TREATMENT MODALITIES AND RECURRENCE POTENTIAL FOR LYMPHATIC MALFORMATIONS IN CHILDREN

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ABSTRACT

Lymphatic malformations (LMs) are slow-flow lesions that mainly occur during embryonic development, through disruption of lymphatic drainage. The study aims to evaluate the diagnostic and treatment modalities of LMs, as well as the outcome after operative or non-operative therapy. Thirty seven patients treated for LM were selected from a group of 97 patients, operated on for congenital vascular malformations from 1991 to 2010 at the University Hospital, Department of Pediatric and Adolescent Surgery, in Graz, Austria. Retrospectively were reviewed the data with a special focus on anatomic location, symptoms and signs, the results of conducted imaging, treatments modalities and recurrence after the treatment. During the study period 37 patients (18 females and 19 males) with LMs were treated. Anatomic distributions of these lesions were in head and neck in 27%, in trunk 43%, in upper extremities in 14%, in lower extremities in 11%, in more part of the body were 5% of the patients. The main symptoms were swelling and pain. The most useful diagnostic procedures were magnetic resonance tomography in 52% and ultrasonography in 42%, also helpful were X-rays in 3% and CT in 5% of patients. The preferred treatment modality was complete surgical resection in 70% of patients, followed by sclerotherapy in 19%, partial resection in 8%, lasertherapy alone or in combination with other modalities in 3%. Recurrence is common in 38% of cases. For successful treatment of vascular malformations it is necessary to be able to use all available treatment modalities alone or in combination, with the main goal to completely remove the lesions without damaging the function – in this way the recurrence of these lesions can be avoided. The treatment of children with LMs should always be performed by group of experts from different disciplines.

Keywords: lymphatic malformations, surgical treatment, recurrence

INTRODUCTION

Vascular malformations occur due to congenital development defect of vasculogenesis, angiogenesis and lymphangiogenesis. They are always present at birth, even not always visible, grow in proportion with child and never regress. Depending on the vessel type they affect, capillary, venous and lymphatic are "slow-flow" malformations, arterial and arteriovenous are "fast-flow" malformations, adding a syndromes of complex cases with each other [2,3,4].

Lymphatic malformations (LM) are slow-flow lesions that mainly occur during embryonic development, through disruption of lymphatic drainage. They usually present at birth but can be seen at any age. They can be divided in macro cystic, micro cystic and mixed. The macro cystic lymphangiomias are characterized by cysts in diameter >2 cm. Microcystic malformations also called Lymphangioma circumscription are most common LM [5,6]. LM can be located include neck and axilla with less common locations in mediastinum, pelvis and retroperitoneum. LM that occur in neck and axilla, are often called cystic hygromas [7]. LM usually involve the subcutaneous tissues, but also may be affected muscle, bone and rarely visceral organs such as gastrointestinal tract or lungs [1]. Both genders are equally affected and 1 out of 1700 newborns is born with LM. It has been found that cell signals over VEGF-C may be involved in the formation of LM, causing lymphatic hyperplasia. It has been suggested that VEGF-C and VEGFR-3 represent peripheral dilatation of lymphatic vessel [8,9].

Lymphatic malformations may be present in any part of the body and can be found most commonly in the head and neck region, mediastinum, chest, axilla, peritoneum, retroperitoneum and extremities [10,11]. In case of dermal involvement these malformations cause severe disfigurement with discoloration, with dark red small vesicles. Complication of LMs with a result of intralesional hemorrhage can affect up to 12% of cases [12]. LMs of the cervicofacial region may be associated with ophtalmologic symptoms, dental and airway
problems, and may necessitate tracheostomy [13,14].

Diagnostic modalities of LMs

A number of investigations are needed for correct diagnosis of lymphatic malformations. First of all a good history and physical examination is needed, but also a number of noninvasive and invasive diagnostic tests. The aim of all these diagnostic procedures is to correctly define the type, localization and the hemodynamic characteristics of lymphatic malformation, in order to be able to make up a guideline schema for appropriate therapy and successful treatment of patients with lymphatic malformations.

Ultrasonography is a noninvasive method, useful to differentiate a slow-flow from a high-flow lesion. It is ideal for children when examining superficial lesions, because it is painless, however in very young ages when children move a lot also this techniques needs to be done under some sedation of children to achieve correct results. In cases of lymphatic malformations ultrasound can detect edema and the presence of cysts [2, 15]. Ultrasound can be extremely useful during percutaneous sclerotherapy and to follow the distribution of the sclerosing agents [16].

CT and MRI give important results with a great value about anatomic extension of vascular malformations [2,17]. CT has some advantages, as it is better at revealing the calcification and skeletal or visceral involvement, but in practice CT is indicated when MRI cannot be used.

The best imaging modality for LM is MRI. Lymphatic channels disclose no enhancement after gadolinium infusion, and enhancement can be seen in the septa of the lymphatic cysts or in the presence of combined venous and lymphatic lesions [18].

Treatment of LMs

Sclerotherapy is performed in lymphatic malformations when they are deep and difficult to access surgically with injection directly into the lesion leading to swelling, then fibrosis and regression of the cysts [19]. For lymphatic malformations OK-432 (picibanil) is commonly used.

Puncture incision or drainage: in this therapeutic approach the secretion obtained in the tumor is removed manually, resulting in a decreasing in size of mass and thus to protect the surrounding tissue from pressure-related injury. However, this can only be performed by cystic cavernous forms.

Bonding of cystic structures: The introduction of fibrin glue after removal of the tumor secretion by puncturing the cyst walls should be placed in an adherent state, so that a new secretion accumulation and thus tumor recurrence can be prevented. Also by the application of Bleomycin which is usually used as a chemotherapeutic agent for tumors of the skin, genital tract or the lung, can be obtained. The injection of picibanil or OK432, the vaccine of Streptococcus pyogenes, can also lead to adhesion of the cyst walls. Also complications of sclerotherapy may include swelling, skin and mucosal injury, infections and nerve injury [19].

Surgical treatment

Surgical treatment is a common method to treat lymphatic malformations. Dubois et al. [22] stated that after sclerotherapy when treatment is incomplete or when an aesthetic disfigurement requires correction, this can be done by surgical procedure.

Non-operative treatment methods used for treatment of vascular malformations are compression dressings, such as an elastic garment or bandage, physiotherapy, lymphatic drainage and anti-inflammatory therapies [21]. When a microcystic lymphatic malformation of the extremities or trunk cannot be completely resected, they are treated by non-operative methods.

METHODS

Thirty seven patients treated for LM were selected from a group of 97 patients, operated on for congenital vascular malformations from 1991 to 2010 at the University Hospital, Department of Pediatric and Adolescent Surgery, in Graz, Austria. Retrospectively were reviewed the data with a special focus on anatomic location, symptoms and signs, the results of conducted imaging, treatments modalities and recurrence after the treatment. Data were collected from the open MEDOCS (Medical Documentation and Communications System) and from the KIS system.

RESULTS

The present study found that the gender distribution is equal.

The locations of the lymphatic malformations were in the head and neck in 10 patients (27%), trunk in 16 patients (43%), upper extremities in 5 patients (14%), lower extremities in 4 patients (11%) and generalized in more parts of the body were in two patients (5%).
Results of conducted imaging

The clinical diagnosis has been further evaluated by plain films (X-rays), ultrasonography (US), magnetic resonance tomography (MRT) and computed tomography (CT). The summary of various imaging modalities is given in figure 3.

Figure 3 shows that in the majority of cases with lymphatic malformations there is a need for a MRT in order to get the correct diagnosis.

From Fig.3 we can see that the most useful diagnostic procedures are magnetic resonance tomography and ultrasonography. For other cases, where it was more difficult to differentiate between different vascular malformations, it was necessary to use also other imaging methods.

Treatment modalities of lymphatic malformations

The figure 4 shows an overview of the performed treatment modalities.

Figures 1, 2, 3, and 4. Anatomic distribution of lymphatic malformations in 37 patients. The most common localization of lymphatic malformation was in the trunk and head-neck region, followed by the LMs in the upper and lower extremities. Treatment indications All of 37 patients with lymphatic malformations presented symptoms and signs as shown in the Fig. The main symptoms were swelling and pain. The other symptoms such as cosmetic disturbance, impaired function and skin changes were less frequent.
In 37 patients with lymphatic malformations, different treatment methods were performed. The main therapy was surgical resection, followed by sclerotherapy and only a few cases were treated with partial resection or laser therapy.

**Recurrence after the treatment**

According to the follow-up data, 62% of cases were successfully treated. After they were treated, 38% of patients got recurrence, and another treatment was necessary.

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Figure 5. 14 patients got recurrence after the treatment

**DISCUSSION**

Vascular malformations occur due to congenital development defect of vasculogenesis, angiogenesis and lymphangiogenesis. They are always present at birth, even not always visible, grow in proportion with child and never regress. Depending on the vessel type they affect, capillary, venous and lymphatic are "slow-flow" malformations, arterial and arteriovenous are "fast-flow" malformations, adding a syndromes of complex cases with each other [2,3,4]. In 1982, Mulliken and Glowacki introduced the biological classification of vascular anomalies. They divided all vascular lesions into vascular tumors and vascular malformations [2,3]. In 1996 at the International Society for the Study of Vascular Anomalies (ISSVA) meeting in Rome, the first classification of vascular malformations was proposed, as single vessel type and combined forms [2]. The nomenclature has always been presented as a major problem. A universal classification is of great importance, because the distinct vascular tumors and vascular malformations may require different therapeutic techniques.

The present study found that the gender distribution of females to males was equal and corresponds to the data for gender distribution of patients with lymphatic malformations found in the literature [2,14,20].

They can furthermore occur anywhere in the body, but their most common occurrence is especially in the head and neck region. Anatomic distributions of these lesions in the present study were in the neck in 22%, trunk in 31%, and all together in the upper and lower extremities in 45% of all patients.

The most common symptoms in patients with lymphatic malformations were swelling and pain. Other symptoms such as cosmetic disturbance, skin changes and impaired function were less frequent in the patients in our study group. These were however very common in patients with large LM in the head and neck regions.

In the present study, the clinical diagnosis has been further evaluated by various imaging modalities. The main imaging techniques performed were magnetic resonance imaging with angiography (MRI) in 52% of patients and ultrasonography (US) in 42% of patients, also helpful were X-rays in 3% and CT in 3% of patients.

The preferred therapies in the present study were complete resection, partial resection, sclerotherapy non-operative therapy, lasertherapy, or combinations between them. The preferred treatment modality was complete surgical resection in 70% of patients, followed by sclerotherapy in 19%, partial resection in 8%, lasertherapy alone or in combination with other modalities in 3%. For localized LMs best therapeutic option seems to be the surgical resection, however in cases with infiltrative growth or microcystic pattern combinations of treatment with sclerotherapy and non-operative treatment modalities are common.

The surgical resection is a very useful treatment method in cases when the LMs are localized and do not involve vital structures like nerves or any other functionally important organs. When LMs are localized deep and involve vital structures it is impossible to remove them by surgical resection without damaging the function. Therefore, in such cases it is necessary to use other treatment modalities such as sclerotherapy and in some cases...
also lasertherapy. Sclerosing agents commonly used are ethanol, OK-432 and bleomycin. These are effective because they lead to endothelial damage and/or thrombosis of vascular spaces in the malformed vascular tissues [2,19,20].

CONCLUSIONS

For successful treatment of vascular malformations it is necessary to be able to use all available treatment modalities alone or in combination, with the main goal to completely remove the lesions without damaging the function – in this way the recurrence of these lesions can be avoided. The treatment of children with LMs should always be performed by group of experts from different disciplines.

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