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The Cover: Karabakh horse

The Karabakh horses are the national heritage of Azerbaijan. The fabled mountain-steppe racing and riding Karabakh horses are one of the world’s oldest breeds. Azerbaijan's national animal gets its name from the Karabakh region, where it was originally developed. The Karabakh is one of the historically rich and ancient regions of Azerbaijan. The mountainous part of Karabakh (Nagorno-Karabakh) and surrounding seven Azerbaijani districts (Lowland Karabakh) have been illegally occupied by Armenian military forces since 1992. Karabakh horses are notable for their beautiful golden chestnut color. These horses are valued for endurance and good temper, loyalty, strength, and exceptional speed. In 2004, a Karabakh horse named Kishmish from the Agdam stud in Azerbaijan set two world speed records: a 1,000-meter dash in 1 minute and 9 seconds; and a 1,600-meter dash in 1 minute, 52 seconds. Azerbaijan’s traditional Karabakh horse-riding game “Chovqan” was mentioned in the UNESCO Intangible Cultural Heritage Lists in 2013.

Photo: The Karabakh horse “Golden Boy II” performance during the jubilee of British Queen Elizabeth II’s reign in 2012.

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Trichotilloses Totalis and Trichotilloses of the Wig as a Consequence of Long-lasting Trichotillomania

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Background: Trichotillomania usually evolves in patchy form. Clinicians may confuse patchy form of alopecia areata with trichotillomania because of their similar clinical manifestation which consequently may lead to a misdiagnosis. Alopecia totalis rarely can be confused with trichotillomania. Here we report a case, where trichotillomania shows similar clinical appearance with alopecia totalis.

Objective: To demonstrate the rare variant of trichotillomania which share similar clinical features with alopecia totalis. In order to escape from misdiagnosing and mistreating of trichotillomania, we recommend a new nomenclature and classification for hair pulling disease.

Material & methods: Case discussion and brief review.

Results: Total hair loss and patchy alopecia of the wig due to trichotillomania, very rarely reported in the literature. Present case and literature review demonstrate that psychogenic total hair loss of the scalp and alopecia of the wig, maybe sign of untreated and long-lasting trichotillomania.

Conclusion: Terms like “trichotillosis areata” and “trichotillosis totalis” could be used in order to avoid confuseness of alopecia areata and alopecia totalis, respectively.

Keywords: Trichotillomania, Trichotillosis Totalis, Trichotillosis Areata, Trichotillosis of the Wig, Alopecia Totalis, Alopecia Areata.

Introduction

Hair pulling and skin picking are body-focused repetitive behaviors induced by preceding anxiety and increasing sense of tension.[1] Above mentioned behaviors is a part of psychocutaneous disorders like trichotillomania (TTM) and dermatotillomania respectively, which were listed in the section of obsessive-compulsive and related disorders (OCDR) in DSM-5.

[1] In patients with TTM, preceding anxiety and increasing sense of tension leads to consciously or unconsciously hair pulling from own scalp, eyebrow, eyelash, axillar and pubic region which may endure for months and years.[1,2] Some patients may pull hairs from pets, dolls, sweaters and carpets. [1] Scalp most common affected region in TTM. Due to continuous hair pulling from one side or multiple sides of scalp, patchy alopecias may evolve in these patients.[1,2] Most common pulling sites on scalp are vertex and parietal region.[3] Usually, hairs are in different length and configuraton in TTM patients.[2,3] Because of noninflammatory nature of the disease, redness, desquamation and any other symptoms are absent in these patients. Therefore, TTM can be confused with alopecia areata (AA), in which macroinflammation and any other symptoms also is not presents.[2,3] Alopecia totalis (AT) rarely can be confused with TTM. Because, total hair loss due to hair pulling, is not common in TTM. Here we report an extreme case of TTM, in which AT considered in differential diagnosis.
Case Presentation

Nineteen-year-old female patient referred to dermatology department with massive hair loss on scalp. Patient’s hairs started to loss when she was twelve-year-old. Hair loss was started when she changed her school to another one. Patient was on wig, at first meeting with a dermatologist. On physical examination of scalp, massive hair loss and hair shafts in different length was found. Hairs of eyebrow and eyelash was almost completely pulled out. Furthermore, single large alopecia patch was found at vertex of the has got a total hair loss. (fig. 1). Genital and axillar hairs was intact. Nail examination revealed severe onycophagia. On trichoscopic evaluation, coiled hair shaft, flamme sign, v-sign and black dots were detected on scalp (fig. 2). Histopathologic evaluation of skin sample taken from scalp, revealed noninflammatory empty anagen phase hair follicules (fig. 3). Patients routine blood test was normal. Ferritin and Zn level was normal. Thyroid gland abnormalities was absent. All autoimmune markers was negative. Patient at the end, referred to psychiatrist and sertraline with risperidon initiated for the treatment of underlying psychiatric disorder.

Discussion

Underlying psychiatric disorders like OCRD may cause both, AA and TTM. In presented case, patient referred to dermatology unit with preliminary diagnosis of AT. However, following detailed examination of the wig and scalp, TTM was considered at first. Patient with AT apperance, diagnosed as a severe TTM following trichoscopic and histopathologic examination. Exclamation mark on trichoscopy, swarm of bee on histopathology and autoimmune markers on blood examinations was negative. So, AT ruled out by these results. Furthermore, on trichoscopy flamme hairs, coiled hairs, V-sign and black dots was positive for TTM. This patient suffered from TTM for seven year. First time she referred to a specialist when she already has got a total hair loss. Patient misdiagnosed and treated as a AT several time, before hospitalisation in our department. Probably, the severity of TTM is time dependent in present case. Long-lasting anxieties, led to long-lasting trichotillar repetative behaviors, as a consequence total hair loss was evolved. Once total hair loss established following continous anxieties and hair pulling tic, this patient started to drag out hairs of the wig from the vertex until tonsure pattern alopecia evolved. Later, patient confessed that first hair pulling site was vertex. The first hair pulling site of the wig was also vertex. Therefore, patients with AT, wig examination should be implemented also, for diagnostic purpose. Because, in severe and long-lasting TTM cases, trichotillosis of the wig may evolve following the total trichotillar hair loss, which clinically could be similar to AT. In the literature, reports regarding total hair loss due to TTM is very limited. However, TTM of the wig, is an exceptionally rare case and never reported in the literature. In one report, patient suffered from TTM for four year, another one for nine year.[4] In both patient alopecia initially was patchy type, then hair loss gradullay became totally. So, patient should be diagnosed and treated in early patchy stages of TTM, otherwise long-lasting TTM can cause total trichotillar hair loss, even trichotillosis of the wig. In present case, patient diagnosed TTM and treatment against underlying psychiatric disorder was initiated, seven years after the first signs of hair losses.

First time Dimino-Emme et al. described the “Friar Tuck sign” or tonsure pattern of hair loss in TTM patients which is a single large alopecia patch at the vertex.[5] In present case, alopeci patches also was started in a tonsure pattern which later generelised due to long-lasting hair pulling, according to confession of the patient. ”Friar Tuck sign” on the wig confirm the righteous confession of patient. Unfortunately, we lost the
chance to evaluate the wig trichoscopically in order to find the clues for confirmation of TTM. However, hair shafts in different length is visible when zooming the macropicture of the wig (fig. 4).

Following the brief review of the literature regarding total hair losses in TTM, we recommend to separate the terms TTM and trichotillnosis in order to better understand the severity dependent clinic of the disease. TTM derived from greek: trhix (hair), tillein (to pull) and mania (madness). First time this term coined in 1889, by french dermatologist François Henri Hallopeau.[6,7] Aljabre in his article recommended different names for TTM, like trichotillosis, trichotillotic and tic trichotillosis. [8] Horenstein et al. used the term trichotillnosis instead of TTM, in their article.[9] Castelo-Soccio used TTM and trichotillnosis as a synonym terms.[10] Shelleh et al. preferred to accept the term “trichotillotic” in their article.[11] Probably, the meaning of that term is a “hair pulling tic”. However, the term “trichotillotic” at first glance, pronouncing like an adjective of unkown noun, in which adjective alone dont make a sense. The word “trichotillotic” as an adjective could be used in the terminology like “Trichotillotic alopecia” as in “Herpetic gingivastomatitis” or “Neurotic person” but it doesn’t open the whole spectrum and severity of the disease. Therefore, we think that trichotillnosis is more relevant term. The term TTM should be considred as psychiatric conception like ‘kleptomania’ and ‘pyromania’. However, trichotillnosis (trhix+tillein without mania) should be accepted as a dermatological concept of TTM syndrome. In other word, underlying anxieties and increasing sense of tension, beside trichotillotic body-focused repetetive behaviors together making the OCRD, so called TTM. Probably, the severity of trichotillnosis depends on severity and duration of obsession. At the early stages of TTM, patchy form of alopecia or trichotillnosis areata evolves. Trichotillnosis areata is a most common form hair loss in TTM. Trichotillnosis totalis is massive hair loss which is uncommon subtype and probably it develops in long-lasting untreated TTM patients like in presented case (Table 1).

Conclusion
In conclusion, by this article we are trying to demostrate the extremely rare case of TTM with a wig involvement. In present case, patients diagnosed as TTM after seven year later. Probably, due to untreated and long-lasting course of the disease caused development of trichotillnosis areata of tonsure pattern which consequently generelised and became trichotillnosis totalis and trichotillnosis of the wig with a positive friar tuck sign. Patients with trichotillnosis totalis could be confused with AT and mistreated. Therefore, patient with AT on wig, have to be carefully evaluated and wig examination also should be done in order to exclude severe trichotillnosis totalis, since OCRD can cause both, AT and TT by different pathogenic pathways.
Table 1. Recommended clinical subtypes of hair loss in TTM.

<table>
<thead>
<tr>
<th>Clinical subtypes</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichotillosis areata</td>
<td>Patchy alopecia. Patches start usually from vertex and parietal region. Extensive patchy alopecia of vertex correspond to tonsure pattern of TTM. Early stages of TTM maybe multipatchy and very oftenly can be confused with AA.</td>
</tr>
<tr>
<td>Trichotillosis totalis</td>
<td>Total hair loss of the scalp. Rare form TTM. It develops in long-lasting and untreated TTM patients. Can be confused with AT.</td>
</tr>
<tr>
<td>Trichotillosis of the wig</td>
<td>Patchy alopecia of the wig. The location of the patches probably correspond to initial hair pulling site on scalp. Could be sign of severe TTM.</td>
</tr>
<tr>
<td>Trichotillosis universalis</td>
<td>Never reported form. Theoretically, in a long-lasting anxieties patient may pull out all terminal hairs, including scalp, eyebrow, eyelash, axilla and pubis.</td>
</tr>
</tbody>
</table>

TTM - trichotillomania, AA - alopecia areata, AT - alopecia totalis.

References

Tracheal stenosis after tracheotomy requiring two plastic surgeries

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Background: Tracheal stenosis is rarely encountered by otolaryngologists and its treatment is difficult.

Material & methods: This study was conducted in accordance with the Declaration of Helsinki. We experienced a case of tracheal stenosis after a tracheostomy in a 74-year-old male patient. First, tracheostomy was performed under the constricted part. The procedure was observed from above using a laryngoscope, and a narrowed part was caught by forceps. After half a year, stenosis reappeared, and another tracheoplasty was performed in August 2016. In the second surgery, we made a local skin flap, and formed the trachea wall. In the two years that have passed since the last surgery, restenosis has not appeared and the patient follows a good course.

Results: We successfully treated a patient with tracheal stenosis using two types of tracheoplasty, and the postoperative course was satisfactory.

Conclusion: Tracheal stenosis suspected when respiratory distress occurs following tracheotomy. It is necessary to select the procedure based on the shape of the stenosis.

Keywords: tracheal stenosis, surgery, tracheotomy, skin flap, restenosis

Introduction

Tracheal stenosis is rare, but it can be fatal. In recent years, the use of tracheotomy has increased due to the advancement in medical care, the use of tracheostomy has increased for treatment of tracheal injuries caused due to long-term ventilator use. Here, we report the case of a patient who required resection of tracheal stenosis and trachea formation using a local flap 10 years after undergoing tracheotomy.

Case Presentation

A 74-year-old male presented to our department complaining nighttime respiratory distress and cough. He had undergone a right lung upper lobectomy due to lung cancer at 60 years old. When he was 62 years old, he underwent tracheostomy due to pneumonia. 10 years after tracheotomy, he complained of respiratory distress. He was referred to our department in July 2015. Laryngeal fiber examination and CT revealed tracheal stenosis due to scar tissue on the mouth side about 87.5 mm from the tracheal branch. (fig. 1a, b)

The first surgery was performed on August 24, 2015. Ventilation was possible by oral intubation. Skin incision was placed just above the previous tracheostomy. The anterior tracheal wall covered with scar tissue was identified. The trachea was fenestrated right under the stenotic area and ventilation from tracheostomy was switched. The stenotic area was visible above the fenestration. To confirm the stenosis from the mouth side, a direct laryngoscope for laryngo-microsurgery was inserted. Scar tissue in the stricture was excised with a stanze while confirming the stenosis from the fenestration and mouth sides. (fig. 1c, d)
After that treatment, he was followed-up on an outpatient basis. There was a relapse of respiratory distress, and fibroscopic examination confirmed stenosis again 7 months after the surgery (fig. 2a, b). We scheduled a second surgery, aiming to open the right side of the stenosed portion. If the effect was insufficient, we planned to adopt the same procedure on the left side. Specifically, we designed the local flap as shown in fig. 2c, d, e cutting off the right side of the restenosis area together with the cricoid cartilage, sewing the skin on the collarbone into the prepared space, and finally inserting the cuffed cannula. Endotracheal closure was performed 2 weeks later.

The postoperative course was satisfactory without the reappearance of respiratory distress 3 years after the second operation.

**Discussion**

Tracheal stenosis can be caused due to congenital, inflammatory, neoplastic, and traumatic causes. The case reported in the present study is classified as traumatic based on the incision of the duct. In cases where there is no emergency tracheotomy or otolaryngological intervention, as in the present case, caution must be exercised in cases where neck extension is challenging. Stenosis after tracheotomy was observed in 27 patients (25.7%) of the 105 patients with tracheal stenosis. [1]

Maeda et al. classified tracheal stenosis after tracheotomy as 1) cricoid stenosis, 2) infracricoid stenosis, 3) stomal stenosis, 4) cuff stenosis, or 5) tube tip stenosis. In our case, classified as cricoid stenosis, the history of upper lung lobectomy may also have influenced the damage of the cricoid cartilage. Laryngeal fiber examination and CT were useful for diagnosis. In high stenosis cases, surgical treatment should be performed. Especially, the partial stenosis cases, it is required that the narrowed part should be resected and sutured directly. On the other hand, some kinds of artificial tracheas have been applied for reconstruction of the trachea. [2,3] Regarding end-to-end anastomosis after tracheal tubular resection, end-to-end anastomosis is reportedly possible even if the trachea is resected tubularly up to 6.4 cm.2 Tracheal tubular resection and end-to-end anastomosis of about 7.5–9 cm was considered to be possible by passive movement of the cervical and thoracic trachea. Although trachea can be reportedly safely constructed up to 8 cartilage rings, Suzuki et al, reported the resection and reconstruction of 12 trabeculae. [3]
Conclusion

We present the case of a patient with a tracheal stenosis 10 years after tracheotomy. The findings of this case suggest that tracheal stenosis should always be considered respiratory distress emerging following tracheotomy. In addition, the results emphasize that it is necessary to select the procedure based on the shape of the stenosis. However, to verify these findings, studies involving larger sample sizes should be conducted in the future.

References

Evaluation of Injury to Firearms Attending the Emergency Service

Objective: Firearm injuries are forensic cases with high mortality among emergency patients. In this study, it was aimed to compare the cases of firearm injuries applied to the literature.

Material & methods: 432 patients who applied to Emergency Department were included in the study. The cases were evaluated in terms of age, gender, date of event, origin, area of injury, number of firearm entry and exit, and clinical status.

Results: 91.0% (n = 393) of the cases were male and the mean age was determined 34.33 ± 13.55. The most frequent murder origin was detected with 54.6%. Of the cases, 38.2% (n = 165) had soft tissue injuries and only one firearm entry hole was detected in 188 cases. It was determined that 7.2% (n = 32) of the cases died during treatment. When the files of the cases were examined, it was seen that they did not contain any information about the shoot distance.

Conclusion: The high incidence of young adults among the injured requires the development of preventive measures targeting this group. The high rate of murder in this study may be related to the high mortality of firearm injuries. Failure to adequately describe the initial examination findings of such cases leads to difficulties in determining the weight of the injury and in determining the origin.

Keywords: firearm, forensic medicine, injuries, emergency.

Introduction

Firearm injuries are an important public health problem affecting all levels of society [1]. In Turkey, tens of thousands of people are injured and three thousand people die annually due to firearm injuries [2]. Factors such as deficiencies in legal regulations, easy availability of weapons, honour crime and terrorism increase the rate of deaths due to firearm injuries [3]. The aim of this study is to evaluate cases with firearm injuries, which applied to the emergency department, and examine their reports and compare the data with similar studies in the literature.

Material and Methods

In this study, the files and forensic reports of 432 cases, who were admitted to Firat University Hospital Emergency Department between 2013 and 2017 due to a firearm (n=368) or explosive (n=64) injuries, were retrospectively analysed. The cases were examined in terms of gender, age, date of incident, origin, and injury location, number of bullet holes, shooting distance, and clinical status. The data were recorded in SPSS, and the tables and graphs were made by this program.

Results

Out of 18,016 forensic cases, who were admitted to the emergency department between 2013 and 2017, 432 (2.39%) cases had injuries due to firearms and explosive substances. Of the cases, 91% (n=393) were male and 9% (n=39) were female. The youngest of the cases was 6 years old and the...
oldest was 86 years, and the mean age was 34.33 ± 13.5 years.

The cases were mostly in the 30-39 age group (30.1%) (Fig. 1).

It was determined that 54.6% of the cases were of homicide origin. The homicide and accident cases were mostly in the 20-29 age range (28% and 45.5%) (Table 1).

When the cases were evaluated based on the months, it was seen that they mostly occurred in the month of August (21.5%) (Fig. 2).

When the cases were evaluated in terms of injury location, extremity injuries were the most common with a rate of 52.3% (Table 2).

38.2% of the cases were soft tissue injuries (Table 3).

In 300 cases with a specified number of bullet holes, a single bullet hole (62.6%) was the most common, followed by five and more bullet holes (16.6%) (Fig. 3).

It was determined that 293 (67.8%) of the cases were hospitalized, 81 (18.8%) were discharged from the emergency department, 32 (7.4%) died and 26 (6%) were referred to another institution.

The shooting distance could not be determined due to lack of detailed wound description in all of the files examined.

**Discussion**

In this study, 2.39% (n= 432) of 18,016 forensic cases were admitted to the emergency department due to firearm and explosive injuries. Similarly, this rate was 1.55% in Bursa, 2.39% in Isparta and 3.6% in Edirne [4-6]. In a study conducted in Los Angeles, it was stated that 3.89% of 12,136 cases were firearm injuries [7]; in USA, 1,565 cases (approximately 400,000 people in 5 years) were admitted weekly to hospital due to firearm injuries and 645 of them died [8]; in South Africa, an average of 127,000 people were admitted annually to hospital due to firearm injuries and 20,000 of them died [9]. This rate was significantly lower in our study. The reason for this is financial and legal difficulties in obtaining firearms in our country.

In this study, 91% (n= 393) of the cases were male and 9% female.

**Table 1. Distribution of age groups according to the origin.**

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Homicide n (%)</th>
<th>Accident n (%)</th>
<th>Suicide n (%)</th>
<th>War n (%)</th>
<th>Terror n (%)</th>
<th>Explosive n (%)</th>
<th>Unspecified n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>32 (66,6)</td>
<td>6 (12,5)</td>
<td>3 (6,25)</td>
<td>1 (2,08)</td>
<td>2 (4,16)</td>
<td>1 (2,08)</td>
<td>3 (6,25)</td>
<td>48 (100)</td>
</tr>
<tr>
<td>20-29</td>
<td>66 (52,8)</td>
<td>20 (16,8)</td>
<td>4 (3,2)</td>
<td>3 (2,4)</td>
<td>18 (14,4)</td>
<td>9 (7,2)</td>
<td>5 (4)</td>
<td>125 (100)</td>
</tr>
<tr>
<td>30-39</td>
<td>60 (46,2)</td>
<td>6 (4,6)</td>
<td>7 (5,4)</td>
<td>9 (6,9)</td>
<td>7 (5,4)</td>
<td>31 (23,8)</td>
<td>10 (7,7)</td>
<td>130 (100)</td>
</tr>
<tr>
<td>40-49</td>
<td>36 (56,3)</td>
<td>4 (6,3)</td>
<td>2 (3,1)</td>
<td>2 (3,1)</td>
<td>1 (1,6)</td>
<td>17 (26,6)</td>
<td>2 (3,1)</td>
<td>64 (100)</td>
</tr>
<tr>
<td>50-59</td>
<td>26 (61,9)</td>
<td>7 (16,7)</td>
<td>1 (2,4)</td>
<td>1 (2,4)</td>
<td>0 (0)</td>
<td>5 (11,9)</td>
<td>2 (4,8)</td>
<td>42 (100)</td>
</tr>
<tr>
<td>≥60</td>
<td>16 (69,5)</td>
<td>1 (4,3)</td>
<td>2 (8,6)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (4,3)</td>
<td>3 (13)</td>
<td>23 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>236 (54,6)</td>
<td>44 (10,2)</td>
<td>19 (4,4)</td>
<td>16 (3,7)</td>
<td>28 (6,5)</td>
<td>64 (14,8)</td>
<td>25 (5,8)</td>
<td>432 (100)</td>
</tr>
</tbody>
</table>

**Table 2. Distribution of injuries area.**

<table>
<thead>
<tr>
<th>Area of injury</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head-Neck</td>
<td>56</td>
<td>13</td>
</tr>
<tr>
<td>Chest</td>
<td>19</td>
<td>4,4</td>
</tr>
<tr>
<td>Abdomen</td>
<td>33</td>
<td>7,6</td>
</tr>
<tr>
<td>Extremity only</td>
<td>226</td>
<td>52,3</td>
</tr>
<tr>
<td>Chest + Abdomen</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Head-Neck + Chest</td>
<td>4</td>
<td>0,9</td>
</tr>
<tr>
<td>Head-Neck + Abdomen</td>
<td>21</td>
<td>4,9</td>
</tr>
<tr>
<td>Abdomen + Extremity</td>
<td>7</td>
<td>1,6</td>
</tr>
<tr>
<td>Chest + Extremity</td>
<td>17</td>
<td>3,9</td>
</tr>
<tr>
<td>Head-Neck + Abdomen + Extremity</td>
<td>3</td>
<td>0,7</td>
</tr>
<tr>
<td>Chest + Abdomen + Extremity</td>
<td>7</td>
<td>1,6</td>
</tr>
<tr>
<td>Genitourinary System</td>
<td>1</td>
<td>0,2</td>
</tr>
<tr>
<td>Genitourinary System + Extremity</td>
<td>2</td>
<td>0,5</td>
</tr>
<tr>
<td>Multiple Injury</td>
<td>23</td>
<td>5,3</td>
</tr>
<tr>
<td>Total</td>
<td>432</td>
<td>100</td>
</tr>
</tbody>
</table>

**Figure 1. Distribution of age groups.**
were female (n= 39). The male-to-female ratio was found to be higher than other studies conducted in Turkey and abroad [7, 8, 10]. This is due to the fact that men have easier access to firearms and take part in social life more actively, and that terrorist incidents are more frequent in this region.

The mean age in the study was determined to be 34.33 ± 13.5 years. In similar studies, the mean age was 32.96 in Samsun, 34.3 in Trabzon and 31.28 in Erzurum [2, 10, 11]. This rate was found to be 27.9 in Iran [12]. This ratio is similar to that of the studies in the literature.

In this study, the most common age range was 30-39 (30.1%) years, followed by age range of 20-29 years (28.9%) (60% in the 20-39 age range). In similar studies, this rate was found to be 57.8% in the 21-30 years age group in Thailand and 61.5% in the 20-39 years age group in Brazil [13-14]. The rate found in our study is similar to that of the studies in the literature.

In this study, the most common origin of cases was homicide (54.6%). The homicide and accident cases were most common in the 20-29 age group (28% and 45.5%, respectively), while suicide cases were most common in the 30-39 age group (36.8%). In this study, suicide rates were lower than those of similar studies [8, 14]. The homicide and accident rates were similar to those in the literature [2, 12]. The low suicide rates were due to difficulty of obtaining firearms in suicide attempts.

When firearm injuries were evaluated in terms of seasons, they were more common in summer (40.2%) while their rate significantly decreased in winter (15.7%). These results were consistent with similar studies [3, 11]. The fact that people spend more time in social life in the summer months due to long days may explain the frequency of forensic cases in these months.

In this study, since extremities (52.3%) are the most common injury location, the most commonly observed condition was soft tissue injury (38.2%). In USA, extremity injuries were seen in 77% of unintentional firearm injuries and 49% of intentional firearm injuries. In Nigeria, extremity injuries occurred in 41% of firearm injuries [8, 15]. These results were consistent with similar studies.

In the study, a single bullet hole (62.6%) was the most commonly observed number of bullet holes, which was consistent with similar studies [16, 17]. In this study, no information was found about the firearm entry wound in the medical documents of 68 cases. In these cases, emergency physicians had not made a sufficient wound description, which causes difficulties in writing a final report and determining the shooting distance. In order to prevent this, physicians should be educated and given in-service training on these topics.

In the study, 293 (67.8%) of the cases received in-patient treatment. The mortality rate was lower than that of similar studies conducted abroad [8, 14, 18]. This is a natural result of the fact that extremity injuries were more common in this study.

### Table 3. Distribution of injured organ.

<table>
<thead>
<tr>
<th>Injured organ</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft tissue</td>
<td>165</td>
<td>38.2</td>
</tr>
<tr>
<td>Extremity-bone</td>
<td>107</td>
<td>24.7</td>
</tr>
<tr>
<td>Lung-rib</td>
<td>47</td>
<td>10.8</td>
</tr>
<tr>
<td>Vascular structures</td>
<td>42</td>
<td>9.7</td>
</tr>
<tr>
<td>Stomach-intestinal</td>
<td>39</td>
<td>9.0</td>
</tr>
<tr>
<td>Brain</td>
<td>33</td>
<td>7.6</td>
</tr>
<tr>
<td>Maxillofacial region</td>
<td>33</td>
<td>7.6</td>
</tr>
<tr>
<td>Liver-bile</td>
<td>14</td>
<td>3.9</td>
</tr>
<tr>
<td>Genitourinary System</td>
<td>12</td>
<td>2.7</td>
</tr>
<tr>
<td>Spleen-pancreas</td>
<td>11</td>
<td>2.5</td>
</tr>
<tr>
<td>Heart</td>
<td>4</td>
<td>0.9</td>
</tr>
<tr>
<td>Unspecified</td>
<td>18</td>
<td>4.1</td>
</tr>
</tbody>
</table>

In 178 cases there was more than one injured organ.
Conclusion

Since the portion of young adults among such patients is high, we believe that new preventive measures aimed at this age group need to be developed. The high number of cases with homicide origin may be associated with the high mortality rate in firearm injuries. Physicians’ failure to sufficiently represent the initial examination findings in such cases leads to difficulties in determining the severity and origin of injuries in the future.

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Subarachnoid Hemorrhage with Type 2 Myocardial Infarction: A Case Report

Abstract: Acute myocardial infarction (AMI), stroke and subarachnoid hemorrhage (SAH) are all associated with high mortality following hospitalization. Electrocardiographic (ECG) changes occurring during SAH have been described frequently. To the best of our knowledge, there is no reported case with SAH and existing Q waves, ST elevations on anterior and lateral walls, and Atrial fibrillation on ECG.

We describe a 47-year-old female patient with a SAH that presented electrocardiographic evidence of MI. By reporting this case, we share our uncommon experience, the increasing reports will allow identifying the clinical features useful for differentiating diagnosis from myocardial infarction in order to avoid treatment with anticoagulants and antiplatelets, potentially dangerous particularly in the group of patients with a hemorrhagic cerebral accident.

Keywords: Subarachnoid hemorrhage, SAH, Type 2 MI, Myocardial infarction.

Introduction

Acute myocardial infarction (MI), stroke and subarachnoid hemorrhage (SAH) are all associated with high mortality following hospitalization [1]. In instances of myocardial injury with necrosis, where a condition other than coronary artery disease (CAD) contributes to an imbalance between myocardial oxygen supply and/or demand, the term “MI type 2” is employed [2]. In critically ill patients, or in patients undergoing major (non-cardiac) surgery, elevated values of cardiac biomarkers may appear, due to the direct toxic effects of endogenous or exogenous high circulating catecholamine levels. Also, coronary vasospasm and/or endothelial dysfunction have the potential to cause MI [2-5]. Electrocardiographic (ECG) alterations occurring during the course of subarachnoid hemorrhage (SAH) have been described frequently. In patients with acute aneurysmal SAH, repolarization abnormalities are the commonest ECG alterations, and ST depression is more common in patients with poor outcome. (6). Transient left ventricular dysfunction with an akinetic or dyskinetic apex has also been described in SAH patients without significant coronary heart disease [7-9]. We describe a patient with a SAH that presented electrocardiographic evidence of MI.

Case Presentation

A 47-year-old female patient with background of neurofibroma in bowels and underwent several surgeries due to bowel obstruction. She had ileostomy and was receiving TPN through Hickman catheter. The patient hospitalized several times due to pneumonia and sepsis and was received two times successfully CPR during hospitalizations. She had no any cardiac history. Her last hospitalization was due to leukocytosis, diagnosed with sepsis. During hospitalization she complained with facial numbness and consulted to neurology. She had nystagmus, anisocoric pupils and positive Babinski reflex. Computerized Tomography (CT) findings was diffuse acute SAH within resultant effacement of the basal cisterns and also acute intraventricular hemorrhage.
Alekberli et al. Subarachnoid Hemorrhage with Myocardial Infarction
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途中で経過を示しながら、フローチャートで示したが、She was diagnosed with type 2 MI but did not receive antiplatelet therapy because of the SAH. After positive blood cultures (Staph. epidermidis) the patient transferred to ICU with hemodynamically unstable profile and suspicion of endocarditis. In ICU the patient was intubated, sedated and mechanically ventilated. Started inotropes (noradrenaline and adrenaline drips) and antibiotics (meropenem, vancomycin and tazocin). Poor global function, thickened, pathological MV and AV was seen on bed side echocardiography. Neurosurgeons were waiting to perform any procedure because of the unstable hemodynamically condition and poor prognosis of the procedure for SAH. Decided to perform TEE by cardiologist but unfortunately the patient died on 4th ICU hospitalization due to severe sepsis and multiorgan dysfunction.

Discussion

Myocardial damage occurring in association with SAH is a well-described phenomenon [10-13]. It has been reported that abnormalities of electrocardiography, echocardiography and serum cardiac specific markers are associated with cerebrovascular disease [14]. The most common cause is subarachnoid hemorrhage, but additional causes include head injury, meningitis and brain tumor [15-17]. The real pathophysiology remains unclear till now, coronary artery spasm, coronary thrombosis, and catecholamine induced oxygen supply-demand mismatch had been mentioned [18, 19].

Unconscious cerebral hemorrhage patients with electrocardiograms showing ST segment elevation, we have a tendency to misdiagnose as acute myocardial infarction and treat with multiple antiplatelet and anticoagulate agents, which can cause harmful effects. Furthermore, delaying accurate diagnosis may result in catastrophic outcome.

Conclusion

In critically ill patients with SAH, elevated cardiac biomarkers may appear, due to the direct toxic effects of endogenous or exogenous high circulating catecholamine levels. Also coronary vasospasm and/or endothelial dysfunction have the potential to cause MI. By reporting this case, we wish to share our uncommon experience and hope that it may be helpful in future cases. We hope that the increasing reports will allow to identify the clinical features useful for differentiate diagnosis from myocardial infarction in order to avoid treatment with anticoagulants and antiplatelets, potentially dangerous particularly in the group of patients with hemorrhagic cerebral accident.

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12. Woon Je Heo, MD1, Jin Ho Kang, MD1, Woo Shin Jeong, MD1, Mi Yeon Jeong, MD1, Sang Hyuk Lee, MD1, Jeong Yeun Seo , MD1, and Sang Won Jo, MD2 1 Departments of Internal Medicine and 2 Radiology, Kangbuk Samsung Medical Center, Seoul, Korea. Subarachnoid Hemorrhage Misdiagnosed as an Acute ST Elevation Myocardial Infarction. http://dx.doi.org/10.4070/kcj.2012.42.3.216 Print ISSN 1738-5520 • On-line ISSN 1738-5555
Case Report

New approach to one-stop hybrid valve/PCI operation

Abstract: Ambition to perform more esthetic and less traumatic operations leads the surgeons to less painfulness, less blood loss and probability of infection and finally to their patients fast recovery and early returning to physical activity. Also, minimally invasive operations have been promoted by hybrid procedures. We would like to present you our new approach in a future of which we deeply believe.

Keywords: hybrid valve/PCI, minimally invasive valve operation, bioprosthetic mitral valve, LAD stenting, single-stage hybrid operation

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Introduction

For a long period two different pathologies – valve and coronary artery diseases met in one patient were treated via sternotomy incision. But it is fact that complex heart operations through this approach possess high mortality. Newly introduced minimally invasive technologies allow to avoid sternotomy incision. When compared with a standard median sternotomy potential benefits of minimally invasive valve surgery include less trauma, less pain and blood loss, less infection and antibiotic use and faster recovery time leading to improved outcomes [1-3]. But in the presence of concomitant coronary artery disease accomplishment of such incision requires stenting procedure before or after the valve operation. Unfortunately, this two-staged treatment option does not create a patient satisfaction because of two separate preparations for two different procedures performed in two different days and therefore utilizes a lot of resources of the hospital. Also, many questions remain unanswered about hybrid valve/PCI procedures, including the optimal order and timing for the procedures [4]. Some surgeons hypothesize that 1-stop approach is more convenient for the patient and more cost effective than a 2-stage approach [5]. But this method requires a high level of coordination between the cardiologist and cardiac surgeon and also demands the presence of a “hybrid” operating room [4]. Although, some groups have observed an increased incidence of acute kidney injury when both PCI and valve procedure are performed on the same day and recommended of creating a period of three weeks between the PCI and valve operation [6, 7]. Also some problems with hemorrhagic complications are emphasized by some authors. Despite this, some surgeons achieved very promising results with single stage valve/PCI procedures for aortic valve [5], as well as for mitral valve (8). The latter performed their procedures in such general manner: PCI to non-LAD lesion and subsequent minimally invasive mitral valve operation. They included both non-reoperative and reoperative patients. But unfortunately, there are only few reports of single-stage (one-stop) hybrid valve/PCI operations in the literature.

We would like to present our case of non-reoperative hybrid valve/PCI operation with the stenting of LAD and oppositely different order of procedures than usually used in such operations.
Figure 1. Hybrid operating room of Baku heart center.

Figure 2. Preparation of patient for hybrid valve/PCI procedure.

Figure 3. Transthoracic echocardiography before operation. IV degree mitral insufficiency is seen in systole.

Figure 4. Transthoracic echocardiography after hybrid operation. Bioprosthetic valve is well functioning.

Figure 5. Coronary angiography. LAD stenosis before stenting. Already implanted bioprosthetic valve is also seen.

Figure 6. Coronary angiography. LAD after successful stenting.
Case Presentation

62-year-old male patient was admitted to our hospital complaining of shortness of breath and non-irradiating retrosternal pain during effort. These complains started abruptly since one week. Transthoracic echocardiography revealed mitral valve anterior leaflet prolapsus owing to chordal rupture- flail AML and IV degree of mitral insufficiency with preserved ejection fraction (Figure 3). Cardiac catheterization revealed mid-LAD stenosis of 80%. The patient's laboratory analysis and other investigations was unremarkable. Surgical consensus was one-stop hybrid procedure on hybrid room (Fig. 1).

Procedural technique: Patient was placed in the supine position and underwent intubation with a double-lumen endotracheal tube and a roll was placed underneath the right scapula (Fig. 2). A transesophageal echocardiogram probe was placed intraoperatively to evaluate the mitral valve and to assess the postoperative results. 3 cm incision was made in the right inguinal fold and femoral vessels are prepared. Then 10 cm skin incision was made in the IV intercostal space and anterior thoracotomy was done with right lung deflated. Pericardium was opened. After full heparinization right femoral vessels was cannulated. Aortic root cannula and superior venous cannula were placed via thoracotomy incision. Once on cardiopulmonary bypass a patient was cooled, ascending aorta was cross-clamped and the heart arrested. The mitral valve was accessed through the left atriotomy incision and found to be not amenable for repair. Mitral replacement with Hancock II bioprosthetic heart valve (Medtronic, Minneapolis, MN) was carried out in the standard fashion (Fig. 4). 3-0 polypropylene suture was used to close the left atrium. Cardiopulmonary bypass had been discontinued. After decannulation purse-string sutures were tied, only 1/2 of protamine administered and the femoral vessels were repaired. A single chest tube was placed to the pleural space. The thoracotomy incision was closed in the routine manner. Surgical team finished their part of operation and 2nd part of hybrid procedure started. 300 mg clopidogrel was given via nasogastric tube and a roll was placed underneath the right scapula (Fig. 2). A transesophageal echocardiogram probe was placed intraoperatively to evaluate the mitral valve and to assess the postoperative results. 3 cm incision was made in the right inguinal fold and femoral vessels are prepared. Then 10 cm skin incision was made in the IV intercostal space and anterior thoracotomy was done with right lung deflated. Pericardium was opened. After full heparinization right femoral vessels was cannulated. Aortic root cannula and superior venous cannula were placed via thoracotomy incision. Once on cardiopulmonary bypass a patient was cooled, ascending aorta was cross-clamped and the heart arrested. The mitral valve was accessed through the left atriotomy incision and found to be not amenable for repair. Mitral replacement with Hancock II bioprosthetic heart valve (Medtronic, Minneapolis, MN) was carried out in the standard fashion (Fig. 4). 3-0 polypropylene suture was used to close the left atrium. Cardiopulmonary bypass had been discontinued. After decannulation purse-string sutures were tied, only 1/2 of protamine administered and the femoral vessels were repaired. A single chest tube was placed to the pleural space. The thoracotomy incision was closed in the routine manner. Surgical team finished their part of operation and 2nd part of hybrid procedure started. 300 mg clopidogrel was given via nasogastric tube. LAD was successfully stented via left femoral artery enter (Fig. 5, 6). The patient received clopidogrel 75 mg starting on postoperative day 1. Aortic cross clamp time was 45 min, cardio-pulmonary bypass time was 63 min. Total blood loss composed 450 ml. A patient extubated in 12 hours and discharged home on postoperative day 7.

Discussion

Our case of hybrid valve/PCI has two different points: at first we used oppositely different order than usually used in such procedures and second we used a stenting of LAD- the vessel which is believed to be more convenient to be bypassed by LIMA. Generally, in single-stage valve/PCI procedures in non-reoperative patient klopidogrel is given before induction of anesthesia. Then, incision for valve operation (thoracotomy) is completed and PCI is performed (before 5000 unit of heparin is administered). Hereafter surgery of the valve is accomplished (before full dose of heparin is administered). We think that performing of procedure in such order is more laborious unless coronary artery stenosis is critical. Obviously, stenting of coronary arteries as first procedure is considered in order to avoid the problems associated with inadequate cardiac protection during the valvular part of operation. We think that in situations when coronary artery stenosis is less than 95% (so non-critical) valvular part could be performed first without compromising the heart muscle viability. This could allow to obviate any mechanical traction damage to the stent itself, especially in proximal and mid portion of right coronary artery. In our case the LAD stenosis was not more than 80%. We did not consider surgery to this lesion.

Conclusion

Usage of one-stop valve → PCI approach is possible in case of non-critical coronary artery stenosis (when there is no risk of reduction of quality of myocardial protection). We consider hybrid PCI → valve order in one-stop procedures in patients with critically stenotic coronary arteries and in staged hybrid procedures when patient with valvular disease comes with acute coronary syndrome. Undoubtedly, for wide use of our approach future randomized trials are required.

References

Sarcoidosis with hepatic and splenic involvement

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Abstract: Sarcoidosis is a systemic granulomatous disease of unknown etiology characterized by presence of non-caseating granulomas in the involved organs. The pulmonary interstitium is most commonly affected but extrapulmonary involvement can occur in almost any other organ system. Isolated extrapulmonary involvement has been noted only in around 10% of cases. Here, we describe the case of a 59-year-old patient with isolated hepato-splenic involvement.

Keywords: sarcoidosis, spleen, liver

Introduction

Sarcoidosis is a multisystem disease characterized by the presence of non-caseating granulomas in affected organs. The pulmonary system is the most common site of involvement, and is affected in about 90% of cases [1, 2]. Sites affected include peripheral lymph nodes (30%), the hepatic system, the spleen, stomach, small bowel, bone, and skin [3]. Bilateral hilar lymphadenopathy is the most common radiological finding. Radiological studies may also show lymphadenopathy, splenomegaly, hepatomegaly, multiple hypointense liver and spleen nodules [4]. However in biopsy and autopsy studies of patients with systemic sarcoidosis, liver involvement was found in about 50–80%, evidence of organ dysfunction is uncommon [5, 6]. Most patients with liver and spleen involvement are asymptomatic. Therefore, the majority of cases are discovered incidentally, frequently by the finding of elevated liver enzymes. Pain in the right upper quadrant of the abdomen, fatigue, pruritus, and jaundice may be associated with liver involvement. Portal hypertension and cirrhosis are complications linked to long-standing hepatic sarcoidosis. Asymptomatic cases do not require treatment. For symptomatic patients, the first line treatment includes corticosteroids or ursodeoxycholic acid. Various immunosuppressant agents can be used as second line agents. Rarely, severe cases require liver transplantation [3].

Case Presentation

A 59-year-old female patient presented to our clinic with a 1-week history of fever, malaise, and fatigue, which began after coronary angiography. She also complained of night sweats, loss of appetite and weight loss (10 kg) in 3 months. She had a medical history of hypertension, type 2 diabetes, and coronary artery disease. Laboratory studies revealed elevated liver enzymes (ALT-62.81 U/L, ALP-524.5 U/L, GGT-301.64 U/L, Total bilirubin-3.98 mg/dL, CRP-36.33 mg/L). Ultrasonography of the abdomen showed hepatosplenomegaly with multiple hypoechoic lesions in the spleen, enlarged lymph nodes at the hepatic and splenic hilum. Chest X-ray showed no significant findings. Abdominal MRI revealed multiple T2 hypointense lesions in the liver and spleen up to 7 mm and 23 mm in size, respectively (lymphoma?); enlarged left paraaortic, interaortocaval, portal lymph nodes up to 12 mm; hepatosplenomegaly; gallbladder sludge (Fig. 1).
Figure 1. A. Multiple T2 hypointense lesions in the liver and spleen; B. Enlarged lymph node at the hepatic hilum.

Figure 2. Intraoperative findings: A. Multiple nodules throughout spleen; B. Enlarged lymph node at the hepatic hilum; C. Lesions in the liver.

Figure 3. Non-caseating granulomatous inflammation. (H&E) A. Lymph node; B. Liver tissue
Sarcoidosis is a systemic disease which can affect different organs and tissues. It is characterized by the presence of non-caseating granulomas, which can involve multiple organs, in the absence of infections, autoimmune diseases. The prevalence of sarcoidosis is 2–60 per 100,000 people. The most common site of sarcoidosis is the pulmonary system, in more than 90% of cases, patients have pulmonary and mediastinal lymph nodes involvement. Extrapulmonary involvement is rare. Extrapulmonary involvement, in particular in the liver and spleen, is unusual and clinically challenging [1, 2].

Most patients with hepatosplenic sarcoidosis have no symptoms. Abdominal pain, fever, malaise, and weight loss are the most common symptoms in 5–7% of patients. Only 1% of cases, complicated by cirrhosis and portal hypertension, present with ascites and gastroesophageal variceal bleeding [3]. As noted above, our patient presented with a complaint fever, fatigue, night sweats, loss of appetite and weight loss.

Laboratory studies are usually nonspecific, dysfunction of liver function tests such as elevated ALT, AST, GGT, and ALP can be observed.

In a minority of patients abnormal findings are revealed on imaging studies. Commonly, USG shows hepatosplenoomegaly and enlarged abdominal lymph nodes. Nodular pattern can be detected in low percentage. In these cases, lesions are revealed as small hypoechoic nodules. CT and MRI are more sensitive to detect granulomas. Lesions are detected as hypodense nodules on contrast-enhanced CT. MRI scan reveals T2-hypointense nodules in 5–15% of cases [4, 6]. In our patient, multiple T2 hypointense lesions and enlarged lymph nodes at the hepatic and splenic hilum were detected on MRI. These findings with systemic symptoms raised high suspicion for lymphoma. To establish a specific diagnosis, histopathologic examination was required. We performed laparoscopic biopsy, and the histopathologic examination suggested sarcoidosis.

Pharmacological therapy should be considered for symptomatic patients. Corticosteroids and ursoodeoxycholic acid are used as the first line agents. Several immunosuppressants such as azathioprine, methotrexate, cyclosporine have been reported to be effective [3]. About 60% of all symptomatic patients show spontaneous remission as our patient. Asymptomatic patients do not require treatment. Observation is indicated for asymptomatic patients and symptomatic patients who show spontaneous resolution. These patients usually have a good prognosis any medical therapy and remain stable for many years [5, 7].

Conclusion
Sarcoidosis with hepatic and splenic involvement, although rare, should be considered in the differential diagnosis of the patients presenting with systemic symptoms and hepatosplenomegaly with multiple lesions. Histologic examination is necessary for establishing the diagnosis of sarcoidosis. Immunosuppressive therapy should be reserved only for symptomatic patients with sarcoidosis who fails to resolve spontaneously. In our case, we did not give any treatment. The patient demonstrated spontaneous improvement.

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Vaccine Efficacy of Hepatitis A and B in Pediatric Oncology Patients

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**Background:** To investigate the factors affecting pre-, and post-treatment hepatitis A and B vaccine antibody titers and the responses to vaccine in the post-treatment period of pediatric patients with the diagnosis of cancer.

**Objective:** The archival data of the patients with an oncologic diagnosis followed up in the Pediatric Oncology and Healthy Children Polyclinics of Tepecik Training and Research Hospital between 2011 and 2018 were retrospectively reviewed. The age at diagnosis, sex, primary diagnosis, average number of days elapsed between the diagnosis, and initiation of chemotherapy, antibody titers at the time of diagnosis, preoperative status of Hepatitis B, Hepatitis A vaccine and Hepatitis B Ig administration, duration of treatment and titers in the second assessment after treatment were evaluated.

**Material & methods:** Medical files of a total of 123 cases including 74 (60%) male patients could be accessed. The mean age of the patients at diagnosis was 98.2 ± 66.2 (0.5-214) months. The primary diagnoses were leukemia in 50 (40.7%), lymphoma in 27 (22.0%) and solid tumors in 46 (37.4%) patients. The mean duration of treatment was 14.8 ± 9.0 (1.54-39.6) months. Serologically post-treatment HB-negativity was comparatively higher in male patients who were HB-positive before, but HB-negative treatment after treatment (p = 0.039). In cases with hepatitis A, a significant correlation was detected duration of treatment was prolonged (p = 0.021).

**Results:** Medical files of a total of 123 cases including 74 (60%) male patients could be accessed. The mean age of the patients at diagnosis was 98.2 ± 66.2 (0.5-214) months. The primary diagnoses were leukemia in 50 (40.7%), lymphoma in 27 (22.0%) and solid tumors in 46 (37.4%) patients. The mean duration of treatment was 14.8 ± 9.0 (1.54-39.6) months. Serologically post-treatment HB-negativity was comparatively higher in male patients who were HB-positive before, but HB-negative treatment after treatment (p = 0.039). In cases with hepatitis A, a significant correlation was detected duration of treatment was prolonged (p = 0.021).

**Conclusion:** Antibody loss was found to be more prominent in male gender for Hepatitis B vaccination. For hepatitis A, antibody loss was more pronounced with treatment duration.

**Keywords:** hepatitis A, hepatitis B, pediatric oncology, vaccine

**Introduction**

In the last century, rates of morbidity and mortality related to prevalent infectious diseases in developed countries have decreased significantly thanks to advances in vaccination practice [1]. Today, vaccination programs represent a universally recognized tool both to prevent the spread of many infectious agents and to reduce death and disability worldwide [1]. Definitive eradication of certain vaccine-preventable diseases has been thus achieved against diseases such as smallpox worldwide and polio in the United States and Europe [2]. Vaccination programs are constantly updated. The use of novel vaccines such as herpes, varicel-
la-zoster virus (VZV), pneumococcal, meningococcus C, and human papilloma virus (HPV) has been introduced in the last two decades [3].

Nowadays, pediatric malignant diseases are the second most common cause of death in developed countries. Survival rates have increased significantly in the last 30 years thanks to multidisciplinary approach based on chemotherapy, and surgery, radiotherapy, hematopoietic stem cell transplantation and supportive treatments [4]. An important disadvantage of chemotherapy is that it suppresses immunity which persists up to 6-12 months after end of the treatment [5]. It adversely affects the effectiveness of these vaccines which may be due to a complete or partial loss of protective serum antibody titers or a combination of other immune deficiencies such as the presence of functional asplenia [6]. In general, patients treated for pediatric malignancies are not at high risk except for patients with splenectomy or functional asplenia when compared to healthy population. However, there is a limited number of literature data on serious conditions caused by insufficiency of vaccine against Haemophilus influenzae or Streptococcus pneumoniae, measles and rubella in cases where long-term humoral response is defective [7]. Therefore, actual need for vaccines is still an important issue in pediatric cancer patients during and after treatment. The aim of this study was to investigate the Hepatitis B and Hepatitis A vaccine antibody titers, the vaccine or immunoglobulin treatments administered before and after treatment of pediatric cancer patients, and the factors affecting the vaccine response in the post-treatment period.

Material & Methods

The study was performed by retrospectively examining the file data of children with oncological diagnosis followed up in Pediatric Oncology and Healthy Children Polyclinics of Tepecik Training and Research Hospital of Health Sciences University between 2011-2018. Age, gender, primary diagnosis, average number of days elapsed between diagnosis and initiation of chemotherapy, anti HBs and anti HAV titers at the time of diagnosis, administration status of Hepatitis B and Hepatitis A vaccines and Hepatitis B Ig before treatment, duration of treatment were evaluated and second assessments of Anti-HBs titer and anti HAV Ig parameters were performed local ethics committee approval was obtained. It was taken into consideration that the patients to be included in the study group were between 0-18 years of age and that cancer treatments were completed at least 6 months before collection of data. All patients screened for hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBcAb), hepatitis B e-antigen (HBeAg) and anti Hepatitis A Ig (anti HAV Ig) were taken into consideration. In order to maintain the integrity and validity of the data, only patients with a complete clinical and medical data record set that were found to be in remission were included in the study sample. Patients who were receiving active cancer treatment, those who had anticancer treatment, recently vaccinated patients or individuals who recently received blood transfusions or IVIG treatment were not included in the study. In addition, patients with active hepatitis B infection, cases previously diagnosed with immunodeficiency or having low immunoglobulin G (Ig G) levels for their age were excluded from the study. Before initiation of cancer treatment, serologic tests for hepatitis A, and B and had to be performed in all patients and their primary HBV vaccinations had to be realized according to National immunization program of Republic of Turkey (three doses i.e. at birth, 2 and 6 months). All seronegative patients (HbsAb <10 mIU/ml) received hepatitis B Ig IM prior to treatment according to the protocol of the center. Hepatitis A vaccine was administered to patients with negative hepatitis A serology. All patients were reevaluated with serologic tests at least 6 months after the end of the treatment, and those with missing data were excluded from the study. Antibody titers were evaluated with enzyme-linked immunosassay. Patients with HBsAb titers of <10 mIU / ml for hepatitis B and negative results for hepatitis A were considered to be seronegative. Statistical Package for Social Sciences (SPSS) version 24.0 for Windows (SPSS, Inc., Chicago, IL, USA) was utilized for pertinent data analysis. The Mann-Whitney U test and chi-square test were used to compare variables and p value of <0.05 was considered to be statistically significant.

Results

Medical files of a total of 123 cases including 74 (60%) male, and 49 (40%) female patients could be accessed. The mean age of the patients at diagnosis was 98.2 ± 66.2 (0.5-214) months. The primary diagnoses were leukemia in 50 (40.7%) lymphoma in 27 (22.0%) and solid tumors in 46 (37.4%) patients. The mean time interval up to treatment was 9.3 ± 26.2 (1-172) days. Hepatitis B IgG was given to all 41 patients who had negative hepatitis B (HB) serology before the treatment. Hepatitis A vaccination had been performed in anti-HAV IgG negative 65 cases. The mean duration of treatment was 14.8 ± 9.0 (1.54-39.6) months. (Table 1). Hepatitis B and Hepatitis A patients whose serologic tests were achieved were divided into four groups. Group 1 consisted of patients with negative serologies both before and after treatment, Group 2 comprised patients with negative, and positive serologies before and after treatment, Group 3 comprised patients with negative, and positive serologies before but positive after treatment, and Group 4 comprised patients with positive serologies before but negative after treatment.

<table>
<thead>
<tr>
<th>Feature</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74 (60.2%)</td>
</tr>
<tr>
<td>Female</td>
<td>49 (39.8%)</td>
</tr>
<tr>
<td>Age of at diagnosis</td>
<td>98.2 ± 66.2 (0.5-214) months</td>
</tr>
<tr>
<td>Primary diagnosis</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>50 (% 40.7)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>27 ( %22.0)</td>
</tr>
<tr>
<td>Solid tumor</td>
<td>46 (%37.4)</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>9.3 ± 26.2 (1-172) days</td>
</tr>
<tr>
<td>Pre-treatment serology</td>
<td></td>
</tr>
<tr>
<td>Hep B (-)</td>
<td>41 (%37.3)</td>
</tr>
<tr>
<td>Hep A (-)</td>
<td>65 (%52.8)</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>14.8 ± 9.0 (1.54-39.6) months</td>
</tr>
</tbody>
</table>
Table 2. Definition of groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>BT (-) / AT (-)</th>
<th>BT (-) / AT (+)</th>
<th>BT (+) / AT (-)</th>
<th>BT (+) / AT (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>BT (-) / AT (-)</td>
<td>BT (-) / AT (+)</td>
<td>BT (+) / AT (-)</td>
<td>BT (+) / AT (+)</td>
</tr>
<tr>
<td>Group 2</td>
<td>BT (+) / AT (-)</td>
<td>BT (+) / AT (+)</td>
<td>BT (-) / AT (-)</td>
<td>BT (-) / AT (+)</td>
</tr>
</tbody>
</table>

AT: after treatment, BT: before treatment

Discussion

The aim of this study was to evaluate the vaccine responses and the factors affecting this response in children with established diagnosis of cancer. Since there are still no clear answers on this subject, it presumably has contributed to the literature. Acquired Hepatitis B infection or reactivation of HBV in patients undergoing malignancy treatment is a known complication in those receiving cytotoxic or immunosuppressive therapy. These conditions have been also reported in HbsAg positive patients after chemotherapy and transplantation [8]. Although there are many vaccines in the national vaccination program, two serologies with the most commonly analyzed and easily accessible data have been evaluated in order to introduce a certain standardization. Although there are no clear answers about the routine to be followed after chemotherapy, some studies have reported that booster vaccination should be administered 6 months after chemotherapy. Another study proposed this practice 12 months after chemotherapy [9,10]. However, Fioredda et al. stated that the vaccination scheme should be maintained after treatment in this group of children as in normal healthy individuals [11]. Guidelines for the immunization of children after chemotherapy also vary among countries. US CDC [1993] has recommended re-vaccination 2 weeks before the initiation or at least 3 months after chemotherapy [12]. UK RCPCH [2002] recommends vaccination of seronegative high-risk cases only [13]. The updated Australian guidelines for vaccination recommend a single adjuvant dose for HBV after chemotherapy if the patient has completed primary vaccination at the time of diagnosis [14]. Esposito et al. however, recommended two booster doses for HBV at 3-month intervals after chemotherapy in the presence of epidemiological risk without considering any other factor [15]. In our study, all patients who were seronegative prior to chemotherapy were vaccinated with Ig for HBV and HAV for vaccination with the application almost in compliance with CDC recommendations and chemotherapy was initiated. After chemotherapy, serology was re-evaluated at the earliest 6 months and seronegative ones were vaccinated. Hepatitis B and Hepatitis A seronegativities were detected in 33.3% and 52.4% of the patients in this study group, respectively. In their study Faye NY et al. found that HBV seronegativity rate of 86% [16]. In the literature, there are different reported results related to seropositivity after chemotherapy. Seropositivity for HBV has been reported to be between 80-84% at the end of treatment in children with acute lymphoblastic leukemia [17, 18]. Another study reported 50-60% loss of seropositivity in 50-60% of cases [19]. Although Hepatitis B vaccination has been included in the national vaccination program since 1998 and Hepatitis A vaccination since 2012, considering the age at diagnosis of the patients was 98 months, they should have all completed the primary vaccination program. However, it was tragic that the seronegativity before treatment ranged between 33% and 52%. This cannot be explained alone by incomplete implementation of national vaccination program. Because the country’s ministry of health has strict controls and sanctions related to vaccination program. Surgical procedures, blood transfusions, immunosuppressive therapies, as well as personal immune response are thought to play an important role. Another known fact is that patients respond differently to chemotherapy. It is not possible to generalize these recommended vaccinations to all patients after chemotherapy. The main purpose of this study was to determine the parameters

Table 3. Distribution of patients by groups and related situations.

| Disability | Hepatitis B | | | p |
|------------|-------------|----------------|----------------|----------------|----------------|----------------|----------------|
|            | Group 1 | Group 2 | Group 3 | Group 4 |            | Group 1 | Group 2 | Group 3 | Group 4 | p |
| Primary diagnosis | Leukemia | 2 | 13 | 13 | 22 | 0,252 | 6 | 21 | 13 | 10 | 0,193 |
| | Lymphoma | 3 | 8 | 7 | 9 | | 2 | 14 | 3 | 8 | |
| | Solid tumour | 8 | 7 | 9 | 22 | | 5 | 23 | 3 | 15 | |
| Gender | Male | 8 | 18 | 23 | 25 | 0,034 | 8 | 36 | 11 | 19 | 0,972 |
| | Female | 5 | 10 | 6 | 28 | | 5 | 22 | 8 | 14 | |
| Duration of treatment | 9.82 | ± 6.3 | 13.3 | ± 8.9 | 17.6 | ± 9.4 | 15.2 | ± 9.08 | 0,230 | 93.5 | ± 53 | 106.2 | ± 67 | 56.5 | ± 44.6 | 110.3 | ± 72.1 | 0,021 |
that would affect the differences in this response. The effect of cancer treatment on immunization by vaccination is not clearly known. Many different factors may affect antibody titers. In previous studies, genetic predisposition, human leukocyte antigen (HLA) haplotypes, interleukin genotypes, and polymorphisms in cytokines or cytokine receptors were found to be effective in generating lower immunogenic response to HBV vaccine [20]. For example, in patients with atopic dermatitis and psoriasis, both these immunological factors and the excessive inflammation caused by the underlying disease are known to inhibit the increase in anti HBs titers. Moreover, although atopic dermatitis is a T helper 2 (TH2) disease and psoriasis is a T helper 1 (TH1) disease, the response is similar. In the presence of a cancer, it is not possible to understand potential changes in the immune system, tumor cell behavior and their relationship with the genetic immunologic, genotypic characteristics of the individual. Therefore, uncertainties remain about prediction of vaccine responses and their potential interaction with the treatment. There are many studies on the factors affecting vaccine antibody titers after treatment. In a serological study, Zignol M et al. detected rates of antibody negativeities for hepatitis B, measles, mumps, rubella, tetanus and polio in 46%, 25%, 26%, 24%, 14% and 7% of the patients respectively. Negativities for rubella, mumps and tetanus antibodies were correlated with age and measles antibody negativeities with age and gender. Antibody loss was found to be more prominent in younger patients and girls [10]. In their study, Karaman S et al. could not find a any correlation between post-treatment antibody titers , age and sex [21]. In contrast to the aforementioned two studies, in this study the rate of antibody negativity in male gender was found to be higher only for Hepatitis B antibody responses. The relationship with age was not determined for both Hepatitis A and Hepatitis B antibody responses. When evaluated in terms of the relationship with the type of the present disease, hepatitis B antibody titers decreased mostly in sarcoïd patients even below the protective level in 64% of the patients [22]. In a study by Karaman S et al. antibody loss was found to be higher in children with leukemia [21]. In this study, primary diagnosis was not important as for both antibody titers. We think that an additional contribution of this study to the literature will be related to hepatitis A vaccination and vaccine response. Although many studies have been performed on this issue, we did not find any study in which Hepatitis A was evaluated in children with cancer. When hepatitis A vaccination was evaluated, it was found that age, sex, primary diagnosis did not affect the response to vaccination after treatment, but the rate of negativity for Hepatitis A was significantly higher as the duration of anticancer treatment was prolonged . The limitation of this study was that it was a single-center, retrospective study performed with a small sample group. In addition, the types of chemotherapy that patients received were not specified. It is known that viral reinfecion is more prominent with some chemotherapy agents and serology may be affected. In conclusion, although there are guidelines on vaccination programs that have already been identified and recommended for children with the diagnosis of cancer, we have seen that individual differences are at the forefront due to many factors that we do not know.

Conclusion

In conclusion, male sex and long-term exposure to hepatitis seem to be risk factors for Hepatitis B antibody responses, prospective multicenter, studies involving genotypic characteristics of the patients with established, and detailed immunological maps, times, and routes of vaccination where immune responses after each vaccination are evaluated should be conducted. Perhaps this protocol will be told us by an artificial intelligence to be developed in the future.

References

Efficiency of Endothelial Dysfunction Correction with Methylethylpyridinol in Patients with Type 1 Diabetes Mellitus

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Objective: This study evaluated the effectiveness of methylethylpyridinol and sulodexide therapy in correcting endothelial dysfunction in patients with type 1 diabetes.

Material & methods: The study included 89 patients with type 1 diabetes divided into 2 groups: group 1 received sulodexide therapy, while group 2 received methylethylpyridinol therapy.

Results: The parameters of endothelial dysfunction, hemostasis and renal function were determined before and after the course of therapy. Results of the study demonstrated the treatment with sulodexide to have led to decrease in the concentration of vascular endothelial growth factor, and normalization of endothelial dysfunction and renal function. Similar changes were noted in patients treated with methylethylpyridinol. The use of sulodexide had a positive effect on decreasing the endothelial dysfunction activity; in addition, methylethylpyridinol increased the antithrombin III activity.

Conclusion: Methylethylpyridinol helps improve the endothelial status and normalize the indicators of hemostasis and microcirculation.

Keywords: diabetes mellitus, endothelial dysfunction, vascular endothelial growth factor, methylethylpyridinol, sulodexide.

Introduction

Some recent researches including large multicentre ones, DCCT from 1993 and UKPDS from 1998 [1,2] have been focused on the exclusive role of chronic hyperglycemia in the process of diabetic microangiopathy development. Hyperglycemia provokes an increase in aldose reductase activity, stimulates glucose oxidation along the polyol pathway and accumulation of final glycation products, aggravates the severity of oxidative stress, and increases blood viscosity and prothrombotic activity [3-5]. These changes lead to damage to endotheliocytes and development of endothelial dysfunction (ED). It is characterized by impairment of the vascular tone regulation and intercellular interaction, aggravates imbalance of the factors of coagulation and anticoagulation systems towards hypercoagulability, and contributes to a decrease in the activity of fibrinolytic properties of blood serum [6,7].

During the whole life, endotheliocytes synthesize a moderate amount of vascular endothelial growth factor (VEGF), which is necessary to ensure endothelial migration, differentiation, and cell survival. The term VEGF unites a whole group of signal proteins that are stimulants of angiogenesis in pathologic conditions (inadequate blood supply and chronic hypoxia).

In patients with diabetes mellitus (DM), hyperproduction of VEGF by endotheliocytes is a protective reaction, indicating an active process of damaging vascular wall and development of microvascular complications (primarily retinopathy and nephropathy) [8-10]. Therefore, more attention has recently been paid to maintaining an adequate level of vascular endothelial re-
generation factors and slowing the progression levels of diabetic microangiopathies [3]. These concepts have raised interest in searching and investigating the agents that are acting simultaneously on ED, rheology and hemodynamics in the vessels of the microcirculatory bed.

For several years, endocrinologists and nephrologists have used sulodexide medication for correction of ED and microcirculatory disorders, owing to its complex pharmacological effect as an anticoagulant, antiadhesive, fibrinolytic, angioprotective, antithrombotic and hypolipidemic agent.

Sulodexide also contributes to restoration of the structural integrity and function of endothelial cells and normalization of the negative charge of the endothelial basal membrane. However, the high cost of the drug prevents its use for the prevention and correction of ED in the vast majority of DM patients. Therefore, there is particular interest in the investigation of the domestic preparation methylethylpyridinol and its effectiveness. Methylethylpyridinol has a number of therapeutic effects including angioprotective, antiplatelet, fibrinolytic and antioxidant.

The aim of this study was to investigate the efficacy of methylethylpyridinol and sulodexide in correcting ED in patients with type 1 DM.

**Material and Methods**

The study included 89 patients (37 men and 52 women) with type 1 DM according to the WHO diabetes diagnostic criteria from 1999, with the mean disease duration of 8.4±3.7 years and mean age 27.2±4.3 years. The patients with duration of the disease of 10 years were not included in the investigation.

Thirty-seven (41.6%) patients were in the stage of subcompensation and 52 (58.4%) were in the stage of decompensation. The mean level of glycated hemoglobin (HbA1c) was 9.6±0.8%, which was a very high risk factor for development of diabetic microangiopathy. Forty-eight (53.9%) patients had elevated urine albumin level. Hypertension was recorded in ten (11.2%), hyperfiltration was recorded in both groups. Thus, the number of patients with hypo- and/or hyperfiltration was lower in both patient groups as compared with control group: 63 [51; 82]% (p=0.019) and 61 [48; 81]% (p=0.014) in groups 1 and 2, respectively, versus 101 [87; 115]% in control group.

Exclusion criteria were uncontrolled arterial hypertension, chronic kidney disease (CKD) stage 3b and higher according to the K/DOQI CKD classification (National Kidney Foundation, 2002 ), chronic arterial insufficiency (CAI) stage Ib and higher (Fontaine stages, 1954), chronic heart failure (CHF) stage III and higher (New York Heart Association Functional Classification, 1964), acute cerebrovascular impairment (ACVII), myocardial infarction (MI) in history, proliferative retinopathy, and alcohol abuse. Study patients underwent complex work-up and treatment (baseline bolus therapy with insulin, statins and angiotensin-convert ing enzyme inhibitor (ACE inhibitor) and angiotensin II receptor blockers, according to the adopted protocols.

Study patients were divided into 2 groups: group 1 including 42 (47.2%) patients administered sulodexide (Vesel Doue F®, Alfa Wassermann, Italy) as add-on therapy at a dose of 600 LE/day intravenous drip in saline solution for the course of 14 injections; and group 2 including 47 (52.8%) patients administered methylethylpyridinol (Cardiosipin®, JSC Biosynthesis, Russia) as add-on therapy at a dose of 600 mg/day intravenous drip in saline solution for the course of 14 injections.

The following parameters were determined in both groups before and after the course of treatment: level of albuminuria by enzyme immunoassay (EIA), von Willebrand factor (vWF) by platelet agglutination in the presence of ristocetin (ristomycin) (SPA Renam, Russia), antithrombin III activity by optic recording technique of paranitroaniline count expressed following thrombin III neutralization with antithrombin (SPA Renam, Russia), and VEGF by EIA in blood serum (LLC Hema, Russia). Desquamated endothelial cell counting in peripheral blood was done by use of J. Hladecy method. Glomerular filtration rate (GFR) was estimated by the CKD-EPI formula.

Control group included 20 age- and sex-matched healthy subjects. All trials (research studies) were carried out on admission to the hospital and in 14 days.

For statistical analysis we used statistical packages Plan Maker Professional 2012 and Statistica 8.0 for Windows. Data were expressed as median and interquartile range (Me, 25% quartile; 75 quartiles). For figure comparison, we used Mann-Whitney U test and McNemar test (to compare 2 sets of associated data). Statistically significant difference was considered to be at p<0.05.

**Results**

Data analysis showed urinary excretion of albumin to be increased by factor 5.2 in type 1 DM patients before treatment as compared to control group: 54.3 [42.8; 61.3] mg/day (p=0.002) in group 1 and 55.7 [43.7; 64.2] mg/day (p=0.001) in group 2. Sixteen (38.1%) group 1 patients and 18 (38.3%) group 2 patients showed GFR index lowering by factor 17% (p=0.027 and p=0.024 in groups 1 and 2, respectively), simultaneously with filtration recovery.

Signs of ED were revealed in randomized patients of both groups. ED was indicated by more than twofold increase of vWF activity as compared with control group (p=0.011 in group 1 and p=0.008 in group 2), of VEGF by more than 5 times (p=0.002 in group 1 and p=0.002 in group 2), and of desquamated endothelial cells in peripheral blood by more than 5 times (p=0.001 in group 1 and p=0.002 in group 2) in comparison with control group.

The activity of antithrombin III, a primary plasma factor of anticoagulation system synthesized by endothelialcytes, was lower in both patient groups as compared with control group: 63 [51; 82]% (p=0.019) and 61 [48; 81]% (p=0.014) in groups 1 and 2, respectively, versus 101 [87; 115]% in control group.

After the course of treatment, albumin level in urine decreased by 25% in group 1 and by 24% in group 2: 40.7 [31.9; 54.2] mg/day (p=0.031) and 42.3 [33.7; 57.5] mg/day (p=0.034), respectively, as compared with pre-treatment figures.

After the course of sulodexide therapy in group 1 and methylethylpyridinol therapy in group 2, GFR index tended to be normal. Reduction in the number of patients with hypo- and/or hyperfiltration was recorded in both groups. Thus, the number of patients with normal GFR index increased to 22 (52.4%) in
After the course of treatment, group 1 showed a significant decrease in vWF activity as compared to pre-treatment figures (p=0.004). Similar changes were recorded in group 2 (p=0.005). However, these changes were more pronounced in group 1, i.e. vWF activity after the course of treatment was almost normal (p=0.037) as compared with group 2 post-treatment (Fig. 1).

In type 1 DM patients, VEGF index in blood serum after the course of the treatment tended to be normal in both groups 1 and 2 (Fig. 2). In the group of patients treated with sulodexide, VEGF concentration was reduced by almost 38% (p=0.007) as compared to pre-treatment values. In the group of patients treated with methylethylpyridinol, VEGF was reduced by 34% (p=0.001). There were no statistically significant differences between the two groups.

The treatment protocols resulted in a statistically significant reduction in desquamated endothelial cells in both groups. The number of desquamated endothelial cell decreased twofold (p=0.002) in group 1 patients and 1.4-fold in group 2 patients (p=0.005).

After treatment, an increase in the activity of antithrombin III to 73 [59; 94]% (p=0.027 compared with the value before treatment) was recorded in group 1. In group 2, this indicator was 88 [69; 111]% (p=0.018 compared with the value before treatment), which was statistically significantly higher than the results obtained in group 1 after treatment with sulodexide (p=0.022).

**Discussion**

In type 1 DM patients, ED is detected with high activity of vWF, a sharp increase in the level of VEGF and the number of desquamated endothelial cells. These changes may be primarily explained by inducing the glucose metabolism polyol pathway with persistent hyperglycemia and activation of protein kinase C, accumulation of advanced glycation end-products, lipid peroxidation, etc. Hyperfiltration, increased intracapillary pressure and chronic hypoxia enhance the adverse effects of high VEGF concentrations on microvascular wall. It enhances the activity of ED and desquamation of endothelial cells, and subsequently triggers fibrotic processes and capillary occlusion [11,12].

Thus, in the study patients with type 1 DM, ED indicated initial impaired renal function. The therapy applied had a positive effect on glomerular endothelial function and status in both groups.

Our study results revealed reduction of antithrombin III activity, which may also accelerate the development of diabetic microvascular deterioration by blood rheology in microvasculature. These changes increase the severity of chronic hypoxia and trophic disorders of endothelial cells.

Therapy with sulodexide caused a decrease in VEGF concentration, normalization of ED and renal function. Our findings pointed to a complex therapeutic effect of the drug on the basic pathogenetic mechanisms of diabetic microangiopathy.

Similar changes were observed in patients treated with methylethylpyridinol. However, the latter had greater hemodynamic effects (GFR normalization and decrease of albuminuria). This drug did not only improve endothelial cells and slowed down development of microvascular complications, but also normalized the parameters of hemostasis (pronounced increase in antithrombin III activity as compared with group 1), which could possibly contribute to improvement of the cardiovascular system in patients with diabetes.

Thus, the use of methylethylpyridinol, which has already been recommended as an angioprotector in the treatment of diabetic retinopathy, can be extended to the setting of diabetic
nephropathy. Having angioprotective, antiplatelet, fibrinolytic and anti-oxidant properties, methylethylpyridinol cannot only slow down the development of ED, but can also slightly improve renal function in patients with type 1 DM.

**Conclusion**

The sulodexide and methylethylpyridinol therapy leads to improvement of endothelial and kidney functions by reducing the activity of vWF, VEGF and number of desquamated endothelial cells, and moderately normalizing the levels of albuminuria. GFR rate was not significantly changed at 14 days. The administration of sulodexide had the greatest positive impact on decrease in the ED activity, while methylethylpyridinol led to further increase in the activity of antithrombin III. The use of methylethylpyridinol contributed not only to improved endothelium status, but also normalized the indicators of hemostasis and microcirculation.

**References**

WMA International Code of Medical Ethics


DUTIES OF PHYSICIANS IN GENERAL

A PHYSICIAN SHALL always exercise his/her independent professional judgment and maintain the highest standards of professional conduct.

A PHYSICIAN SHALL respect a competent patient’s right to accept or refuse treatment.

A PHYSICIAN SHALL not allow his/her judgment to be influenced by personal profit or unfair discrimination.

A PHYSICIAN SHALL be dedicated to providing competent medical service in full professional and moral independence, with compassion and respect for human dignity.

A PHYSICIAN SHALL deal honestly with patients and colleagues, and report to the appropriate authorities those physicians who practice unethically or incompetently or who engage in fraud or deception.

A PHYSICIAN SHALL not receive any financial benefits or other incentives solely for referring patients or prescribing specific products.

A PHYSICIAN SHALL respect the rights and preferences of patients, colleagues, and other health professionals.

A PHYSICIAN SHALL recognize his/her important role in educating the public but should use due caution in divulging discoveries or new techniques or treatment through non-professional channels.

A PHYSICIAN SHALL certify only that which he/she has personally verified.

A PHYSICIAN SHALL strive to use health care resources in the best way to benefit patients and their community.

A PHYSICIAN SHALL respect the local and national codes of ethics.

DUTIES OF PHYSICIANS TO PATIENTS

A PHYSICIAN SHALL always bear in mind the obligation to respect human life.

A PHYSICIAN SHALL act in the patient’s best interest when providing medical care.

A PHYSICIAN SHALL owe his/her patients complete loyalty and all the scientific resources available to him/her. Whenever an examination or treatment is beyond the physician’s capacity, he/she should consult with or refer to another physician who has the necessary ability.

A PHYSICIAN SHALL respect a patient’s right to confidentiality. It is ethical to disclose confidential information when the patient consents to it or when there is a real and imminent threat of harm to the patient or to others and this threat can be only removed by a breach of confidentiality.

A PHYSICIAN SHALL give emergency care as a humanitarian duty unless he/she is assured that others are willing and able to give such care.

A PHYSICIAN SHALL in situations when he/she is acting for a third party, ensure that the patient has full knowledge of that situation.

A PHYSICIAN SHALL not enter into a sexual relationship with his/her current patient or into any other abusive or exploitative relationship.

DUTIES OF PHYSICIANS TO COLLEAGUES

A PHYSICIAN SHALL behave towards colleagues as he/she would have them behave towards him/her.

A PHYSICIAN SHALL NOT undermine the patient-physician relationship of colleagues in order to attract patients.

A PHYSICIAN SHALL when medically necessary, communicate with colleagues who are involved in the care of the same patient. This communication should respect patient confidentiality and be confined to necessary information.
ABOUT

The Azerbaijan Medical Association (AzMA) is the country's leading voluntary, independent, non-governmental, professional membership medical organization for physicians, residents and medical students who represent all medical specialties in Azerbaijan.

Association was founded by Dr. Nariman Safarli and his colleagues in 1999. At the founding meeting, the physicians adopted the Statutes and Code of Ethics of the Association. The AzMA was officially registered by Ministry of Justice of Azerbaijan Republic in December 22, 1999.

Since its inception, the AzMA continues serving for a singular purpose: to advance healthcare in Azerbaijan.

• Founded in 1999, the AzMA provides a way for members of the medical profession to unite and act on matters affecting public health and the practice of medicine.
• We are the voice of physicians who support the need for organized medicine and want to be active within their profession.
• We are the representative for Azerbaijan doctors on the world–wide level and the voice of Azeri physicians throughout the world.

MISSION

The mission of the Azerbaijan Medical Association -is to unite all members of the medical profession, to serve as the premier advocate for its members and their patients, to promote the science of medicine and to advance healthcare in Azerbaijan.

GOALS

• Protect the integrity, independence, professional interests and rights of the members;
• Promote high standards in medical education and ethics;
• Promote laws and regulation that protect and enhance the physician-patient relationship;
• Improve access and delivery of quality medical care;
• Promote and advance ethical behavior by the medical profession;
• Support members in their scientific and public activities;
• Promote and coordinate the activity of member-specialty societies and sections;
• Represent members' professional interests at national and international level;
• Create relationship with other international medical associations;
• Increase health awareness of the population.

The association's vision for the future, and all its goals and objectives are intended to support the principles and ideals of the AzMA's mission.

INTERNATIONAL RELATIONSHIPS

Since its establishment, AzMA built close relationships with many international medical organizations and national medical associations of more than 80 countries. The following are the AzMA's international affiliations:

• Full membership in the World Medical Associations (WMA) (since 2002)
• Full membership in the European Forum of Medical Associations (EFMA) (since 2000)
• Full membership in the Federation of Islamic Medical Associations (FIMA) (since 2002)
• Associate membership in the European Union of Medical Specialists (UEMS) (since 2002)

Especially the year 2002 remained with memorable and historical events for AzMA such as membership to the World Medical Association (WMA). Today we are extremely pleased to represent our Association and to be a part of the WMA family.

MEMBERSHIP

A person with medical background, who accepts and follows the AzMA Statutes and AzMA Code of Ethics, may become a member of the Association. The Code of Ethics of the Association shall be the members' guide to professional conduct.

Membership in the AzMA is open to:

• Physicians residing and practicing in Azerbaijan and in abroad.
• Medical students enrolled at medical universities or schools
• Retired physicians

Members can access a special members only area of the AzMA website designed to provide the most up-to-date, and timely information about organized medicine in our country.

To the non-member, we hope you'll discover, through our website how valuable Azerbaijan Medical Association is to medicine in Azerbaijan and will join us.

MEDICINE'S VOICE IN AZERBAIJAN

As the largest physician membership organization in Azerbaijan the AzMA devotes itself to representing the interests of physicians, protecting the quality of patient care and as an indispensable association of busy professionals, speaks out with a clear and unified voice to inform the general public and be heard in the highest councils of government.

The AzMA strives to serve as the Medicine's Voice in Azerbaijan.

For more information, please visit our website: www.azmed.az
We work together for the sake of healthy future of Azerbaijan!

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