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Different clinical presentation of pyogenic granuloma in children and different therapeutic approach – case series

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Abstract

Introduction. Vascular tumors are one of the most common tumors in children. Pyogenic granuloma (also known as lobular capillary hemangioma) is a type of benign vascular tumor according to the ISSVA classification of vascular tumors. The treatment of choice is surgery. However, there are many treatment options, for example, topical timolol. ***Case series.*** The article presents three patients treated due to pyogenic granuloma. Patient 1 was a 10-month-old boy with a vascular skin lesion on the left side of the bridge of the nose (the tumor macroscopically resembled pyogenic granuloma) was referred due to the bleeding from the lesion. The mother did not accept surgical treatment. The local timolol eyedrops 0.5% twice a day were prescribed. During the therapy, no adverse effects were noticed. After two months of treatment, the lesion diminished in each dimension. The bleeding was no longer observed. Patient 2 was a 13-year-old boy with a lesion of the skin of the left frontal region treated surgically. Patient 3 was a 10-year-old girl with a lesion of the anterior chest wall skin treated surgically. ***Conclusions.*** The topical treatment with timolol eyedrops 0.5% is a treatment option worth considering in the youngest children. *(Farm Współ 2023; 16: 115-119) doi: 10.53139/FW.20231611*

Keywords: vascular lesions, children, beta-blockers

Introduction

Vascular tumors are one of the most common tumors in children [1,2]. Pyogenic granuloma (also known as lobular capillary hemangioma) is a type of benign vascular tumor according to the ISSVA (The International Society for the Study of Vascular Anomalies) classification of vascular tumors [3,4]. It can arise in the skin and mucous membranes [5].

It is usually present as a solitary, red, pedunculated papule or a sessile plaque [5]. The most common locations of the lesion are the head, neck, and upper extremities [6].

The etiology of the lesion is unclear [7]. Among the causal genes of pyogenic granuloma are BRAF, RAS, and GNA14 [3,4]. Moreover, chronic irritation and trauma are potential risk factors for the development of pyogenic granuloma [7]. The role of female sex hormones as a risk factor is also suspected because pyogenic granuloma is more often found in females than men [6,7].

The treatment of the lesion is surgical excision with histopathological examination. It can be simple excision with root planing or modified excision with deep curettage [8]. The second option is related to the lower recurrence rates [8]. However, the topical beta-blockers' role in children is also discussed in the literature [6]. It must be underlined that their use in diseases other than infantile hemangiomas is off-label [6].

The article presents a series of three cases of children with vascular tumors. Two of them were treated surgically, and one patient was treated with a topical beta-blocker with good effect.

Case report 1

A 10-month-old boy with a vascular skin lesion on the left side of the bridge of the nose was referred by a pediatrician due to bleeding from the lesion (figure 1). According to the mother, the lesion was present at birth but looked like "dilated capillaries". After a few months, it has grown. A few days ago, the lesion was bleeding.

At the admission, on the skin on the left side of the nose bridge, there was a ruby-colored vascular

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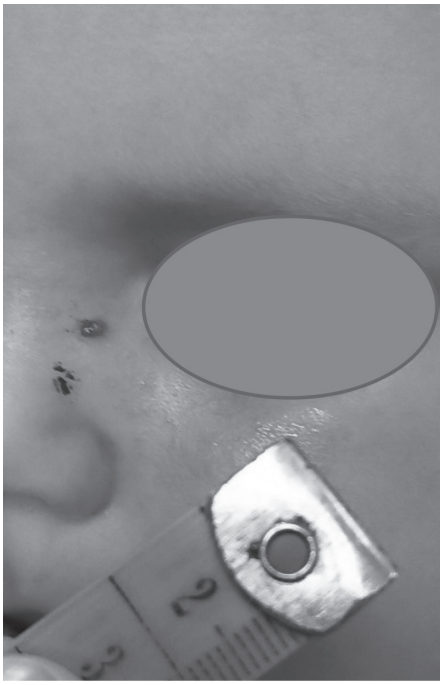

Figure 1. A 10-month-old boy with a vascular skin lesion on the left side of the bridge of the nose (non-intensive bleeding from the lesion is visible)

lesion, elevated over the skin level with dimensions of 3 mm x 2 mm, currently with no signs of active bleeding or inflammation.

Because the mother did not accept the surgical treatment or oral propranolol therapy, the local timolol eyedrops 0.5% twice a day was prescribed. The caregivers were asked to take photographs of the lesion every week and were provided with the information that in case of bleeding, the child should be admitted to the Pediatric Surgery Department to stop bleeding and excise the lesion.

During the therapy, no adverse effects were noticed. After two months of the treatment, the lesion diminished in each dimension (figure 2). The diameter was 1 mm x 1 mm. The bleeding was no longer observed. The treatment was stopped. The patient has been in observation for six months.

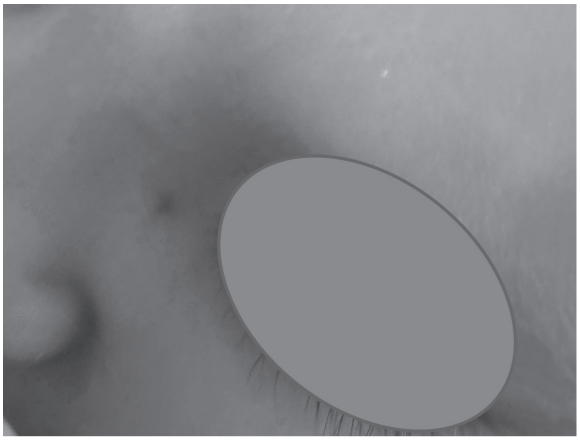

Figure 2. A 12-month-old boy with a vascular skin lesion on the left side of the bridge of the nose (2 months of treatment)

Case report 2

A 13-year-old boy with a lesion of the skin of the left frontal region present for four years. The lesion was enlarging. The history of bleeding from the lesion was positive. A history of skin cancers in the family was negative. Clinically, on the skin of the frontal region on the left side skin the nodule with a diameter of 0.9 cm x 0.5 cm x 0.1 cm, a ruby color. The features of damage to the epidermis on the lesion were observed. Laboratory tests did not show deviations from the norm. The boy was qualified for surgical treatment – excision of a lesion under local anesthesia with the histopathological examination, which revealed "granuloma angioplasticulm parim exulcerans".

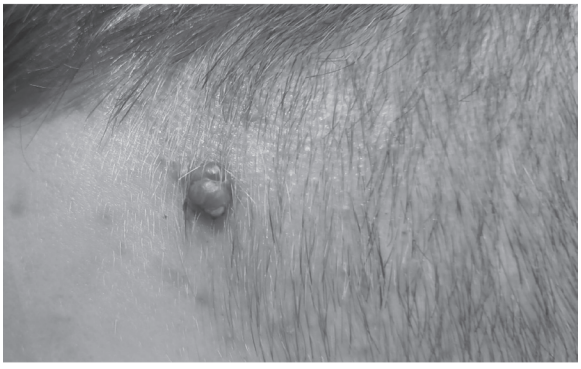

Figure 3. The pyogenic granuloma present at the skin of the left side of the front

Case report 3

A 10-year-old girl with a lesion of the skin of the anterior chest wall. The lesion was present for about a month and was bleeding periodically. Clinically a lesion of the skin of the anterior thoracic wall was seen (pyogenic granuloma-like) with a diameter of less than 1 cm. Laboratory tests did not show deviations from the norm. The patient was qualified for surgical treatment – excision of a lesion under local anesthesia with the histopathological examination, which revealed "partially necro-hemorrhagic pyogenic granuloma".

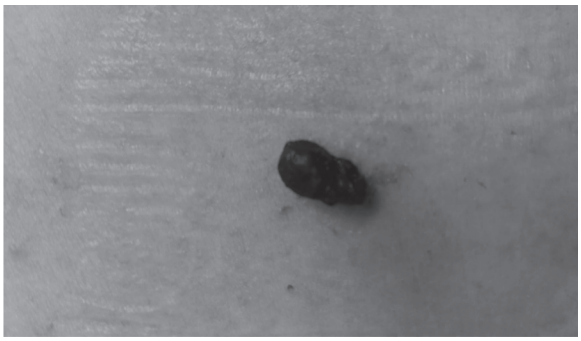

Figure 4. The pyogenic granuloma present at the skin of the anterior surface of the thorax

Discussion

The case series presents the different clinical presentations of pyogenic granuloma in children and therapeutic approaches. Patient number 2 and 3 were treated surgically. These children were mature enough to perform the procedure under local anesthesia. In patient number 1, the risk of disfigurement was not high; the problem was persistent bleeding. No recurrence was observed in all presented cases.

The treatment of choice in the presented case is surgical treatment (lesion excision). However, in the case of younger children, the procedure of skin lesion excision requires general anesthesia. That is why conservative treatment would be a valuable option. Effective conservative treatment can help reduce the lesion's size or postpone or obviate surgery [6]. However, it must be underlined that it is also related to the impossibility of performing histological examination [6]. The use of topical beta-blockers in infantile pyogenic granuloma treatment is off-label [6,9]. In the literature, there are some case reports of successful treatment of pyogenic granuloma with topical timolol.

Chiriac et al. effectively treated a 2-year-old boy presented with a solitary rapidly growing red pedunculated nodule on the left palpebral with the timolol (0.1% obtained from the ophthalmic formulation of 0.5% timolol) applied in occlusive dressings twice daily for two weeks, followed by one application of 70% Trichloroacetic Acid [10]. They also described the complete resolution of a small pyogenic granuloma on the left side of the face in a 13-month-old girl after two weeks of application of 0.1% timolol and one application of 70% Trichloroacetic Acid [10]. Gupta et al. reported a series of 10 patients with pyogenic granulomas who received treatment with 0.5% timolol maleate ophthalmic solution applied four times a day, two drops per dose [11]. Four patients showed complete response within 3-24 days, with no recurrence at a 3-month follow-up. Three patients each showed partial or no response [11]. The treatment seems to be safe, and no adverse effects were noticed [11]. The advantages of the treatment option are also the ease of administration and better cosmetic outcomes [11]. However, the authors underlined that the response to topical beta-blockers is variable, and the efficacy is not as universal as in cases of infantile hemangiomas [11]. Similar observations were made by McGinness et al. who reported 3 patients with pyogenic granulomas treated with topical timolol 0.5% solution [12]. Neri et al. realized the single-arm, open-label, prospective study to evaluate the efficacy of topical propranolol (topical propranolol ointment 1% with occlusion) for the treatment of pyogenic granulomas in 22 children in the Dermatology Pediatric Outpatient Service of the University of Bologna [13]. The complete regression was observed in 59.0% (in a mean of 66 days) [13]. Approximately one-fifth (22.7%) did not respond to the treatment. However, the authors did not observe any side effects [13]. Oke et al. reported a case series of 4 children treated with topical timolol 0.5% twice daily for a minimum of 21 days in Boston Children's Hospital [14]. The authors suggest that ocular surface pyogenic granulomas respond to topical timolol treatment [14]. Moreover, they pay attention to the fact that this treatment option has a lower adverse-effect profile than conventional topical steroid treatments or other medical or surgical therapies [14]. Mashiash et al. performed a retrospective study of 18 cases of pyogenic granuloma treated with topical propranolol 4% gel and reported one patient with local side effects, including irritation, redness, and scaling of the treated

area leading to discontinuation of the treatment and curettage of the pyogenic granuloma [15].

The pyogenic granuloma belongs to the benign cutaneous RAS-opathies (a group of medical genetic syndromes caused by germline mutations in genes that encode components or regulators of the Ras/mitogen-activated protein kinase (MAPK) pathway; the name of the oncogene, ras, has its origin in studies of murine leukemia viruses which, at high doses, produced sarcomas in rats; transforming retroviruses were isolated, and its oncogene was named "ras" after rat sarcoma) with causative mutations described in BRAF (the BRAF gene codes for a protein called B-Raf) and KRAS (the name comes from "Kirsten rat sarcoma virus"; the KRAS gene provides instructions for making a protein called K-Ras) [15,16]. The role of the Ras pathway in angiogenesis and vascular proliferation through hypoxia-inducible factor 1-alpha (HIF-1a) and vascular endothelial growth factor (VEGF) was previously confirmed in infantile hemangiomas [17]. Beta-blockers probably inhibit HIF1a and VEGF, leading to vasoconstriction [18]. They also cause a decrease in angiogenesis and stimulate the endothelial cells' apoptosis [18].

Conclusions

The topical beta-blockers can be a valuable option for the treatment of children with pyogenic granuloma. Especially for the youngest patients, for whom general anesthesia is required for surgical treatment. However, studies on larger patient groups are needed to estimate the concentration of topical timolol and the optimal duration of the therapy. In older patients, it is essential to first consider the surgical treatment under local anesthesia to avoid the risk related to general anesthesia.

Conflict of interest
None

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