CLINICAL EVOLUTION OF LYMPHANGIOMA CIRCUMSCRIPTUM: OBSERVATIONS ON THREE CASES

LIMFANGIOMUL CIRCUMSCRIS, OBSERVAŢII CLINICO-EVOLUTIVE PRIVIND TREI CAZURI

Keywords: lymphangioma circumscriptum, clinical, treatment.

Abstract

Introduction: Lymphangiomas are rare congenital dysplasia of lymphatic vessels, which may affect the tegument, mucous membranes and viscera. They are superficial cavernous or cystic. In 80-90% of cases they are diagnosed prior to the age of 2 years.

Patients and Methods: We present 3 patients with lymphangioma circumscriptum, aimed to highlight aspects of this tumor clinical course, based on clinical examination, laboratory investigations, histopathological examination and Doppler ultrasound. Patients were investigated for diagnosis and comorbidities. The treatment was surgical (excision and electrocautery of tumors) for the first two cases and by medication in the third case.

Results: Our patients had no associated comorbidities. Correct diagnosis was established based on histopathological examination and the treatment has conducted good results. We obtained healing by surgically treating cases I and II and correction by medical treatment bleeding complications in case III. However regular follow up is necessary in these patients.

Conclusion: Lymphangioma circumscriptum is a benign condition, but difficult to treat and recurrent due to the deep hypodermal component.
INTRODUCTION
Lymphangiomas are rare congenital dysplasia of lymphatic vessels, which may affect the skin, mucous membranes and viscera. About 80-90% of cases are diagnosed before the age of 2 years. They are classified based on microscopic features in the following subtypes: capillary, cavernous and cystic hygroma. A fourth subtype is hemolymphangioma. The classification of lymphangiomas has no clearly standard defined and universal application due to the clinicopathological nature of those lesions. The classification most commonly used divided lymphangiomas into two major groups based on depth and the size of these lymphatic vessels tumors: superficial group are called lymphangioma circumscriptum, the deeper group including cavernous lymphangioma and cystic hygroma. Some of the literature data classifies cystic hygroma as a variant of lymphangioma cavernosum. Capillary lymphangiomas are composed of small size vessels and are located in the epidermis. Cavernous lymphangiomas usually arise at birth or within the first 2 years of life, with an equal incidence by gender. Most common sites are the head and neck area, especially the oral cavity and rarely extremities. It appears as subcutaneous masses fluctuent diffuse delineated and consist in lymphatic dilated and irregularly shaped spaces and they can invade surrounding tissues. Frequently recur after a limited excision. Cystic hygroma are large, making the overall appearance of a “honeycomb” and they are developing within 75% of cases in the head or neck, most commonly on the left side of the body, but can also occur in the axilla, groins or other areas, equally affecting both genders. They tend to be better circumscribed than cavernous lymphangiomas and also have the tendency for local recurrence if the excision is not wide enough. Hemolymphangiomas have both types of components in their structure: lymphatic vessels and blood vessels also. Another classification of lymphangiomas divides them into the following subtypes: microcystic, macrocystic and mixed type. Microcystic lymphangiomas measure less than 2-3 cm and the macrocystic lymphangiomas have more than 2-3 cm in diameter. Mixed lymphangiomas contain both components.
PATIENTS AND METHOD
We present 3 patients with lymphangioma circumscriptum, with the objective of highlighting aspects of this tumor clinical course, based on clinical examination, laboratory investigations, histopathological examination and Doppler ultrasound. Patients were also investigated for possible comorbidities. In all three cases lesion biopsy was obtained and surgical specimens were sent in order to achieve histopathological result. The pieces were processed by classical histological technique and histopathological interpretation was performed using Hematoxylin - Eosin standard staining. Two of the cases were treated by surgical excision and electrosurgery of the tumor, while the third case was treated with drugs.

RESULTS
The first case is a 22-years-old male, from urban area, requesting a dermatological consult for two vegetable tumors, having dimensions of 1.5 cm and 2 cm, partially keratotic and also with ulcerated areas, located left thigh and internal side. The tumors are located on the edge of a surgical procedure scar at the age of 4 years for similar lesions and several translucent vesicles were located in the neighborhood (Fig. 1). From history we retain electrocautery at 7 years old of other injuries with the same location. The usual investigations were normal and Doppler ultrasound excluded other vascular malformations. Histopathology revealed microscopic structure of lymphangioma, containing a network of spaces coated by endothelial cells, identifiable as lymphatic vessels only because they do not contain red blood cells (Fig. 2). These spaces contain a protein-rich liquid identifiable in HE staining as a material eosinophilic homogeneous. A small number of lymphocytes is present in the stroma (Fig 3). We performed excision of tumor lesions and electrocautery for the translucent vesicles.

The second case that we present is a 10-year-old boy, from rural area, underweight (BMI = 20), who was hospitalized in Dermatology Clinic for a tumor with irregular surface, covered by haematic crusts and purulent deposit (2 5 / 3.5 cm), front of the right leg and a similar lesion (1 cm) in proximity. From history we retain the appearance of this tumor when he was 7 years old, after a local me-
Mechanical trauma. Over time the tumor has grown relatively slowly in size, and later a new injury occurred near the first one. X-ray of right leg did not show bone alterations near the tumor. We have established the diagnosis of hemolymphangioma based on clinical examination, laboratory and histopathological exams, which revealed lymphatic vessels and blood vessels (Fig 5). We performed excision of the two tumors with the scalpel blade from the skin plane, then curettage and electrocautery of the bases. In Fig. 6 we present the clinical aspect one month after this treatment.

The third case is a 43-years old woman who requested dermatological consult, being concerned about some old skin lesions changing their appearance, after a recently mechanical trauma at this level. The patient reports this lesion since she was 5 years old. Clinical examination revealed multiple vesicles, some with yellowish others with hemorrhagic content, located on the left iliac region, the proximal part of the left thigh and the buttock on the same side.

She also presents a painful induration about 4/3 cm below the left inguinal fold and one bruising about 5 / 2.5 cm wide on the left buttock (Fig 7). Following clinical examination, histopathological exam, skin ultrasound, CT scanner and biological investigations we have established the diagnosis of lymphangioma circumscriptum. Under general treatment with antibiotics, pain relievers, hepatoprotectors and local care of the injury the outcome of complications was favorable.

**Discussion**

Lymphangiomas consist in isolated lymph cisterns of varying sizes located in the dermis and hypodermis, without connections with the normal lymphatic system. Depending on the size of those cisterns the lymphangiomas can have different aspects: microcystic (lymphangioma simplex and lymphangioma circumscriptum) and macrocystic (cavernous lymphangioma and cystic hygroma). (3)

**Etiopathogeny**

A racial predominance in lymphangiomas was not reported. It is an approximately equal gender incidence. (4)

In 1976, Whimster (5) studied the pathogenesis of lymphangioma circumscriptum. According to him, the basic pathological process is the formation of lymphatic cisterns deep into the subcutaneous tissue. These reservoirs are separated from the normal network of lymphatic vessels. However they communicate with superficial lymphatic vesicles and with vertical channels through the dilated lymphatics. Whimster found that those cisterns could arise from a primitive lymphatic vessel who fails to connect with the rest of the lymphatic system during its embryonic development. The rhythmic contractions of muscle fibers can cause a sequester of a primitive lymphatic vessel. These contractions increase intramural pressure, forming channels that cross the walls of the dilated cisterns to skin. Whimster’s observations are supported by lymphangiographic and radiographic studies. These studies have shown that large cisterns, multilobulated, are extended deep into the dermis and laterally beyond the clinically apparent lesions. (6) Cases of lymphangiomas secondary to trauma have been reported, likewise our second case or following an infection.

**Clinical aspects**

Lymphangioma circumscriptum is the most common type of lymphangioma and it is characterized by translucent vesicles having dimensions around 2-4 mm, which can be present at birth or appear shortly after, having a tendency to expansion. The lesions are asymptomatic, but occasionally patients may experience spontaneous episodes of minor bleeding or leakage of fluid from broken vesicles. These vesicles represent dilated superficial lymphatic vessels involving the upper dermis and containing clear or pinkish - purple fluid (serosanguinolent or haemorrhagic content).

Lymphangioma circumscriptum has a high rate of recurrence after excision, because of its deep component. (3)

Cavernous lymphangioma is less common and usually occurs in childhood. It is located at the cephalic extremity frequently and rarely in other areas. The lesions develop as nodules with elastic consistency, painless, in the dermis and subcutaneous tissue. Unlike lymphangioma circumscriptum, the covering tegument is usually undamaged. These lesions often have a rapid growth phase similar to hemangiomas. The tumor can measure 1 cm or involve an entire anatomical area. There is no family history of the lymphangioma. Some patients experience pain when tumor makes compression on adjacent structures.
Lymphangioma circumscriptum may be associated in some cases with cavernous lymphangioma and cystic hygroma.\(^3\) Cystic hygroma occurs in childhood, it is large and located in the soft tissues, usually in the head and neck but can occur in axillaries or inguinal areas. It has elastic consistency, varies in size and shape, and tends to increase if it is not excised. Typical lesions are multilocular cysts filled with clear or serocitrin lymph fluid. These congenital lesions are located deep into the connective tissue. When drained, they tend to fill up quickly with lymphatic fluid. Usually cystic hygroma is diagnosed clinically based on the large size, location and translucency\(^1\). Cystic hygroma may be associated with congenital disorders as follows: Turner syndrome, Chromosome Aneuploidy, fetal hydrops, fetal alcohol syndrome, Noonan syndrome, Down syndrome and other disorders with trisomy\(^7\). Patients with cystic hygroma should be cytogenetic investigated for chromosome aneuploidy. Parents will receive genetic counseling because chromosome changes may recur in future pregnancies.\(^8\) Diffuse lymphangiomas are characterized by asymptomatic, erythematous, indurate or atrophic plaques without changes in their surface and sometimes can go unnoticed. If not completely excised the lesions may grow to large sizes.\(^2\) Hemolymphangiomas develop from vascular and lymphatic congenital malformation. They occur mostly in younger patients, especially newborns and infants, and 6.5% of them are located on the extremities.

**Diagnosis**

Lymphangioma diagnosis is mainly based on lesion history, clinical examination and histopathological exam. Microscopically the vesicles in lymphangioma circumscriptum are dilated lymphatic channels that develop into the papillary dermis. This may be associated with hyperkeratosis and acanthosis of the epidermis. Channels are numerous in the superficial dermis and often extend into the deep dermis. These deep vessels seem to have a wide caliber and thick wall containing smooth muscle fibers. The lumen is filled with lymphatic fluid, but often contains red cells, lymphocytes, macrophages and neutrophils. These channels are lined by flattened endothelial cells. The gap has often numerous lymphatic cells and presents evidence of fibrosis. The nodules in cavernous lymphangioma are characterized by large, irregular channels comprising a single layer of endothelial cells, being located in the reticular dermis and subcutaneous tissue. The surrounding stroma consist in loose connective tissue or fibrous tissue and contains a big amount of inflammatory cells. Cystic hygroma is histologically indistinguishable from cavernous lymphangioma.\(^6\) Immunohistochemical study is effective to differentiate lymphangiomas from hemangiomas in difficult cases. Test results for VIII factor antigen reveal the fact that this is positive for hemangiomas endothelium and negative or weakly positive for lymphangiomas endothelium. In case of normal blood vessels and hemlymphangiomas, immunohistochemistry for laminine indicates a typical multilayered basal membrane, and a discontinued basal membrane in lymphangiomas. Dermoscopy can be helpful in lymphangioma circumscriptum diagnostic.\(^9\) Clear fluid lesions present brown lightning gaps, surrounded by palisading septae.
Those with haemorrhagic areas can show focal reddish shades inside the gaps while the diffused pink and/or red color is present in the purple gap structures.

Thus, they are characterised by a gap model with a blood content that may not be differentiated from a hemangioma. Monoclonal D2-40 antibody expression or Podoplanin and VEGFR-3 markers may establish the differential diagnostic with a hemangioma.\(^{(10,11)}\)

Invasion of the surrounding tissues and tumor relation with them is evidenced by MRI. This can help to prevent unnecessary extensive resection or incomplete resection.\(^{(12)}\)

**Differential Diagnostic**

Usually, lymphangioma circumscriptum must be differentiated from skin metastases, lymphangiectasias, simplex herpes, zoster herpes\(^{(13)}\), molluscum contagiosum.

Other cystic lesions and elastic subcutaneous masses must be considered. Other differential diagnostics regarding the clinical aspects are: melanoma, Dabska tumor, lipomas, type 1 neurofibromatosis, Stewart-Treves syndrome, angiokeratomas.

**Treatment**

First choice treatment for lymphangiomas is complete surgical excision.\(^{(14)}\) Based on Whimster hypothesis, the large subcutaneous cisterns must be removed to prevent tumor recurrence.

The complete excision of lymphangiomias may be difficult and sometimes unachievable and this is the main reason for the high rate of recurrence. The tumors limited to the superficial dermis are surgically removed easily, being associated with a higher success rate.

Lymphangiomas are not responding to radiotherapy and corticosteroids. Although, Propranolol is a new treatment option, which can be helpful even for the diffuse lymphangiomias.\(^{(15)}\) The antibiotic therapy is indicated only in secondary cellulitis. Cryotherapy, sclerotherapy and electrocauterity represent other possibilities of therapy.\(^{(16)}\) Lymphangioma circumscriptum can also be treated by electroextraction.\(^{(17)}\)

It does not always respond to the pulsed laser, and the CO\(_2\) laser vaporization has been successfully tested.\(^{(18)}\) but also other types of lasers (argon, pulsed-dye) can be used.\(^{(19)}\) Another therapeutical option for lymphangioma circumscriptum is sclerotherapy with bleomycin solution or NaCl 23.4% hypertonic saline.\(^{(20)}\)

Intralesional OK432 (Picibanil) is a new and efficient treatment in macrocystic lesions, but in the cases of microcystic or cavernous lesions, the response to OK-432 was disappointing, surgery remaining the main option.\(^{(21)}\) Postoperative vacuum assisted closure devices may decrease the recidive and infection risk.\(^{(22)}\)

**Evolution**

Rarely, lymphangiomas interferes with the well-being of the patients. They usually present to the medical doctor for aesthetic issues. Lymphangioma circumscriptum is associated with minor bleedings, recurrent cellulitis and lymphorrhoea.

Two cases of lymphangiosarcoma complicating a lymphangioma circumscriptum were reported. Lesions from both patients were treated for a long time with X-ray therapy. Therefore, radiotherapy must be avoided in lymphangiomas therapy. Dabska tumor can complicate a lymphangioma circumscriptum.\(^{(24)}\)

In case of cervical cystic hygroma, a complete surgical excision is necessary to prevent complications like: breath alteration, aspiration and superinfections.\(^{(25)}\)

Lymphangiomas tend to recur, except the ones with complete surgical excision. In the first and the second cases the evolution was favorable after the surgical treatment obtaining healing, and in the third case we obtained the correction of bleeding complication by oral medication. Patients will be surveilled to capture possible recidives.

**CONCLUSIONS**

Lymphangioma circumscriptum is a benign lesion, but difficult to treat and recurrent due to the deep hypodermic component.

During lifetime, lymphangiomas can lead to complications like spontaneous or posttraumatic hemorrhages. Regular examination of skin is necessary to evaluate the treatment response and to capture possible recurrence or complications.

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