INTRODUCTION

Glomuvenous malformations (GVM) are benign venous anomalies characterized by glomus cells (modified smooth muscle cells) surrounding venous channels [1,2]. GVMs are also known by the name of "glomangioma". However, as they are not of neoplastic nature, the term "glomangioma" was challenged by recent literature, authors considering that GVM represents the proper name [1]. GVMs were described as early as the 18th century. However, it was William Wood in 1812 to first coin a name, specifically "painful subcutaneous tubercle," to describe the painful lesion treatable by surgical extirpation [3]. In 1924, Pierre Masson, reported that the lesion described by Wood was a pathology of the dermal arteriovenous (AV) shunt [4]. Further development in understanding GVMs was made with the discovery of the Sucquet-Hoyer canal, which has a thick medial coat consisting of glomus cells (large, cuboidal cells) [4]. The Sucquet-Hoyer canal is an AV anastomosis with role in thermoregulation [5].

GVMs are commonly inherited and it is believed that they are caused by a mutation in the glomulin gene, which has a key role in the differentiation of vascular smooth-muscle cells (VSMCs), especially those belonging to cutaneous veins [1]. Inherited GVMs have
been linked to chromosome 1p21-22 and are the result of truncating mutations in glomulin; these mutations have been found in all cases of familial GVM [6]. Most lesions occur in the dermis or subcutaneous tissue of the upper and lower extremities and have a diameter of less than 1 cm [5]. Two forms have been described: the solitary form (90% of cases) and a multiple variant (10% of cases), the latter being more common in children and believed to have an autosomal dominant pattern of inheritance [5]. The most common location for solitary, sporadic GVMs is the nail bed, which is characterized by the presence of numerous glomus bodies [7]. Approximately 80% of GVMs are affecting the upper extremities and 75% of these can be found subungally [8]. GVMs usually present as pink to purple nodular, hyperkeratotic lesions that are limited to the subcutaneous tissue and illicit pain when compressed [9]. Pain in GVMs correlates with the size of the lesion; the bigger the lesion, the more painful it is; in lesions greater than 5 cm, an approximate 80% of patients feel pain [9].

CASE PRESENTATION

A 16-year old female was referred to our clinic for evaluation of a violaceous tumor-like mass of the left forearm, which began growing 2 years ago. The onset of growth was not related to any trauma to the area. The patient reported discomfort when wearing a watch and/or tight blouses. She had no other medical problems. Family history revealed, in the maternal grandmother, vascular anomalies located on the right laterocervical area and at the level of the right ear (Fig. 1). Despite no such similar lesion being present in other family members, the clinical picture supports a familial mode of inheritance. Physical exam showed an oval mass (5x2x1 cm) located on the distal 1/3 on the ventral side of the left forearm. Compression of the mass could not completely empty it (Fig. 2) and led to sensation of pain.

On Doppler studies (Fig. 3), the lesion appeared as a conglomerate of serpiginous vascular tracts, which did not extend beneath the subcutaneous tissue; there was no muscle infiltration. In longitudinal plane, the dimension of the lesion was below 6 cm while in axial plane, it was below 0.5 cm. Upon compression with the transducer, the vascular formation did not undergo complete emptying. There were no thromboses.

Fig.1. Patient's grandmother presenting vascular anomalies on the right laterocervical area and the right ear

Fig.2. Patient with GVM located on the ventral left forearm

Fig.3. Ultrasound image showing a vascular tumor not extending beneath the subcutaneous tissue. The Median nerve is located at considerable distance from the mass.
MRI (Fig. 4) confirmed the dimensions and localization of the lesion. It also revealed that there were no arteriovenous (AV) communications and that the enhancement of the lesion appeared in the late venous phase. There were no osseous lesions.

The diagnostic on imagistic studies was that of hemangioma. Patient had normal findings on blood tests and X-ray of the thorax. Surgery was scheduled and the mass excised (Fig. 5). The intraoperative findings confirmed the location revealed by the imagistic techniques employed.

Histopathological exam of hematoxylin and eosin stained section of the excised GVM (Fig.6) shows a formation surrounded by endothelium and presenting wide vascular spaces, with one or more layers of glomus cells in the vascular wall. The vascular wall surrounds a lumen filled with RBCs and plasma in which, besides endothelial cells, one can distinguish rows of cells with oval euchromatic nuclei and acidophilic cytoplasm. Periodic acid-Schiff (PAS) -Hematoxylin stain (Fig.7) shows a vascular wall with PAS-positive glomus cells, with an accentuation in the positive coloration towards
the periphery of the cells. The diagnosis on microscopic exam was that of GVM.

The patient had a favorable, uneventful postoperative recovery.

**DISCUSSION**

Once diagnosed and treated, GVMs have an excellent prognosis. However, reports have shown that the approximate period of time from the onset of symptoms to diagnosis is 10 years and that, on average, 2.5 physicians are consulted before the correct diagnosis is attained [8]. As most GVM are located subungually, misdiagnosis and delayed diagnosis is especially true for GVM in extradigital locations [8], as was that of our patient. A lesion that: varies in color from pink in infants to deep purple in children and adults; is not compressible and elicits pain upon palpation; involves the skin and subcutis only and never the deeper layers; has a cobblestone-like appearance; and is slightly hyperkeratotic, should always prompt the clinician to consider a diagnosis of GVM [10].

For the proper management of GVMs, it is important to distinguish them from venous malformations (VMs). In a study on 1685 patients with cutaneous venous anomalies, Boon at el [9] found that GVMs comprised 5.1% of venous anomalies and most of them (63.8%) were familial; of these, 78% were located on the extremities. On the other side, only 1.2% of VMs were inherited, the rest being sporadic. Contrary to GVMs, VMs can involve the surrounding muscles and joints, can be emptied easily by external pressure and can present phleboliths [9,10]. GVMs are only painful when compressed; no other factors (temperature, tumor location, time of the day, hormonal changes, etc) have been found to have an eliciting pain [9]. As far as VMs go, however, they are usually painful in the morning, at the onset of puberty, at menstruation, when the patient is on contraceptive drugs and during pregnancy [9]. While therapeutic methods of external compression (such as compressive garments) are effective in the management of VMs, they aggravate pain in GVMs and should thus be avoided [9]. Full surgical excision is possible in most cases involving small GVMs, and recurrence rates are very low; VMs, on the other side, are difficult to completely excise due to their predilection for infiltrating surrounding and often times deep structures [9]. Some VMs, in contrast to GVMs, are also associated with localized intravascular coagulopathy (LIC), low fibrinogen and high D-dimer levels, which could lead to thromboses and bleeding at wound sites [10].

The clinician can employ two tests in diagnosing GVMs: (1) the "Ischemia test" - inflating a BP cuff to above systolic pressure should alleviate the patient's pain (if the lesion is located in the upper extremity) and (2) "Love's test" - applying pressure with a blunt object over the lesion should elicit local tenderness [8]. In a Mayo Clinic study on 56 patients with extradigital GVMs, the authors reported 11 cases of tumors located at the level of the forearm; the treatment of choice employed in all cases was surgery, with excellent results [11]. While surgical excision is the preferred treatment in the management of isolated GVMs, it can lead to considerable scarring when dealing with multiple lesions. In the latter case, other methods should be first employed. Parsi et al [12] report on successful sclerotherapy treatment with sodium tetracyetyl sulphate, in a patient with multiple glomangiommas who underwent surgery but had postoperative recurrences. Vascular laser, CO2 laser and pulsed dye laser have also been proven useful in the management of multiple GVMs [12,13].

**CONCLUSION**

Misdiagnosis and/or delayed diagnosis of GVMs are common. Providing clinicians with guidelines for the proper identification and treatment of these conditions is crucial for the welfare of patients. Surgical excision is by far the most suitable method of treatment, especially for single GVMs, yielding excellent results. Once these lesions are properly diagnosed and treated, patients can experience an immediate improvement in the quality of their life.
References:


