

Venous malformation of epiglottis and arterio-venous malformation of palate treated by sclerotherapy – case reports

Malformacja żylna nagłośni i malformacja tętniczo-żylna podniebienia leczone metodą skleroterapii – opis przypadków

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Article history: Received: 06.08.2016 Accepted: 20.12.2016 Published: 30.12.2016

ABSTRACT: This study presents two rare clinical entities of vascular anomalies localized in the region of head and neck: the case of woman with venous malformation of the epiglottis and the man with the arterio-venous malformation of palate. Here in the title the term vascular malformation has been used because of conformity with the classification of International Society for the Study of Vascular Anomalies. Another, interchangeably used term hemangioma, defined according to World Health Classification of Tumours, is more familiar in clinics. The foam sclerotherapy treatment has been reported with success. Microfoam prepared from polidocanol was injected directly into malformations. Large, ball-shaped laryngeal malformation decreased. In this case, sclerotherapy provides a good preparation for further surgery. Arteriovenous malformation of palate disappeared and there was no need for supplementary surgery. Authors did not observe any complications of the treatment.

KEYWORDS: vascular malformation, laryngeal venous malformation, arterio-venous malformation of palate, laryngeal cavernous hemangioma, arterio-venous hemangioma of palate, sclerotherapy, polidocanol

STRESZCZENIE: W pracy przedstawiono dwa rzadkie przypadki anomalii naczyniowych w zakresie głowy i szyi: kobietę z malformacją żylną nagłośni i mężczyznę z malformacją tętniczo-żylną podniebienia. Użyte przez autorów w tytule pracy nazwy rozpoznają się zgodnie z aktualną klasyfikacją kliniczną proponowaną przez Międzynarodowe Towarzystwo Badań nad Anomaliami Naczyniowymi (ISSVA). Według innej stosowanej przez patologów WHO klasyfikacji guzów naczyniowych, opisywana malformacja żylna to naczyniak jamisty, zaś malformacja tętniczo-żylna to naczyniak tętniczo-żylny. Pacjentów leczono metodą skleroterapii. Po wstrzyknięciach do malformacji polidokanolu w postaci piany stwierdzono regresję zmian. Duża, kulista malformacja nagłośni znacznie się zmniejszyła, umożliwiając jej wycięcie nożem elektrycznym, zaś malformacja podniebienia uległa całkowitemu zanikowi. Żadnych powikłań leczenia nie zaobserwowano.

SŁOWA KLUCZOWE: malformacja naczyniowa, malformacja żylna krtani, malformacja tętniczo-żylna podniebienia, naczyniak jamisty krtani, naczyniak tętniczo-żylny podniebienia, skleroterapia, polidokanol

INTRODUCTION

Until 1982, the term *angioma* had been used to denote various vascular malformations, which may have resulted in incorrect

therapy [4]. In 1982 Mulliken and Glowacki proposed a revolutionary system for classifying vascular anomalies into two groups: angiomas and developmental malformations [14]. This classification was adopted by the International Society for the

Study of Vascular Anomalies (ISSVA)) [19]. Later on, ISSVA introduced a modification of this classification system and divided vascular anomalies into:

- - vascular tumors – angiomas were classified in this group
- - vascular malformations [30].

The aforementioned classification is based on different biological activity and histopathological features, different clinical course and therapeutic management. According to this classification system, the term angioma should be used for the most frequently encountered tumors of the infancy that usually develop in two phases. Mesothelial cells express significant mitotic activity during the proliferation phase. During the next phase, i.e. the involution stage, metabolic activity of the angioma decreases and the lesion undergoes gradual involution [11]. Angiomas are observed in 5-10% of all infants [24]. They develop frequently within the head and neck (65%), the trunk (25%) and the limbs (15%) [11]. They occur within the late fetal period or in the perinatal period as lively red nevus or telangiectasia. They grow at a fast pace within a few weeks, and regress from the 10.-12. month onwards. The involution process may last from 3 to 10 years. In 40-50% of all cases, the angioma leaves a scar or deformation after involution [24].

Malformations are disorders within the structure of vessels, and there is no pathology within the mesothelium in these cases. As opposed to vascular tumors, cellular hyperplasia that leads to the growth of the lesion is not observed [28]. The type of vascular stroma determines the classification of malformations into simple malformations, i.e. lesions that are composed of one type of vessels, and complex, in which different vessels are found in the same lesion. Simple malformations include capillary, lymphatic, venous, and arteriovenous malformations [30]. The incidence of venous malformations is estimated at one case in 5,000-10,000 people [18, 29], and it is observed with the same incidence in males and in females [13]. 40% of all venous malformations are located within the head and neck [29]. In 90% of the cases, the lesions are solitary [4]. Venous malformations are present at birth, grow during the patient's life, and, in contrast to vascular tumors, do not undergo involution [1, 13, 18]. The etiology of these lesions is unknown. In some of the patients with venous malformation, a mutation of the TIE-2 tyrosine kinase receptor gene within the cells of mesothelium, which led to the loss of receptor function, was observed, [29]. Soblet et al. [20] showed that such mutations were observed in 17 specimens acquired from mesothelial cells out of 30 studied venous malformations. Histological structure of venous malformations is characterized by the presence of dilated venous channels lined by a single layer of mesothelium. These

channels are surrounded by irregularly distributed smooth muscle cells whose structure is pathological, which leads to progressive dilatation of the lumen of the vessels due to hydrostatic pressure [4, 16, 20]. Venous malformations grow bigger as the patient grows older [4], particularly during adolescence [13, 26]. Hemostasis within the vessel promotes the formation of thrombi, phleboliths. Venous malformations located superficially are easy to spot in clinical examination [9]. They are soft in palpation, in contrast to angiomas. As they are dilated venous channels filled with blood, they may easily be pressed, and drain partially [13, 26]. Their temperature is not increased when compared with the surrounding environment, and blood flow cannot be felt in palpation [4]. Exerting pressure on the lesion does not cause pain. Pain on palpation occurs if venous thrombosis develops. The possibility of aspirating blood on injection constitutes an important diagnostic symptom of a venous malformation [29]. Venous malformations are asymptomatic as long as they are small in size. As they grow bigger, they deform organs and lead to their dysfunction [1]. They may also be life-threatening due to such complications as hemorrhage, compression of other organs, or in cases in which they constrain the patency of the respiratory tract.

Case 1

An 84-year-old female patient was admitted to the ENT Department of the Independent Regional Hospital in Piotrków Trybunalski due to dysphagia, the feeling of foreign body retention in the pharynx, and hemoptysis, whose symptoms had been increasing for 4 months prior to admittance. Bleeding had occurred a few times every day during the previous week, and had been more abundant. According to the family, the patient's voice had „always” been of the characteristic pharyngeal, muffled kind. At admittance, the general state of the patient was good, dyspnea during rest was not observed, and stridor was present on exert. In indirect laryngoscopy, a spherical, dark red lesion was observed. Its surface was uneven, aciniform, with an erosion of approximately 0.5 cm in diameter, and it filled the space of the inferior pharynx between the lingual surface of the epiglottis and the base of the tongue.

CT scans showed the presence of a solid, oval-shaped, non-enhancing mass of 30x40x38 mm in diameter, filling the inferior pharynx. In the front, the lesion adjoined the base of the tongue, in the back – the posterior wall of the pharynx at the length of 27 mm, without infiltration. The superior border of the tumor was located at the level of the base of the tongue (Fig. 1). Due to the fact that it was impossible to perform intubation in the patient, tracheostomy was performed in local anesthesia, and, afterwards, surgical biopsy of the tumor



Fig. 1. Tumor of epiglottis visible in neck contrast-enhanced CT. The tumor is non-enhancing.

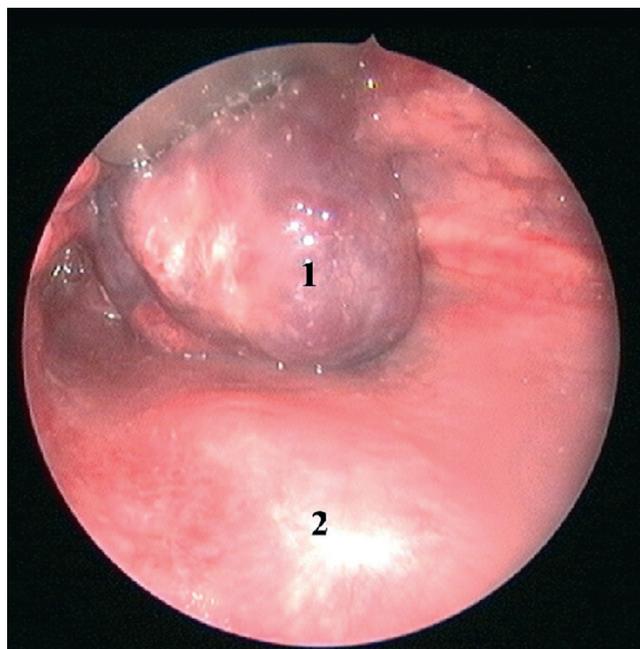


Fig. 3. Histopathological picture of cavernous hemangioma of epiglottis (magnification. 200x).

was performed in general anesthesia. The patient was placed in Rose position, and jaw opener was applied. A tumor filling the whole space of the inferior pharynx was disclosed, and it was quite soft and susceptible to pressure (Fig. 2). A curved vascular clamp was tightened below the inferior border of the tumor, and a specimen of the tissue was dissected for further evaluation. Bleeding was controlled with the use of continuous suture. Following result of histopathological examination was acquired: small tissue specimen including mucous membrane covered with squamous epithelium. Below the epithelium, microscopic imaging after routine hematoxylin-eosin staining showed hyalinating connective tissue with multiple vascular channels filled with blood, showing characteristic features of venous vessels, lined with physiological mesothelium. The diagnosis of cavernous hemangioma was made (Fig. 3). Together with the clinical picture, a venous malformation according to ISSVA was diagnosed. The patient was qualified for sclerotherapy treatment. The treatment was begun 6 weeks after the specimen had been taken. Polidocanol (lauromacrogol 400) in foam that was prepared immediately before application by mixing it with air at 1:1 ratio. In order to achieve even placement of the foam, 3 needle injections in the lesion were performed. Injections were performed every 4 weeks in hospital in indirect laryngoscopy, after applying 10% lidocaine for topical anesthesia to the inferior pharynx. During each appointment, reduction of the malformation in size was observed, and smaller amounts of the drug foam were applied to the lesion.

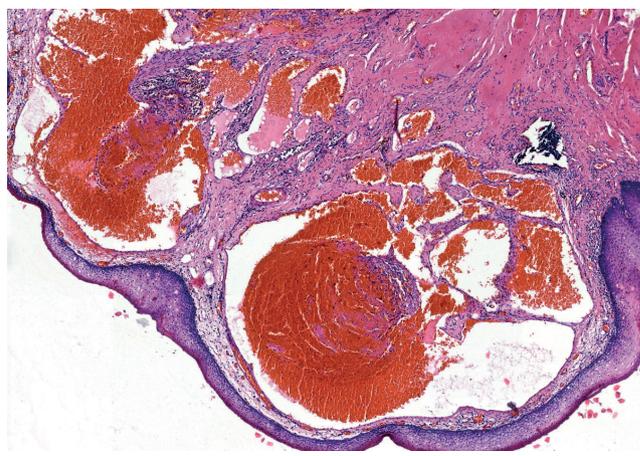


Fig. 2. Opreoperative of inferior pharynx in endoscopy. 1 – venous malformation of epiglottis, 2 – posterior wall of the pharynx.

In total, 5 polidocanol injections were performed, which led to the reduction of the lesion in size to a spherical mass of 8 mm in diameter, originating from the inferior part of the lingual surface of epiglottis. This residual lesion was excised using electrical blade under general anesthesia. The cannula was removed. Control CT examination was performed 1 year after surgery (Fig. 4), and endoscopic examination was performed 1.5 years after surgery (Fig. 5). Recurrence of malformation was not observed in any of the examinations.

Case 2

A 62-year-old patient was admitted to hospital due to the tumor of palate. According to the patient, the non-painful elevation within the palate had been present in childhood. The lesion had been growing for several years. Bleeding occurred after trauma with hard food, and it stopped on its own. For the previous 3 months, bleeding episodes had occurred more frequently, were more abundant and lasted for a longer time, which made eating difficult. The patient reported that it had been possible for him earlier to reduce the size of the lesion by pressing on it with the tongue. Over the last time, however, attempts at this led to bleeding.

Clinical examination revealed an elevation of the mucous membrane within the palate along the midline. The height of the elevation was 1.5 cm, its diameter was 2.0 x 2.0 cm, and it was blue-red in color. In the central part of the lesion, erosion with a small inflammatory reaction around it was observed (Fig. 6). The lesion was soft in palpation and susceptible to pressure. At injection, venous blood was aspirated, and the volume of the lesion did not change.

Contrast-enhanced CT (Fig. 7) revealed a well-demarcated focus within the hard palate along the midline, of 18x19,13 mm diameter, protruding to the oral cavity, showing slightly non-homogenous contrast enhancement. The lesion did not cause resorption of osseous structures. Clamps were used to acquire two tissue specimens for examination from the erosion at the top of the lesion. Bleeding was stopped with pressure dressing. Following result was acquired: Two fragments of mucous membrane covered with physiological squamous epithelium. Within one of the specimens, multiple venous vessels were visible below the epithelium; morphology of some vessels was characteristic of small veins. Within the other specimen, under partially eroded epithelium, small blood vessels were disclosed, embedded in abundant adipose-hyaline stroma. In histopathological terms, arteriovenous hemangioma was diagnosed (Fig. 8). Along with the clinical picture, arteriovenous malformation according to the ISSVA classification was diagnosed. The patient was qualified for sclerotherapy in outpatient clinic. Polidocanol foam was applied, after preparing the foam at 1: 1 ratio with air. The applications were performed every 3 weeks. After 4 sessions, the lesion resolved completely, and only a slight thickening of the mucous membrane remained. Recurrence of the malformation was not observed in control examination performed 5 months after treatment was completed (Fig. 9).

DISCUSSION

The classification of vascular anomalies introduced by Mulliken and Glowacki and modified by ISSVA takes such features



Fig. 4. Picture of the inferior pharynx and larynx in CT, 1 year post-operatively.

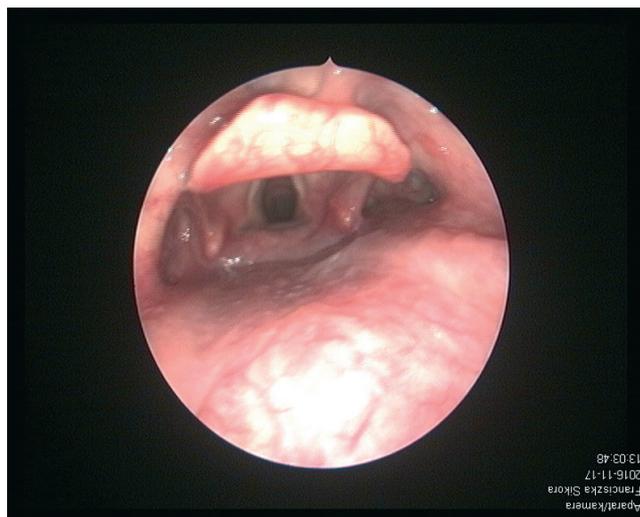


Fig. 5. Picture of the inferior pharynx in endoscopy, 1.5 years post-operatively.

as the time of the development of the lesion, its location, and color into consideration, apart from the histopathological features, and it does not follow the classification of vascular tumors by the WHO used by pathologists [7, 24]. The WHO classifies vascular tumors into benign, borderline (locally malignant and rarely metastasizing), and malignant. Within this classification, angiomas are not differentiated from vascular malformations, both entities are sometimes classified in one category, or both terms are used interchangeably. That is why



Fig. 6. Arteriovenous malformation of the palate.

histopathological picture of small specimens is used mostly for differentiating lesions of vascular origin using the following categories: benign, through borderline, to malignant, but it does not always enable the interpretation of benign lesions of the hemangioma-vascular malformation type, particularly in routine examinations.

Immunohistochemistry is used for differentiating vascular malformations, though it is not a standard procedure. The presence of D2-40 or LYVE-1 markers in mesothelial cells is characteristic of lymphatic malformations, and that is how they differ from other vascular malformations [24]. In order to differentiate hemangioma from vascular malformation, determination of membrane glycoprotein GLUT1 (Glucose transporter 1) expression is used, as this glycoprotein is a commonly accepted marker of early childhood angiomas [1, 15, 24, 23]. This glycoprotein is observed in all stages of hemangioma evolution, and its expression is not elevated in vascular malformations [5]. The WT1 protein (Wilms tumor protein) is another marker that is used for differentiating hemangiomas from vascular malformations. The presence of WT1 is characteristic of vascular tumors, and it is not observed in vascular malformations [12, 23]. The fact that there is no uniform classification of vascular malformations that would be the same for all specialists makes it more difficult to provide a diagnosis and choose appropriate treatment methods [8, 13, 16, 19, 21]. On the basis of histopathological specimen examination, the specimens acquired from the lesions discussed in the article fulfilled all criteria for hemangiomas according to the classification by the WHO. However, according to the classification by ISSVA used by clinicians, they fulfilled the criteria for vascular malformations. Treatment methods appropriate for vascular malformations proved successful.

Described methods for treating venous malformations include: surgical excision, laser surgery, cryotherapy, electrocoagula-



Fig. 7. Tumor of the palate in CT. Contrast enhancement of the tumor can be seen in the scan.

tion, sclerotherapy [29]. In cases of arteriovenous malformations, intra-arterial embolization is used on its own or together with sclerotherapy [3]. Potential difficulties related to surgical treatment of vascular malformations within the head and neck include the lack of complete lesion removal without impairment in the functioning of an organ, abundant hemorrhage, and difficult access. Therefore, management commencing with sclerotherapy followed by surgical excision after reduction of the lesion in size is achieved, seems optimum [4, 29]. The point of sclerotherapy is to cause embolization of vascular channels. This can be achieved by inflicting irreversible damage to the cells of mesothelium followed by inflammation and fibrosis [4, 6, 11]. This method is used by phlebologists for treating lower extremity varicose veins. Different preparations for use in sclerotherapy have been described. According to the way in which the drug affects the wall of the vessel, the medications can be classified into three groups: osmotic agents (e.g. hypertonic sodium chloride solution), detergents (e.g. polidocanol), chemically irritating substances (e.g. ethanol, phenol) [25]. Currently, detergents, i.e. sodium tetradecyl sulfate and polidocanol, are used most frequently [6]. Both preparations are available in Poland.

Polidocanol is a non-ionic surface active substance (a surfactant) [10]. The hydrophobic part of the polidocanol molecule destroys the osmotic barrier by binding with the lipids of the cell membrane of mesothelial cells, which, in turn, leads to cell destruction. Due to exposure to polidocanol, the interior

surface of the vein becomes thrombogenic. A clot that closes the lumen of the vessel is formed. Aseptic inflammation develops and the vessel, closed by the clot, fills with connective tissue [10, 29]. The vessel, transformed into a streak of connective tissue, cannot form a channel again [6]. Polidocanol deactivates after getting contact with blood, and this feature limits its sclerosing influence to the mesothelium at the site of injection [31]. The drug also acts as a local anesthetic and that is why injections are well tolerated by patients [27, 29].

The first attempts at treating lower extremity varicose veins using sclerotherapy were made in the 19th century but the method was discontinued due to complications caused by toxicity of various solutions administered as fluids to the vessels [27]. Sclerotherapy has gained popularity since the mid-1990s when the drug was transformed into foam by mixing the ingredients with carbon dioxide or compressed air. Applying the drug as foam makes it possible to reduce the concentration of the drug as well as its total dose, provides even distribution of the sclerotizing agent in the lumen of the vessel, and provides better and longer-lasting contact of the drug with the walls of the mesothelium [6, 17, 25]. A simple way of transforming a liquid agent used for sclerotherapy into foam was described by Tessari et al. [22]. Two syringes are used in this method – each of them is connected to a different end of a three-way connector with the possibility of regulating the flow direction [2]. The first syringe contains the sclerosing solution, and the other one contains air, in appropriate ratio. A catheter with a needle emerges from the third end of the connector. After the fluid and air are mixed energetically between the syringes, foam forms and the whole produced foam gathers in one of the syringes. It is injected into the lesion through the catheter [6, 27].

CONCLUSIONS

Sclerotherapy with the use of polidocanol proved efficient, simple, and safe for treating a large venous malformation (cavern-

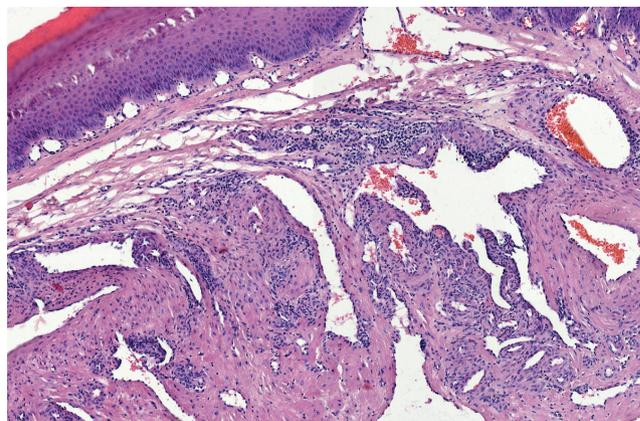


Fig. 8. Histopathological picture of the arteriovenous hemangioma of the palate (magnification 200x).



Fig. 9. Picture of the palate, 5 months after completion of treatment.

ous hemangioma) of epiglottis and an arteriovenous malformation (arteriovenous hemangioma) of the palate. In the first case, sclerotherapy constituted the preparation for surgery, and in the second case it led to total resolution of the lesion.

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Word count: 3000 Tables: – Figures: 9 References: 31

Access the article online: DOI: 10.5604/20845308.1226621 Full-text PDF: www.otorhinolaryngologypl.com/fulltxt.php?CID=1226621

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Competing interests: The authors declare that they have no competing interests.

Cite this article as: Białawczewski L., Maciaszczyk K., Supeł M.: Venous malformation of epiglottis and arterio-venous malformation of palate treated by sclerotherapy – case reports; *Pol Otorhino Rev* 2016; 5(4): 29–35