INTRODUCTION

Vascular anomalies constitute some of the most difficult diagnostic and therapeutic enigmas that can be encountered in the practice of medicine today. Clinical manifestations of these lesions are extremely protean and can range from an asymptomatic birthmark to life-threatening hemorrhage. Venous malformations (VMs) occur in ectatic vessels that have low blood flow and that are morphologically and histologically similar to veins. They are classified as superficial or deep and as localized, multicentric or diffuse. The skin or mucosa that covers such malformations varies in color according to the depth and degree of ectasia of the lesion. The most superficial ones are purple in color, whereas the deeper ones appear more bluish or greenish or may not even be visible.

Vascular malformations can cause significant morbidity and even mortality in both children and adults. Clinical manifestations are extremely protean and because of the rarity of these lesions, diagnosis and management of these lesions by clinicians are limited. Arteriovenous malformation (AVM) is a congenital vascular malformation with direct communications from arteries to veins with lack of normal capillary network. The peripheral or extracranial AVM is usually locally aggressive mainly during puberty or adolescence with an expansive mass causing cosmetic and functional disturbance. With progression, AVM can destroy normal tissues and can lead to complications such as severe disfigurement, uncontrollable bleeding, ulceration, pain and cardiac volume overload. These vascular malformations are subdivided into slow or low flow and fast or high flow malformations. The overall incidence of VM is about one in 10000. These lesions commonly occur in the head and neck with a predilection for the oral cavity, airway and muscle groups. These lesions will continue to grow throughout the patient’s life. Many patients with vascular malformations may be misdiagnosed as hemangiomas. This misdiagnosis delays treatment as hemangiomas are known to regress. These aberrant venous connections lead to venous congestion, thrombosis and gradual expansion of these lesions. As a result, VMs persist and progress until therapeutic intervention. In this interesting case report, authors report and discuss about anomalous development of blood vessels and multiple VMs in the head, neck and shoulder region.

CASE REPORT

Multiple vascular malformations in head and neck - Rare case report

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ABSTRACT

Multiple venous malformations (VMs) pose some of the most difficult challenges in the practice of medicine today. Clinical manifestations of these lesions are extremely protean. Because of the rarity of these lesions, experience in their diagnosis and management by most clinicians is limited. This augments the enormity of the problem and can lead to misdiagnoses, inadequate treatment, high complication rates and poor patient outcomes. Because these lesions can recur, removal of the nidus is the main priority. Vascular malformations are best treated in medical centers where patients with these maladies are seen regularly and the team approach is utilized. The presence of intralosomal nerve in arteriovenous malformation (AVM) and sometimes in VMs, as reported in this study, provides an additional diagnostic criterion that is simple and reliable and can be readily used to differentiate VMs from hemangiomas.

Key words: Head and neck, multiple vascular/venous malformation, multiple vascular malformation, phleboliths
Multiple vascular malformations of head neck

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area [Figure 3], left parietal region of skull [Figure 4], right submandibular region and lower part of right masseter region [Figure 5] and on both the sides of shoulder [Figure 6]. Swellings of all regions were peanut size at birth and they enlarged with the patient’s age to the present size. Swelling on the tongue was bluish in color causing macroglossia and difficulty in mastication. Patient had history of bleeding from the tongue occasionally but not from other sites, also pain from shoulder site on lying down. All swellings were soft in consistency, non-tender, skin was pinchable, compressible, warm with positive pulsation, but the bruit was absent on auscultation. Overall patient had cosmetic and functional disfigurement. Patient gives a history of occasional pain when lying down while sleeping, especially from the shoulder swelling. Patient was poorly built, malnourished and anemic at the time of initial examination. Patient is a field worker/laborer with no family history of the lesion, but the patient gave history of chronic rectal bleeding (blood in feces) sometimes. Stool examination showed positive hookworm infestation. Based on this possibility, worm infestation was suspected and antihelminthic drug albendazole tablet was given.

Because the patient was anemic, peripheral smear showed normocytic hypochromic type of anemia with hemoglobin (Hb) level of 8.5 g% and normal platelets count. There was no disseminated intravascular coagulation (DIC), thus we ruled out the Kasabach-Merritt syndrome (KMS). He was put on Haemup syrup with an albendazole tablet at the time of initial visit.

Although the diagnosis of vascular malformations may be suspected on the basis of subjective symptoms and clinical features, diagnostic imaging is required in order to define the origin and extension of the anomalies; to differentiate between low- and high-flow lesions and to define whether the lesions are isolated or part of syndromes.[7] Magnetic resonance imaging (MRI) is the imaging modality of choice when diagnosing VM and offers superior delineation of disease for treatment planning.[6] A multiplanar and multisequence MRI neck plain and contrast findings showed multiple well-defined lobulated, variably sized, T2 hyperintense and

Figure 1: Swelling on right dorsal surface of tongue extending to ventral surface with bluish color

Figure 2: Prominent soft swelling on right cheek area

Figure 3: Swelling on the left preauricular area and left lateral neck region

Figure 4: Swelling seen on left/ parietal region of skull
T1 hypointense lesions with multiple flow voids and striated appearance both subcutaneously and in the inter/intra muscular regions [Figures 7 and 8].

These lesions also showed multiple vascular flow and circular flow void calcific density i.e., phleboliths. On contrast imaging, most of the lesions showed peripheral Bloch and heterogenous central varying-type enhancement. Great vessels are normal with evidence of multiple feeding arteries noted from external carotid artery. Final impression of multiple subcutaneous, intra/inter muscular lobulated and enhancing faciocervical lesions with calcific densities hemangiomas was given.

**X-ray findings**

Skull anteroposterior (AP)/lateral view showed multiple soft tissue opacities noted in bilateral cheek and in the supraclavicular (right) region. Calcification foci were noted within soft tissue opacities [Figure 9]. There was erosion and sclerotic margin noted in the posterior aspect of the mandible with erosion of left mandibular ramus. A provisional diagnosis of hemangiomas and VMs was given, although plain radiographs are less useful in diagnosis and treatment planning of these lesions; venous lakes and phleboliths are features of VMs that, when present, may help in diagnosis. Magnetic resonance imaging was useful in delineating the extent of disease and differentiating low-and high-flow vascular lesions.

Since the vascular lesions require extensive care, the patient was referred to a major hospital where the lesions on the cheek and right neck region were completely excised. Histopathological examination showed progressively enlarging, dilated vascular channels lined by flattened, endothelium [Figure 10a]. Phleboliths are commonly observed with venous component. There was fatty overgrowth that may be due to skeletal muscle atrophy with fatty replacement, bundles of nerve fibers and some of the veins with collapsed and narrow lumen were observed [Figure 10b and c]. Most common histopathological differential diagnosis is AVM, which are high-flow lesions. No arteriovenous shunts were seen and phleboliths were commonly seen in low-flow lesions than high-flow lesions.

Ultrasound-guided intralesional bleomycin (15 U) was administered, under local anesthesia for right shoulder

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Figure 5: Swelling in the right submandibular region and lower part of right masseter region

Figure 6: Prominent bilateral swellings in the posterior shoulder girdle region

Figure 7: Magnetic resonance imaging showing swellings at right side base of neck is semispinalis capitus muscle measuring 39 × 35 mm at C2 and C3 level and midline posterior subcutaneous locations measuring 50 × 34 mm from C2 to C4 level and extends downwards to left side subcutaneously

Figure 8: Magnetic resonance imaging of left side of cheek in subcutaneous plane lateral to masseter muscle measuring 43 × 26 mm and right anterior surface of cheek lateral to superior alveolar margin in subcutaneous plane measures 44 × 33 mm and deep extends between masseter and medial pterygoid muscle and infratemporal fossa involving tongue
swelling. Patients showed little response to the drug, 6 months after the injection he noticed slight reduction in the size.

**DISCUSSION**

The moot answer for origin of AVM is still not clear. AVMs are the result of errors in morphogenesis and are divided into subtypes based on the constituent vessels: capillary, venous, arterial, lymphatic and combined forms. Genes and the causative mutations have been identified for several inherited vascular anomalies including cutaneous-mucosal venous malformation (VMCM), glomu-venous malformation (GVM), capillary malformation-AVM (CM-AVM), hyperkeratotic cutaneous capillaro-venous malformation (HCCVM) and cerebral cavernous malformation (CCM). Inherited VMCM is mediated by germline mutations in the TEK gene (chromosome 9p), which encodes the endothelial cell (EC) tyrosine kinase receptor TIE2. The mutations result in increased phosphorylation of TIE2 leading to uncoupling between ECs and the normal recruitment of smooth muscle cells (SMCs). Somatic mutations in TIE2 also cause 40% of sporadic VMs. The lesions are frequently encountered in interdisciplinary centers for vascular anomalies.[7] The presence of intralesional nerve in AVM, as reported in this study, provides an additional diagnostic criterion that is simple and reliable and can be readily used to differentiate AVMs from hemangiomas, even in hematoxylin and eosin (H and E)-stained tissue sections. Also, the presence of nerve in AVMs supports the theory that AVMs are hamartomas, which by definition are mass lesions, composed of an abnormal architectural organization of tissues that are normally present at a particular site or organ.[8,9]

Because the clinical and angiographic manifestations can be extremely varied; VMs and vascular malformations in general, have always been difficult to classify. Head and neck AVM are locally aggressive lesions, which can recur after interventions. The most important factors in assessing the success of surgery are complete nidus eradication, complication rate and long-term recurrence rate.[4]

Various classification systems were proposed from the time of Mulliken and Glowacki who described a biological classification of congenital vascular malformations based on the main pathological characteristics of the endothelium and the natural course of the lesion. This classification was later redefined by Mulliken and Young and adopted by the International Society for the Study of Vascular Anomalies (ISSVA) in 1996; today it is the most widely used classification with minimal changes to the original version.[2]

To our best knowledge and literature review, we have not noticed such an extensive multiple vascular/venous low-flow malformation. Because these vascular malformations require extensive care before any surgical procedure, we have referred to a major hospital with vascular anomalies team for complete surgical excision and sclerosing agent therapy. Vascular malformations are true structural anomalies resulting from errors in vascular morphogenesis. Trauma, surgery or hormonal influences caused by birth control pills, puberty and pregnancy may cause vascular malformations to enlarge and become more symptomatic.[11] Several syndromes are associated with VMs including blue rubber bleb nevus syndrome, GVM and multiple VMCM.[12] No syndrome association was found in our case. In certain positions, such as those on the head and neck after the Valsalva maneuver, the malformation fills with blood, whereas malformations at other sites drain when the affected area is raised above the level of the heart. Phleboliths, that is, radiologic markers of this type of malformation, may be present and such malformations appear at early ages. A particular characteristic feature is that early in the morning patients may experience pain that gradually remits with movement. Symptoms may also be exacerbated.

Figure 9: Skull anteroposterior/lateral view showed calcification foci noted within soft tissue opacities

Figure 10: (a) Histopathology showed dilated vascular channels (H&E stain, x40). (b) Histopathology showing fatty overgrowth and fatty replacement and associated nerve bundles (H&E stain, x40). (c) Histopathology showing nerve bundles (H&E stain, x40)
in pregnant women and women with hormonal imbalances.[2] These AVM appear as pink-to-red, warm and pulsatile lesions in the skin and are most dangerous and difficult to treat vascular anomalies. They may worsen at any time of life, especially after trauma or surgical treatment.[10] The turkey wattle sign describes enlargement of a facial mass on dependency of the head and when the sign is present, it is pathognomonic of a vascular malformation or hemangioma.[11] Positive turkey wattle sign was seen in our case that with Valsalva method showed filling of blood when the patient bends or lies down. VM are generally benign with slow growth, expand secondary to venous stasis. Airway obstruction, snoring and sleep apnea may also be present with recumbence. VM can occur anywhere in the body but often are found in the head and neck where they involve the oral cavity, airway or cervical musculature.[6]

VMs are frequently obvious at birth and will cause a constellation of symptoms depending on the locations involved. The lesions vary in color depending on depth of involvement, from undetectable color differences to deep purple. Patients may present with complaints of pain and swelling and this is usually related to clot formation either from trauma or venous stasis.[5] The presence of increased neural cells has been found in both slow-flow and high-flow malformations. A recent study found a significant increase in nerve components in VMs and more so in AVMs, whereas lymphatic malformation and Port-wine stains showed decrease in the neural innervation. These findings suggest that neural elements in each of these lesions play a role in the development. It has long been accepted that these lesions grew by slow expansion, rather than by proliferation (hyperplasia). Clinically, it can be difficult to predict the growth of the lesions, as some appear to expand well beyond their initial clinical boundaries. The patient may even develop multifocal lesions later in life suggesting that proliferation and actual invasion of surrounding tissue may be occur.[5]

The main mechanism of action of bleomycin is deoxyribonucleic acid (DNA) cleavage via oxidative damage caused by free radicals that form when its metal binding core is oxidized. Bleomycin also induces apoptosis in rapidly growing cells and has a sclerosing effect on the vascular endothelium, which makes it useful in the proliferating phase of vascular neoplasms. Additional mechanisms include blocking the cell cycle at G2, degrading cellular ribonucleic acid (RNA) and the induction of tumor necrosis factor. Many investigators have reported the successful use of IBI in treating hemangiomas and lymphangiomas in various anatomic locations.[12]

Based on this, the surgeons have given bleomycin injection as an optional treatment modality for one side of the shoulder; as it was not possible to operate all lesions in one sitting. Patient was advised sclerosing therapy and he responded to the treatment with slight reduction in the size of swelling that was noted after 6 months.

**Management**

Because of the wide variety of management options and patient presentations, it is strongly recommended that patients with vascular malformations undergo treatment at a multidisciplinary center for treating vascular anomalies. Early intervention, especially on extensive lesions, can not only help prevent many symptoms but also decrease the management complexity of a much larger malformation. Complete surgical excision of the cheek [Figure 11] and right neck region in this case was done with the removal of involved overlying skin and mucosa, failing which, would lead to recurrence. Postoperative pictures were taken after 9 months for lesions treated by surgery [Figure 11a and b] and also of areas injected by bleomycin [Figure 12].

**CONCLUSION**

Treatment of vascular anomalies is complex and often involves multiple disciplines and therapeutic options. Referral to a
vascular anomalies team is recommended when considering therapy for “problematic” hemangiomas and vascular malformations. Vascular anomalies represent a wide variety of vessel abnormalities. Their correct classification and diagnosis is imperative to accurately ascertain prognosis and direct treatment. Multimodal therapy is frequently indicated and in complex patients, a referral to a multidisciplinary vascular anomalies team should be considered.

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