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Invited Article

Interdisciplinary Management of Head and Neck Vascular Anomalies: Clinical Presentation, Diagnostic Findings and Minimalinvasive Therapies

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ABSTRACT

Objectives: Vascular anomalies are included in the 30 000 rare diseases worldwide affecting less than 5/10 000 people. Depending on their morphology and biological properties, they can cause varied disorders with organ involvement. Almost 60% of vascular anomalies have a predilection for the head and neck region in children. Clinical and scientific effort to establish interdisciplinary management concepts for vascular anomalies is increasing worldwide.

Methods: Especially in the head and neck region, clinical impairment and organ dysfunction is associated with cosmetic issues that may represent a physical and psychological issue for the patient. Correct diagnosis, based on clinical presentation and symptoms, is a prerequisite for appropriate therapy, ranging from conservative management to a spectrum of minimally invasive treatment options. We searched PubMed for German and English language published data until December 2016 with focus on clinical studies, review articles and case reports on vascular anomalies with a focus on the head and neck region.

Results: The last ISSVA update in 2014 has contributed to a better understanding of vascular anomalies, classifying them in vascular tumors and vascular malformations. The predominant representatives of vascular tumors are congenital and infantile hemangiomas. Infantile hemangiomas have the ability of spontaneous regression in more than 80%. Patients with symptomatic growing hemangiomas with ulcerations, bleeding complications and restriction of hearing, swallowing disorder, impairment of vision, or cosmetic dysfigurement require treatment. Therapies include oral propanolol, transcatheter embolization and surgery. Vascular malformations tend to progress with patientś age and are subdivided in slow flow and fast flow lesions. Symptomatic slow flow lesions, e.g. venous and lymphatic malformations, benefit from percutaneous sclerotherapy. Fast flow lesions, as arteriovenous malformations, are rare but undoubtedly therapeutically the most challenging vascular anomaly. Depending on location and size, they may require multiple transcatheter embolization procedures for successful occlusion of the AVM.

Conclusions: This review provides knowledge on the current ISSVA classification of vascular anomalies, their clinical presentation, diagnostic evaluation and minimally invasive therapy options to encourage the establishment of a comprehensive interdisciplinary management for head and neck vascular anomalies.

1. Introduction

Vascular anomalies comprise of congenital vessel disorders which can be associated with soft tissue and organ involvement. The main representatives are vascular tumors and malformations which can already be clinically apparent in the newborn and might be associated with considerable symptoms [1]. The exact incidence of vascular anomalies, a rare disease that mainly affects children and young adults worldwide, is unknown [2]. In approximately 5 cases per 10 000 individuals a vascular anomaly requiring treatment is diagnosed.

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Almost 60% of vascular anomalies in young patients have a predilection for the head and neck region due to unkown reasons [3–5]. Patients can suffer from ulcerations and bleeding complications combined with restriction of hearing, swallowing disorder, and impairment of vision that require treatment. Associated cosmetic disfigurement in the head and neck region has to be addressed, too. Treatment includes pharmacotherapy with oral propanolol, minimalinvasive percutaneous sclerotherapy and transcatheter embolization, and rarely surgery.

A prerequisite for appropriate therapy, which usually consists of an interdisciplinary multimodal approach, is correct diagnosis of the underlying vascular anomaly. In 1982 a fundamental classification system for vascular anomalies was established by Mulliken and Glowacki. In 1992 it was modified by the International Society for the Study of Vascular Anomalies (ISSVA) [6–8]. The updated and currently available ISSVA classification is well accepted internationally and offers clinicians and researchers an important guideline for diagnosis and appropriate therapy of vascular anomalies avoiding incorrect and often confusing nomenclature [9].

The aim of this review is to describe a comprehensive interdisciplinary management approach for head and neck vascular anomalies, based on the current ISSVA classification of vascular anomalies, their clinical presentation in the head and neck region, radiological diagnostic evaluation tools and treatment options.

2. Materials and Methods

We searched PubMed for German and English language published data until December 2016 with focus on clinical studies, review articles and case reports on vascular anomalies with a focus on the head and neck region. Diagnosis was based on the current ISSVA classification of vascular anomalies.

3. Results

3.1. Pathophysiology and Clinical Presentation

Vascular anomalies are subdivided in vascular tumors and malformations. They can be distinguished by their pathophysiology and morphology (Table 1) [10]. The predominant representative of vascular tumors, characterized by excessive angiogenesis, based on endothelial cell proliferation, are congenital and infantile hemangiomas [11]. They frequently occur in the head and neck region (65%), followed by chest and trunk (25%) and upper or lower extremities (10%) [12]. Congenital hemangiomas have attained their full size at birth and may show fast or no regression. Infantile hemangiomas arise weeks to months after birth and are the most common benign tumors of the infant, showing spontaneous regression in more than 80% and often do not need therapy [13,14]. They express the immunhistochemical marker Glut-1. Only enlarging symptomatic hemangiomas require treatment, especially when neighboring organs, like the aerodigestive tract, hearing and vision are impaired [11–13].

Vascular malformations are characterized by defective vessel-maturation with a varying degree of mesenchymal tissue proliferation, including dermal, subcutaneous, fatty and bone tissue [15]. Depending on the vessels involved and flow characteristics, they are divided in venous (VM 70%), lymphatic (LM 15%), arterio-venous (AVM 6%) and capillary (CM 9%) malformations with slow-flow (VM, LM, CM) or fast-flow properties (AVM) [16–18]. Vascular anomalies progress with patient's age, never regress and require treatment when symptomatic.

The ISSVA update of vascular anomalies in 2014 represents a comprehensive and widely acknowledged classification [9,17,18]. It is an integral part of the clinical work-flow in vascular anomaly centers and allows to diagnose and treat patients based on symptoms, clinical findings and associated syndromes (Table 1) [17,19].

The clinical presentation of head and neck vascular anomalies is versatile. Initially superficial hemangiomas may appear as raspberry colored birthmarks or an enlarging reddish discoloration of the skin. Enlarging hemangiomas with organ involvement can cause ulcerations, bleeding, impairment of hearing or vision, chewing or swallowing disorders and airway obstruction (Fig. 1A) [20,21].

Venous malformations, the most common vascular malformation, can enlarge extensively, become a palpable discolored mass with local blood stasis and cause painful thrombophlebitis (Fig. 1B) [22].

Macrocystic lymphatic malformations (cysts > 1 cm) are diagnosed in the head and neck region in almost 60%, followed by chest wall, axilla and extremities in 30% (combined macro- and microcystic) and visceral involvement in 10% (often microcystic) [23]. They are mostly located superficially and may cause pain after local hemorrhage or infection. Swelling in the head and neck region can be associated with chewing disability, dysphagia and obstructive sleep apnea. Currently treatment with Sirolimus in diffuse lymphatic malformations in neonates and children is being evaluated with good clinical response and

Table 1
Compendium of the ISSVA Classification of Vascular Anomalies.

Vascular Tumors			Vascular Malformations		
Benign Tumors	Borderline Tumors	Malignant Tumors	Simple	Combined	Associated with Other Anomalies
- Infantile Hemangioma - Endothelial Cell Proliferation - GLUT-1 Marker positive	Hemangio-endothelioma	Angio-sarcoma	Venous Malformation (VM) Blue rubber bleb nevus Syndrome Glomovenous malformation	CM + VM CM + LM CM + AVM LM + VM	Klippel-Trénaunay-Syndrome
Congenital Hemangioma Excessive Angiogenesis with Capillary Lobules GLUT-1 Marker negative Fully developed at birth	Others	Others	Lymphatic Malformation (LM) Macrocystic Microcystic Mixed Cystic	CM + LM + VM CM + LM + AVM CM + VM + AVM	CLOVES Syndrome
Tufted Angioma			Capillary Malformation (CM) Teleangiectasia Nevus Simplex Others	CM + LM + VM + AVM	Sturge-Weber-Syndrome
Spindle Cell Hemangioma			- Arterio-Venous Malformation (AVM) -		Parkes-Weber-Syndrome
Epitheloid Cell Hemangioma Others			Arterio-Venous Fistula (AVF) Hereditary Hemorrhagic Teleangiectasia (HHT)		Others

Abbreviations: CM, capillary malformation; VM, venous malformation; LM, lymphatic malformation; AVM, arterio-venous malformation.

Fig. 1. Mixed superficial and deep infantile right neck hemangioma in a one year old child. Red coloured birth mark and local swelling. The patient was suffering from swallowing disorder and airway obstruction (A). Combined extensive capillary-venous malformation with right hemifascial involvement. The patient was suffering from pain after recurrent thrombophlebitis and hearing loss because of inner ear involvement (B).

tolerability [24,25].

In patients with fast-flow arterio-venous malformations initially a local swelling with pulsations can be noticed. Local hyperthermia, exulcerations, hemorrhage and right heart failure due to chronic arterio-venous shunting may occur in untreated patients (Fig. 2).

The autosomal dominantly inherited hereditary hemorrhagic telengiectasia (HHT) represents a vascular anomaly with formation of enlarging arterio-venous fistulas. Affected patients develop cutaneous, mucosal, or visceral telangiectasias and sometimes aneurysms, that may be associated with severe bleeding, for example nose bleed or intracranial hemorrhage [26].

3.2. Assessment and Diagnosis

Ultrasound with color-coded duplex displays high vessel density in symptomatic hemangiomas [27]. Cross-sectional Magnetic Resonance Imaging (MRI) characterizes vascular tumor extension with potential involvement of surrounding structures [28,29]. In pediatric patients sedation or aneasthesia may be required for optimal diagnostic output of MRI.

Venous malformations increase in size with patient‘s age and appear as bluish compressible tumors when located superficially. Intralesional blood stasis can cause recurrent painful thrombophlebitis and cosmetic impairment. Blood sampling displays coagulation disorder in more than 50% of patients. Elevated D-Dimer plasma levels and von Willebrand Factor can be found, indicating localized intravascular coagulopathy (LIC) with increased endothelial dysfunction markers, venous stasis and inflammation [30,31]. On ultrasound VMs are hypoechogenic tubular structures with slow flow pattern and occasionally increased surrounding fatty tissue [32]. Phleboliths represent remnants of thrombophlebitis. With the ongoing clinical discussion on deposition of gadolinium in the brain, especially in pediatric patients, CT imaging on the latest generation of dual-source CT scanners with a low dose radiation protocol should be seriously considered in future [33]. In venous malformations with potential bone involvement, CT also plays an important diagnostic role.

For extensive VMs of the head and neck with involvement of the aerodigestive tract, neural and vascular structures, multiplanar dynamic contrast enhanced MRI still is the imaging modality of choice [34,35]. Especially T2-weighted imaging characterizes VMs as bright hyperintense lesions, unless signal alteration has occured after partial thrombosis with calcified phleboliths. Post contrast T1-weighted sequences differentiate between devascularized and yet remaining slow flow parts of the VM during the treatment course. Direct percutaneous phlebography of the malformation is usually performed during sclerotherapy for assessment of deep venous system drainage [36].

Along with a thin-walled cystic appearance in ultrasound and hyperintense signal in T2-weighted MRI, lymphatic malformations

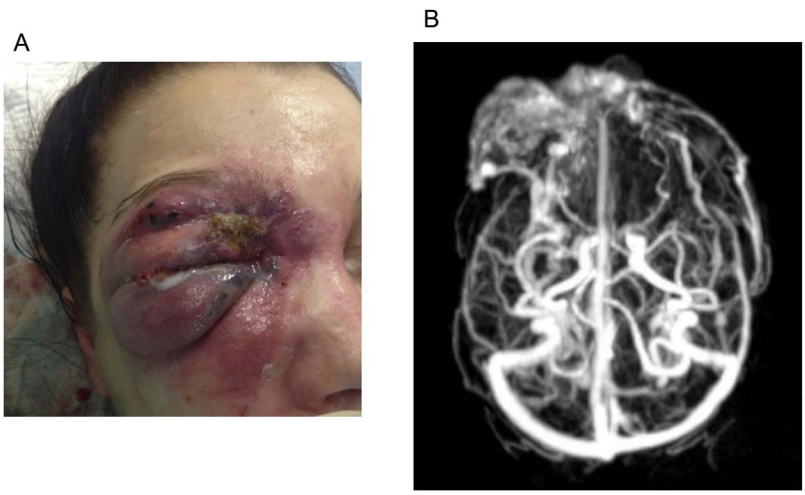

Fig. 2. AVM of the right eye. Pre-and retroorbital arterio-venous fast-flow shunts with clinically apparent swelling, pulsation, hyperthermia of the skin, ulceration and bleeding. The patient complained of almost total loss of vision on the right eye (A). MRI confirms the massive arterio-venous shunts on axial post contrast angiography (B).

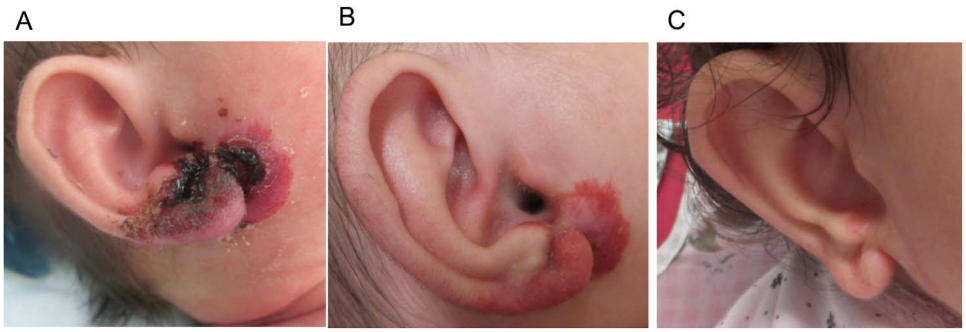

Fig. 3. Mixed superficial and deep infantile hemangioma of the right lobular and preauricular region below the external ear canal in a one year old child. Red coloured birth mark, swelling and crust formation after bleeding (A). Local improvement after 2 months of Propanolol therapy (B). Clinically almost unapparent hemangioma after 1 year of Propanolol therapy (C).

express the immunhistochemical marker Podoplanin D2-40 which is a reliable diagnostic parameter along with clinical findings and imaging [37,38].

Arterio-venous malformations appear as fast-flow pulsating palpable tumors with local skin hyperthermia and redness. Clinical deterioration may lead to venous insufficiency, skin ulcerations and high-output cardiac failure [39,40]. Diagnostic catheter angiography is essential for complete AVM evaluation during treatment [41,42].

3.3. Management Overview

Correct diagnosis is key to appropriate therapy of vascular anomalies. Treatment has to address pain, functional restriction, cosmetic impairment, ulcerations, bleeding and thromboembolic events.

In hemangiomas a “wait and observe” strategy is justified, as spontaneous involution occurs in more than 85% of patients. Rapidly growing hemangiomas with substantial cosmetic disfigurement or impairing vision, hearing and aerodigestive tract, have to be treated. Propranolol was approved by the Food and Drug Administration in 2014, and is currently considered the first line therapy (Fig. 3A–C) [43–45]. It reduces endothelial vessel proliferation in hemangiomas. A systemic oral dose of 2 mg/kg bodyweight is administered up to three times daily for 12 months or longer. In children, careful dose adaption prevents side-effects like bradycardia, hypotension or increased airway resistance and bronchial obstruction. Invasive therapies are hardly required.

Minimally invasive percutaneous sclerotherapy is established for treatment of venous malformations. In extensive VMs, pain relief due to recurrent thrombophlebitis and size reduction can successfully be achieved in more than 90% of patients with Polidocanol or Sodium tetradecyl sulphate foam (STS) foam [46,47]. Interventional management includes ultrasound, phlebography to characterize the VM and its draining veins, sclerotherapy and postprocedural compression therapy for at least 24 hours. In experienced hands, Polidocanol or STS represent cost-effective therapy with excellent safety profile. Sclerosis of the fragile venous endothelium and induction of fibrosis result in devascularization of the VM [48]. Depending on location and extension of the VM, sclerotherapy should be repeated in 8 to 12 weeks intervals for persistent pain management and downsizing (Fig. 4A and B). In less extensive circumscribed VMs, located on lips, earlobe or cheek, sclerotherapy can be performed with Sclerogel (Gelscom/France and ABMedica/Germany), composed of 96% jellied alcohol embedded in a cellulose derivate. Unlike Polidocanol, Sclerogel has a high viscosity which prevents rapid wash-out, enables longer contact with the venous endothelium and increases the sclerosing effect [49,50].

Lymphatic malformations are very frequent in the head and neck region in children. Depending on size and location, LMs can cause compression of the aerodigestive tract and enlarge due to recurrent infection or bleeding into the lesion. In more than 80% of patients with macrocystic LMs, sclerotherapy with Picibanil, also known as OK-432, a lyophilized mixture of streptococcus pyogenes, is effective. [23] Postinterventionally patients may develop local inflammation and fever that require symptomatic therapy. Microcystic LMs do not respond to Picibanil and may need systemic therapy with Sirolimus or surgery.

AVMs are rare but the most challenging lesions to manage. Transarterial and transvenous catheter angiography are prerequisites for anatomical assessment and analysis of the nidus, the site of arterio-venous shunting. The goal of catheter embolization is the occlusion of the AVM nidus in order to prevent further enlargement and hemorrhagic complications [51,52]. Embolization can also play a supportive role in presurgical vessel occlusion to minimize intraprocedural blood loss. For selective flow modulation, mechanical devices as coils and plugs are available, for superselective embolization the liquid agent Ethylene-Vinyl-Alcohol-Copolymer (EVOH) dissolved in Dimethyl-Sulfoxid, is recommended [53,54]. EVOH allows a slow and controlled flow-directed transarterial or transvenous embolization and can efficiently plug the nidus to prevent further arterio-venous shunting.

4. Prognosis

Vascular anomalies present with diverse biological properties and a vast spectrum of clinical symptoms. The majority of infantile hemangiomas show a spontaneous regression without permanent sequels so that a watch-and-wait approach may be justified. Venous malformations and lymphatic malformations may be asymptomatic in small children, but the majority tends to enlarge and cause local swelling and compression effects, together with pain (VMs) or lesion infection (LMs), requiring treatment. Arteriovenous malformations are invariably slowly progressing, almost all of them get symptomatic and need treatment. Incompletely treated AVMs recurr, progressive proliferation can be a consequence of inadequate therapy.

5. Conclusions

Vascular anomalies are rare diseases. Awareness of their pathophysiology, clinical appearance and related complications is increasing. In the head and neck region functional impairment is often associated with serious cosmetic issues that have to be addressed during treatment, too.

An interdisciplinary approach to head and neck vascular anomalies with a dedicated comprehensive treatment concept is key to consistent patient management.

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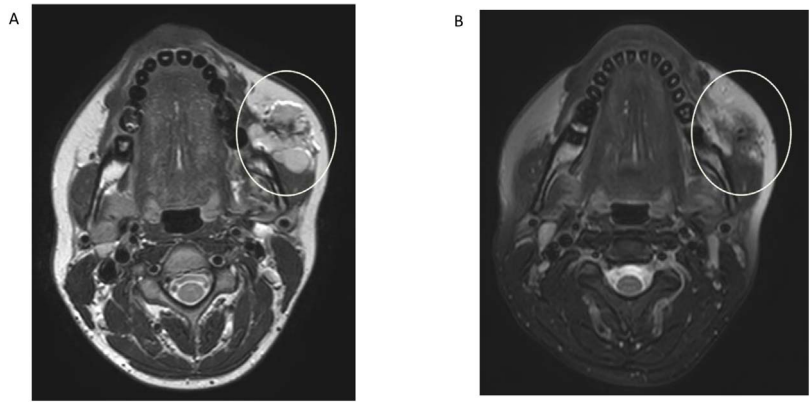

Fig. 4. T2-weighted axial MRI demonstrating a subfascial intramuscular venous malformation involving the left masseter muscle of a 26 year old female. Large hyperintense VM before therapeutic management (A). Decreased signal intensity and massive size reduction after two percutaneous sclerotherapies (B).

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