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Vascular malformations of the orbit (lymphatic, venous, arteriovenous): Diagnosis, management and results

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ABSTRACT

Vascular malformations are often found inside the orbit. Isolated venous malformations (frequently misnamed as cavernous hemangiomas) are the most frequent among these. However, also lymphatic and arteriovenous malformations can affect the orbit. The complex anatomy of the orbit and the fact that its content easily suffers from compartmental syndrome explain why treating orbital vascular malformations can be challenging and technically demanding.

In this study, two institutions have retrospectively collected their cases, consisting in a total of 69 vascular malformations of the orbit. Each type of malformation has been evaluated separately in terms of diagnosis, indications for treatment, techniques and outcomes. Moreover, the authors have analyzed in detail venous malformations, identifying three different types, named orbital venous malformation (OVM) 1, 2 and 3. These behave differently from each other, and a prompt differential diagnosis is mandatory to pose correct indications, minimize risks and improve results.

Overall, surgery was the technique of choice for OVM1, microcystic lymphatic malformations (LM) and arteriovenous malformations (AVM). A pure transnasal approach with mass removal and reconstruction of the medial wall with polyethylene sheets was chosen for OVM1 (intra- or extraconal) located in the medial or superomedial compartment.

Sclerotherapy had a role in treating macrocystic LM and OVM3.

1. Introduction

Despite being quite frequent in the general population, having an overall prevalence of 10%, vascular anomalies are obscured by a blanket of incertitude and confusion.

This is particularly true for orbital vascular malformations that are, along with lymphomas, the most common orbital masses.

A wide range of wrong terms plagues the field of orbital vascular anomalies; lymphangioma and cavernous hemangioma are the most frequently used incorrect terms (Colletti and Deganello, 2016; Colletti, 2018; Dessy et al., 2018; Colletti and Dessy, 2018).

Hooper in 1828 coined the term melanoma and proposed that the ending “oma” be adopted for tumor lesions only (KEIL, 1950).

A tumor is a biological entity in which a pathological cell turnover takes place. This does not apply to vascular malformations. Despite this, in many contemporary papers the word “tumor” is used in the context of cavernous hemangiomas, lymphangiomas and other vascular malformations.

A clear distinction between tumors and malformations does not just have an intellectual and academic relevance: misinterpretation of a disease frequently leads to wrong therapeutic approaches, with an evident burden for the patient.

An up-to-date appropriate description of a vascular anomaly must adhere to the ISSVA classification (ISSVA Classification of Vascular Anomalies ©2014 International Society for the Study of Vascular Anomalies, available at issva.org/classification). The aim of

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this paper is to present the conjoined experience of two centers in the field of orbital vascular malformations and to try to shed light on their features and ideal treatment.

Throughout all the paper, the ISSVA classification was followed as presented in Table 1.

2. Materials and methods

The cohort of the present study comprises patients in whom a definite diagnosis of vascular malformation of the orbit was made either clinically (and confirmed with imaging) or histologically. All malformations were classified according to the 2014 extended ISSVA classification. Overall the cohort consists of 69 patients affected by 9 lymphatic malformations (LM), 57 venous malformations (VM) and 3 arteriovenous malformations (AVM).

The diagnostic workup consisted, for all patients, in the following: clinical examination before and after Valsalva maneuver, an ophthalmological assessment and pre-treatment contrast-enhanced magnetic resonance imaging (MRI). More recently we have added advanced dynamic MRI imaging with DWI (diffusion weighted imaging)–ADC (apparent diffusion coefficient) series and TRICKS (time resolved imaging of contrast kinetics) sequences. TRICKS images were used to identify worrisome outflows from the malformations into highly sensitive regions (in VMs) and to define the different flow patterns (in AVMs).

2.1. Lymphatic malformations

All 9 LMs were of mixed type, micro- and macrocystic. Of these, 8 were intra-/extraconal and 1 LM was extraconal only. This and 6 more intra-/extraconal LMs were treated surgically with a transpalpebral approach. Two intra-/extraconal LMs were treated by means of sclerotherapy with bleomycin (pure liquid 1 mg/ml, total 6 ml); of these 2 patients, 1 was treated elsewhere (dose report not available) but returned to our centre after treatment.

2.2. Venous malformations

Of the 57 VMs, 50 were isolated encapsulated VMs (orbital venous malformation type 1, OVM1, so-called cavernous malformations), 2 were isolated nonencapsulated distensible VMs (orbital venous malformation type 2, OVM2, so-called orbital varix) and 5 were diffuse distensible infiltrating VMs (orbital venous malformation type 3, OVM3 [see Discussion]). A total of 47 OVM1 were removed by means of transpalpebral open surgery. Three cases, all of which were medial to the optic nerve, were removed by means of an endoscopic transnasal approach. Of these, 2 were extraconal and 1 was intraconal and removed with cephalad displacement of the medial rectus muscle. Both OVM2 were removed surgically with a transpalpebral approach. Of the 5 OVM3, 2 were treated by sclerotherapy with gelified ethanol (Sclerogel®, 2.3 ml each patient, one single session) and 2 with bleomycin (pure liquid, 1 mg/ml, 5 ml in patient 1 and 7 ml in patient 2). One more patient was involuntarily treated with 3% Sodium Tetradecyl Sulfate, STS. This patient had a diffuse VM of the right hemiface. He underwent sclerotherapy for the palatal localization of the disease (3% STS foam with air, Tessari method, 1:3 ratio; total 15 ml). However, during the procedure, some sclerosant leaked into the orbital fraction of the VM and caused an acute compartment syndrome. The patient was then immediately decompressed with a bedside canthotomy and cantholysis, and subsequently the lateral orbital wall was osteotomised and laterally luxated. Ten days after, the orbital wall was repositioned and stabilized.

2.3. Arteriovenous malformations

We have treated 3 arteriovenous malformations, all of which were intra-/extraconal. We treated 2 Stage III Shœbinger AVMs and one Stage IV Schœbinger AVM. None of the patients could be treated by means of preoperative embolization. All of them underwent previous intravascular embolization elsewhere and there was no room for subsequent endovascular treatment. Two patients underwent partial resection of an extensive facial AVM (Schœbinger Stage IV) extended to the orbit. In these patients a radical resection was not achievable. Indications were (1) reduction of the bulk of the orbital fraction of the AVM to preserve vision, reduce the proptosis and stop the bleeding; and (2) volumetric reduction of the upper lid to free the eye and allow vision.

The third patient (Schœbinger Stage III) underwent radical removal of a fronto-orbital AVM. Here, the most complete removal was tried and achieved. The AVM involved the entirety of the upper and medial orbital quadrants, but it did spare the cone and the bulb. Thus, the lateral orbital wall was osteotomised and removed. Then the orbital cone was retracted laterally and the entirety of the AVM removed. The bone was then repositioned and stabilized and the lid reconstructed by means of an expanded contralateral forehead flap grafted on the inner surface with cheek mucosa.

2.4. Postoperative assessment

Each patient received, at each follow-up session, including the most recent one, a clinical and ophthalmological evaluation in which the ophthalmologist considered: eyeball position, corneal health, visual acuity, presence or absence of diplopia, and lid cinematics. At 6 and 12 months after surgery and yearly thereafter, each patient underwent instrumental examination with contrast-enhanced MRI. Since the beginning of 2017, DWI-ADC and TRICKS sequences were obtained in each case.

3. Results

3.1. Lymphatic malformations

Pre-treatment ophthalmological assessments revealed proptosis and eyeball dystopia in all patients. All patients suffered

Table 1
2014 revised ISSVA Classification of Vascular Anomalies.

VASCULAR ANOMALIES				
Vascular Tumors			Vascular Malformations	
Benign	Locally Aggressive	Malignant	Simple	Combined
Infantile Hemangioma	Kaposiform hemangio endothelioma	Angiosarcoma	Capillary Malformation (CM)	CVM, CLM
Congenital Hemangioma	Retiform hemangio endothelioma	Epitheloid hemangio endothelioma	Lymphatic Malformation (LM)	LVM, CLVM
Tufted Hemangioma	PILA, Dabska tumor		Venous Malformation (VM)	CAVM
Spindle-cell Hemangioma	Composite hemanigoendothioma		Arteriovenous Malformation (AVM)	CLAVM
Epithelioid Hemangioma	Kaposi Sarcoma		Arteriovenous Fistula	
Pyogenic Granuloma				

episodically from lymphangitis causing pain, exacerbation of the disfigurement and a decrease in visual acuity.

All the LMs that were treated surgically yielded a significant improvement in cosmesis, binocular vision and pain as assessed by ophthalmologists. One patients who underwent sclerotherapy with bleomycin suffered from compartment syndrome and, despite early surgical decompression, lost vision in the affected eye.

At 2 years' follow-up (average; range 18 months 11 years), 2 patients showed disease relapse, which did not require further treatment (minor proptosis being the only consequence of the LM).

3.2. Venous malformations

Pre-treatment ophthalmological assessment revealed the following:

In all OVM1 patients proptosis, eyeball dystopia with diplopia. Of the patients, 38 suffered from acute decrease of visual acuity during bursts of localized intravascular coagulation (LIC) that concomitantly caused severe pain. Four patients with OVM1 located at the level of the optic nerve suffered from episodes of lipothymia, probably caused by direct pressure of the malformation on the eyeball or the optic nerve. All patients had intermittent binocular diplopia.

All 50 OVM1 had good long-term results as assessed by ophthalmologists. In detail, a decrease in visual acuity was not observed, and at 4 years follow up (average; range 1–24 years) there were no recurrences. No residual diplopia, exophthalmos or corneal exposures were detected. Both OVM2 and 5 OVM3 had marked enophthalmos at rest that switched to severe proptosis with dependence and at every increase in the thoracic pressure. Eyeball dystopia was present in all patients. However, no diplopia was revealed at the ophthalmologic evaluation. All patients suffered from cyclical episodes of acute swelling of the orbital content with proptosis, pain and temporary visual acuity impairment. These episodes ware caused by thrombosis that left phlebolites in the malformation as a result. Both OVM2 had a marked decrease of pressure-dependent proptosis without perioperative complications as assessed by ophthalmologists, who did not detect any residual diplopia or visual impairment. Of the 5 OVM3, all had a significant improvement in symptoms, with reduction of dependence-related exophthalmos and vision blurring as assessed after ophthalmological evaluations. No long-term complication was observed except mild lower lid malposition in the patient who underwent orbital decompression.

3.3. Arteriovenous malformations

Two patients underwent operation with palliative purposes with the aims described in Materials and Methods. These results were achieved in both cases. At an average of 1.5 years' follow-up (range 12–24 months), no disease progression was noted. With longer follow-up, however, this may occur.

The third patient underwent operation in March 2016 (follow-up at the time of writing is 2 years); the vision was preserved and no signs of disease progression are present. We are still doing remodeling on the reconstruction. A longer follow-up is needed for this case.

4. Discussion

4.1. Epidemiology

In a frequently cited large case series, orbital vascular malformations appeared to be the most common among all tumor and tumor-like lesions, as they accounted for 12% of 1264 lesions (Shields et al., 2004). In detail, cavernous hemangiomas (OVM1) were found in 6% of the patients, varices (OVM2 and 3) in 2% and lymphangiomas (lymphatic malformations) in 4%. Unfortunately, the authors described 3% of capillary hemangiomas that are difficult to relocate into the ISSVA classification and did not mention a single case of arteriovenous malformation. In another very large case series, "vasculogenic lesions" were encountered in 24% of 2480 orbital masses (Bonavolontà et al., 2013). Specifically, in this latter case series, the authors found that cavernous hemangiomas (OVM1) were found in 9% of the case series, venous flow lesions in 4% (probably OVM 3), varices in 1% (probably OVM 2), no-flow malformations in 4%, lymphangiomas in 4% (lymphatic malformations), combined lymphangioma-varix in 1%, "arterial flow lesion" in 3%, "shunt/fistula" in 3% and "arterial malformation" in 1%. It is immediately obvious that an ISSVA-accepted nomenclature was not used in these landmark papers. However, it would appear that vascular malformations as a whole might, as said, be the most common pathology encountered within the orbit.

4.2. Pathogenesis and pathophysiology

Vascular malformations are developmental errors that take place during embryogenesis just after the primitive capillary plexus has formed. This means that, conceptually, every kind of vascular malformation, as they are classified by the ISSVA (the International Society for the Study of Vascular Anomalies) could take place in the orbit: capillary, lymphatic, venous, and arteriovenous malformations. However, since capillary malformation usually only hits the subdermal capillary plexus, deep capillary malformations of the orbit do not exist.

Vascular malformations are believed to be caused by genetic errors that hit the endothelial cell during embryogenesis. As the basic research continues, more and more data point in this direction. Venous malformations are frequently caused by a mutation in TEK gene, coding for the TIE2 protein, while lymphatic malformations are associated with PIK3CA mutations (Queissier et al., 2018). Recently, mutations in the genes coding for proteins in the RAS/MAPK pathway (like MAP2K1) have been found to be linked to arteriovenous malformations.

Common to most vascular malformations of the orbit is a vivid expression of VEGF receptors (Atchison et al., 2016). This could explain, on one hand, the responsiveness of orbital vascular malformations to hypoxic stimuli. On the other hand. It could justify a tendency to increase in size that is common to them (Colletti and Ierardi, 2017). Finally, vascular malformations can take place in mixed forms, and more frequently, as to what pertains to the orbit, venous-lymphatic malformations can be found (Rootman et al., 2014b). We did not, however encounter mixed vascular malformations in the present case series: no D2-40 (podoplanin)–positive cells were ever found in venous malformations, although small vessels were always identifiable on microscopic examination in lymphatic malformations: this, however, is consistent with the usual structure of lymphatic malformations that have numerous vessels running within the septae and is therefore not indicative of a combined lympho-venous malformation.

Just as the embryology and the pathophysiology explain, since all vascular components are born from the primitive capillary plexus, vascular malformations can take place in the form of pure malformations (more frequently) or there can be mixed forms as well (Colletti et al., 2014). Specifically, the primitive lymphatic vessels are created as "buds" or small saccules. These either bud from the venous channel or anastomose with it later on. It is no surprise, then, that the most typical form of mixed vascular malformation is the lympho-venous.

For unknown reasons, however, these generally accepted principles and classifications have failed, as said, to permeate the beliefs of "orbitologists." Still, it is true that the orbit is a delicate and complex anatomical and surgical site, and therefore some practical distinctions are highly valuable if they help in proper planning.

A multidisciplinary setting where different specialist coordinate treatment planning is advisable for all vascular malformations and the orbit makes no exception. The treatment is to be tailored to the patient's specific disease (Stacey et al., 2015). Considering this point of view, orbital vascular anomalies can be divided as follows.

4.3. Venous malformations

VMs are composed of malformed venous channels of different sizes. VMs frequently lack a continuous sheath of muscular and connective fibers surrounding the endothelial layer. This makes them particularly prone to progressive mechanical dilation. Moreover, venous blood flow can be altered with episodes of stagnation. This in turn causes localized intravascular coagulation (LIC) that is followed by intense inflammation. Acute inflammation is responsible for the typical bursts of pain and proptosis that are typical of orbital VMs. Finally, chronic inflammation is at the root of phlebolith formation. Phleboliths, thus, are pathognomonic (and unique) of VMs (Colletti and Ierardi, 2017). There are 3 clinically distinct forms of orbital VMs that are, to a certain extent, linked to the Puig rheological classification (Puig et al., 2003). The first form is composed of a single VM that is excluded from the surrounding venous system. We call this "orbital VM type 1" ("OVM1"). This type is equivalent to Puig I VMs and is unfortunately often referred to as "cavernous hemangioma." The term cavernous hemangioma is profoundly wrong (Colletti and Deganello, 2016). Hemangiomas are tumors, i.e., there is an altered cellular turnover rate or proliferation. OVM1 are malformations lined by endothelium that increase in size, on average, by 10% per year (Rootman DB et al., 2014a). This increase in size is due to repeated episodes of LIC and not to hyperplasia or neoplastic growth.

Clinically there is usually proptosis with or without visual disturbances. No exacerbation of signs and symptoms is noted with dependence or Valsalva maneuver.

On MRI, they appear as isointense in T1w sequences and mildly or inhomogeneously hyperintense in T2w sequences. This is because there is often a portion of the malformation that is thrombosed and thus not hyperintense. They do not change their features on Valsalva-augmented MRI. On ADC, they usually show values similar to those of other orbital masses (values < 2.1 mm/s^2), tumors included. However, on TRICKS they typically show only late, gradual contrast enhancement (Jayaram et al., 2017). This helps in differentiating this from tumors of the orbit that (usually) have an early, vivid contrast filling in TRICKS sequences (Jayaram et al., 2017). The second form of VM is characterized by a single, ectasic or racemose VM that is connected with the rest of the venous system of the orbit. We call this "orbital VM type 2" ("OVM2)". OVM2 are sometimes referred to as "orbital varices." Although connected with the venous system, they are topographically limited and separated from the surrounding structures. This is very similar to Puig IV VMs. Clinically, there is usually proptosis with or without visual disturbances that are more evident with dependence or with Valsalva maneuver.

On MRI, they appear isointense in T1w, hyperintense in T2w and vividly contrasted. More often than not, phlebolyths are visible as hypointense spots. The malformation, even if is not inflated clinically, increases in size during Valsalva, and this is detectable during the examination. On ADC, they show high values, typically greater than 2.8 mm/s^2. This is a 100% sensible and specific index (Kalin-Hajdu et al., 2018). The third form is made of a plexiform, infiltrating VM that is linked to surrounding orbital and intracranial venous system. We call these "orbital VM type 3" ("OVM3"). At rest they are usually characterized by enophthalmos with or without visual disturbances. With dependence or Valsalva maneuver, significant exophthalmos takes place, and this is usually accompanied by various degrees of visual disturbances such as diplopia or, more rarely, blurring or scotomas.

On MRI they show the same features as OVM2, but they are more extensive and have a clear tendency to intermingle with normal tissues.

The diagnosis of "distensible VM: OVM type 2 and 3" is easily confirmed by specific protocols during contrast-enhanced MRI.

1. Valsalva-augmented MRI. Up to 40% of OVM2-3 that do not present with proptosis clinically during Valsalva will show a measurable increase in size if the thoracic pressure is increased during MRI acquisitions (Figs. 51 and 52).
2. DWI-ADC. Distensible VMs (OVM2-3) will typically show an ADC greater than 2.1 mm/s^2 (100% specificity and 100% sensibility according to Kalin-Hajdu et al. (2018). Accordingly, we found coherent results, with average values exceeding 2.8 mm/s^2 (Fig. 53).
3. TRICKS sequences are most useful to study the dynamic flow of the malformation (Kahana et al., 2007). Orbital VMs might drain into the cavernous sinus (Fig. 54), which renders any procedure much more hazardous to perform.

This classification does not have academic purposes. It should serve as a guide for planning surgery and as an aid to predict surgical difficulties or complications. OVM1 can lie inside or outside the orbital muscle cone and in the superior, inferior, medial, or lateral quadrant of the orbit (Figs. 1–13). The extraconal OVM1 of the medial compartment can be approached by means of an endoscopic transnasal approach (Bleier et al., 2015). This holds true (although in very experienced hands only) even for intraconal OVM1 of the medial orbital compartment (Figs. 24–31). Medial wall reconstruction is advisable to avoid postoperative enophthalmos and can be done with the same transnasal route (Colletti et al., 2016). Yet traditional transpalpebral surgery is a valid option in both cases. On the other hand, OVM1 intervening in one of the other orbital quadrant are usually approached with transpalpebral surgery. OVM1 are characterized by a lack of a significant vascular connection with the remainder of the venous system of the

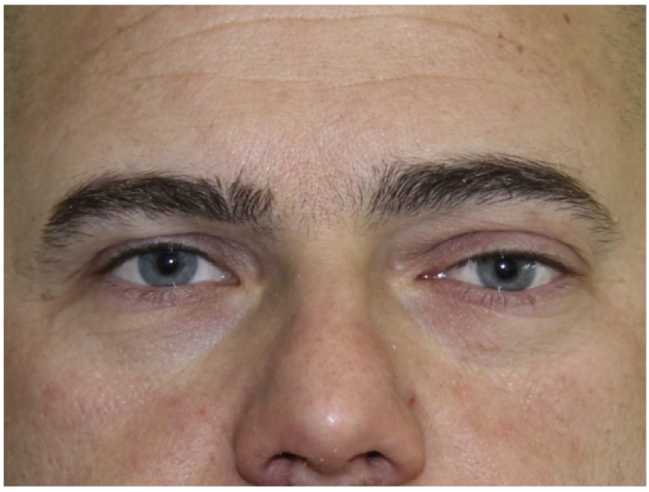

Fig. 1. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Frontal view. The eyeball appears displaced laterally and caudally, causing diplopia.

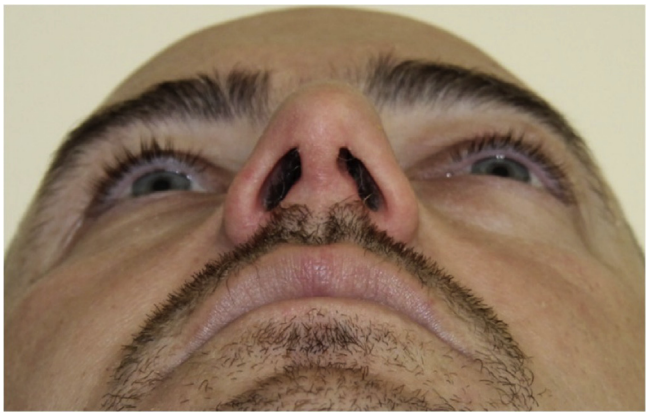

Fig. 2. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Worm's eye view. Left exophthalmos and bulb displacement are evident.

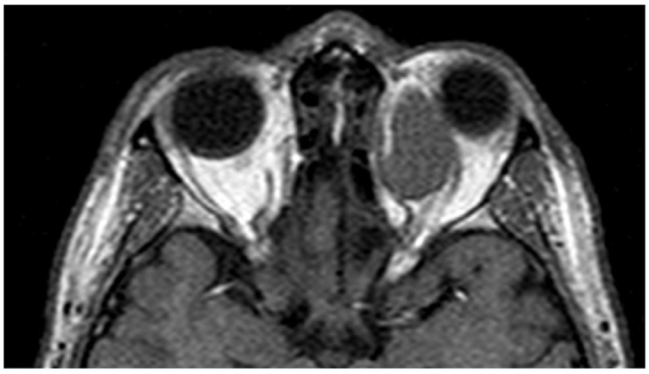

Fig. 3. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Axial T1w MRI. The malformation is intra-extraconal and medially placed.

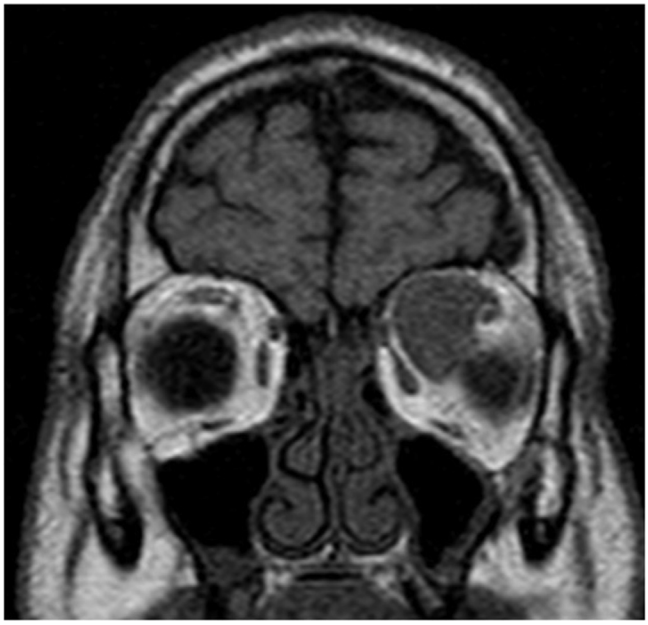

Fig. 4. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Coronal T1w MRI. The malformation is located in the supero-medial compartment of the orbit.

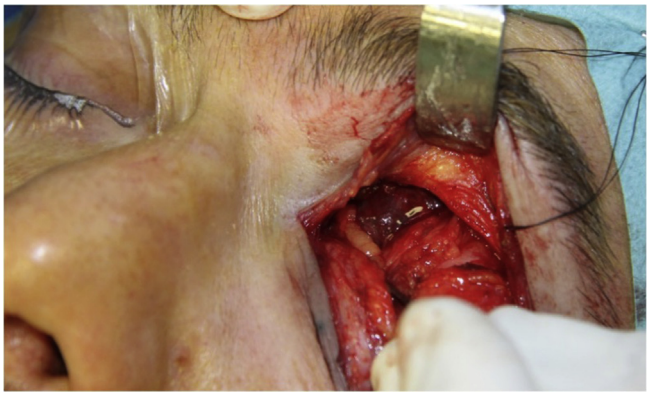

Fig. 5. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Intraoperative detail. Through a blepharoplasty access the lesion is easily reached by gently pushing the orbital content laterally.

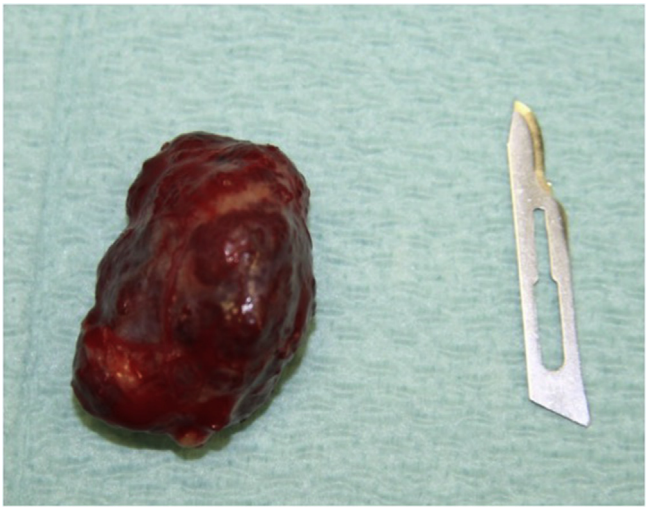

Fig. 6. Patient 1. Orbital Venous Malformation Type 1 (OVM1). The malformation removed.

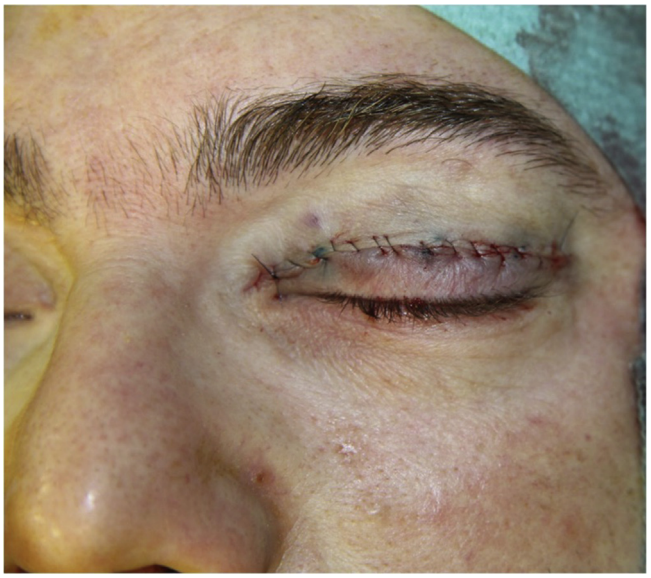

Fig. 7. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Surgical detail at the end of the suture.

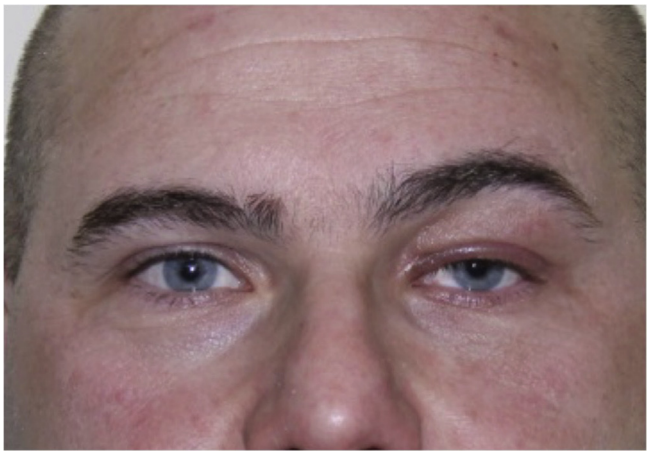

Fig. 8. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Postoperative frontal view. The eyeball is now in the right position. No residual diplopia.

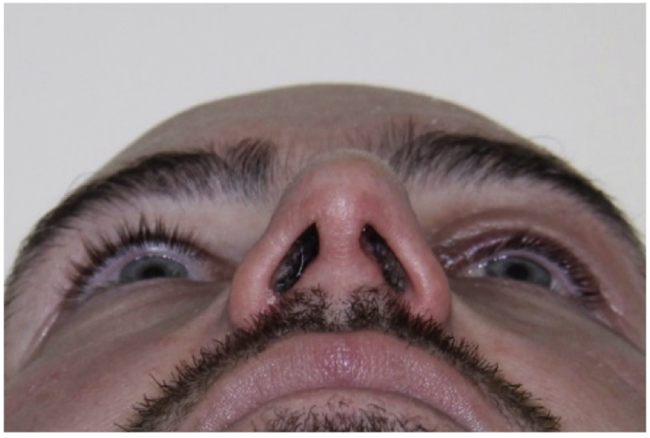

Fig. 9. Patient 1. Orbital Venous Malformation Type 1 (OVM1). Postoperative worm's eye view. The exophthalmos has been corrected.

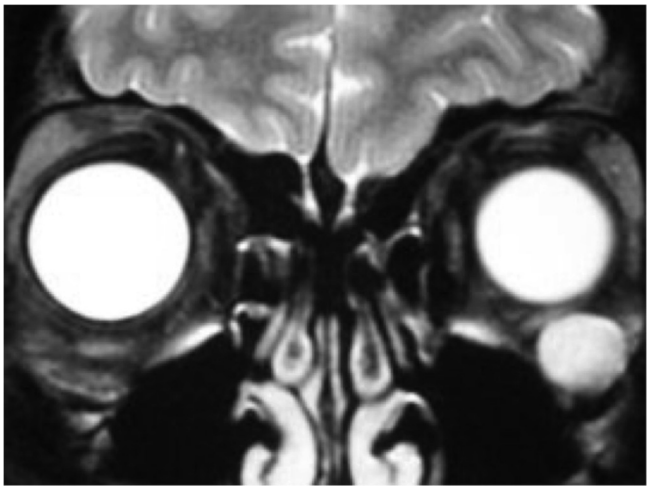

Fig. 10. Patient 2. Orbital Venous Malformation Type 1 (OVM1). Coronal MRI. The malformation is extraconal, located inferomedially. This calls for a direct transpalpebral access.

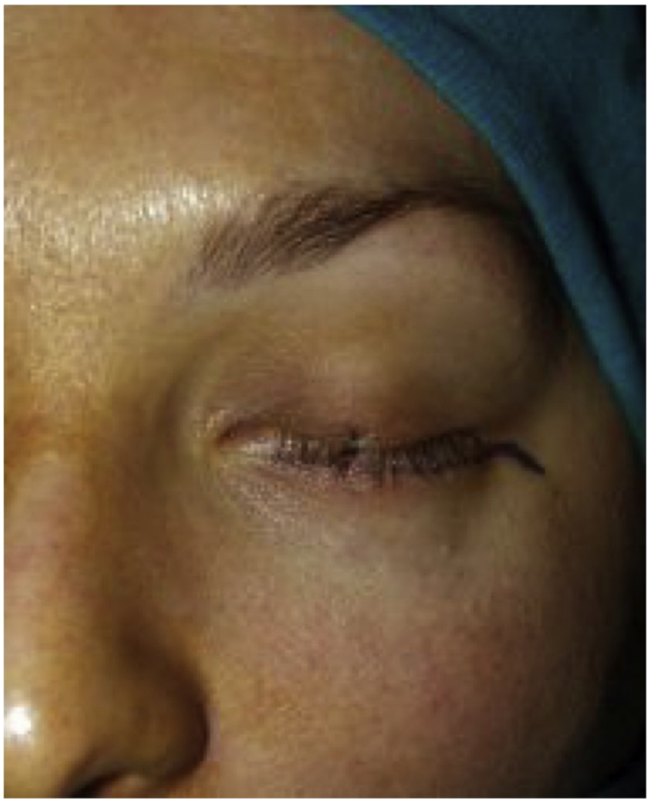

Fig. 11. Patient 2. Orbital Venous Malformation Type 1 (OVM1). Preoperative drawing of a subciliary incision.

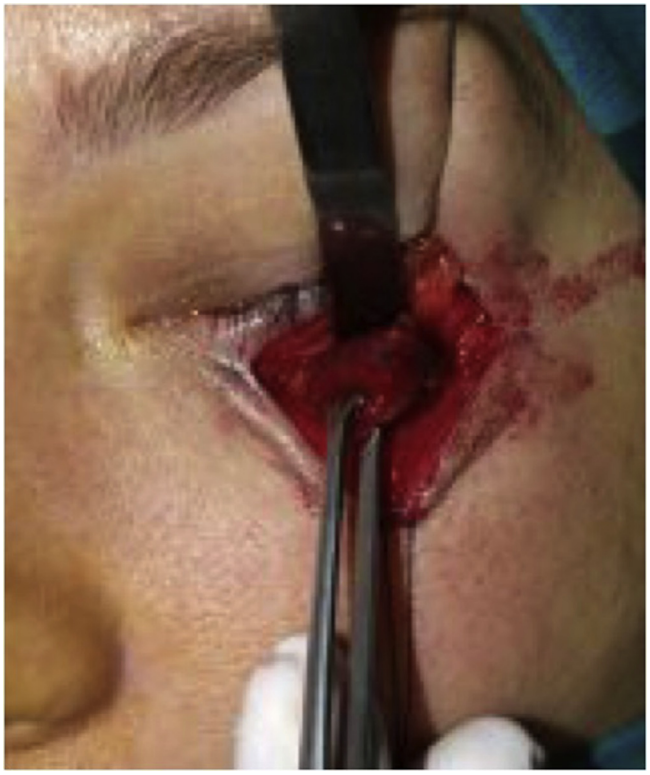

Fig. 12. Patient 2. Orbital Venous Malformation Type 1 (OVM1). Intraoperative detail of the removal of the mass.

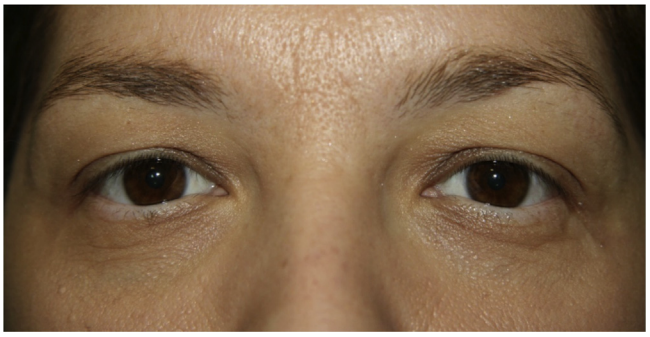

Fig. 13. Patient 2. Orbital Venous Malformation Type 1 (OVM1). Postoperative appearance. The eyeballs are symmetric and no scar is visible.

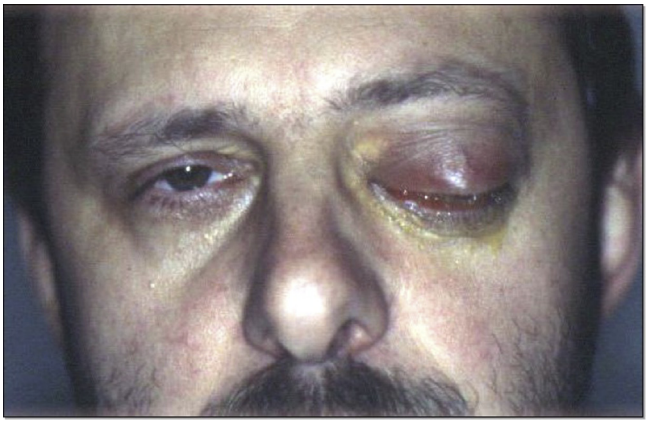

Fig. 14. Patient 3. Orbital Venous Malformation Type 2 (OVM2). Severe exophthalmos and dystopia are evident.

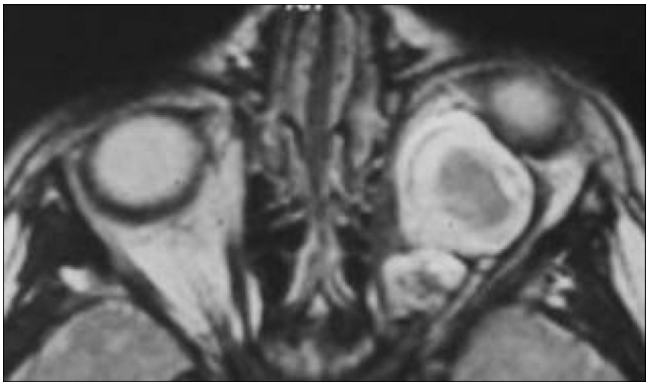

Fig. 15. Patient 3. Orbital Venous Malformation Type 2 (OVM2). Axial MRI. The malformation is intra and extraconal and shows local intravascular coagulation.

orbit. This, with the ubiquitous presence of an adventitial dissection plane, accounts for the relative easiness of their surgical management and the feasibility of a transnasal approach. Yet, surgical removal has absolute indications just when visual disturbances are present. Other authors include esthetically relevant proptosis or dystopia as an additional relative indication.

OVM2 and OVM3 (Figs. 14–23), being rheologically connected to the venous system of the orbit (and sometimes of the brain) involve crucial therapeutic issues. If approached surgically, they are at risk of intraoperative bleeding. Conversely, sclerotherapy due to the intrinsic swelling poses a risk of causing an orbital compartment

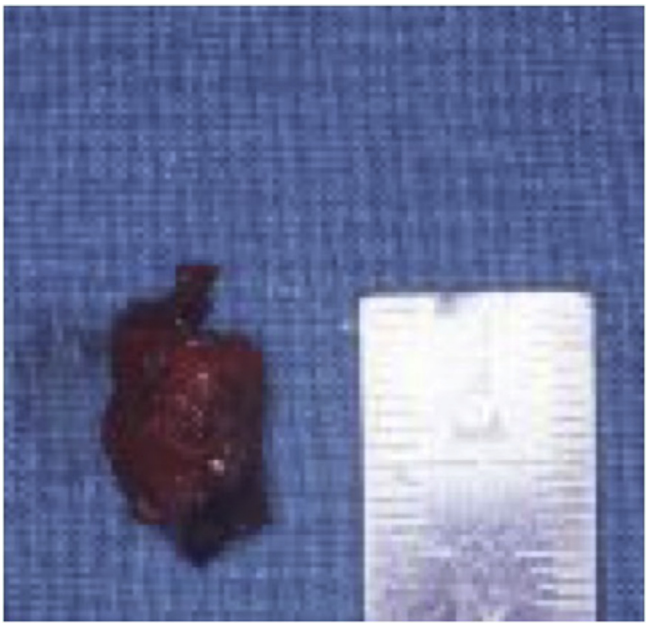

Fig. 16. Patient 3. Orbital Venous Malformation Type 2 (OVM2). The malformation was removed after ligation of the vascular pedicle.

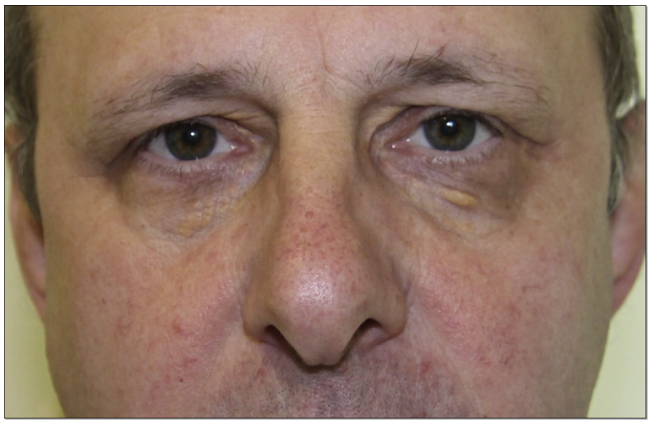

Fig. 17. Patient 3. Orbital Venous Malformation Type 2 (OVM2). Postoperative frontal view. The eyeballs are now symmetrically positioned.

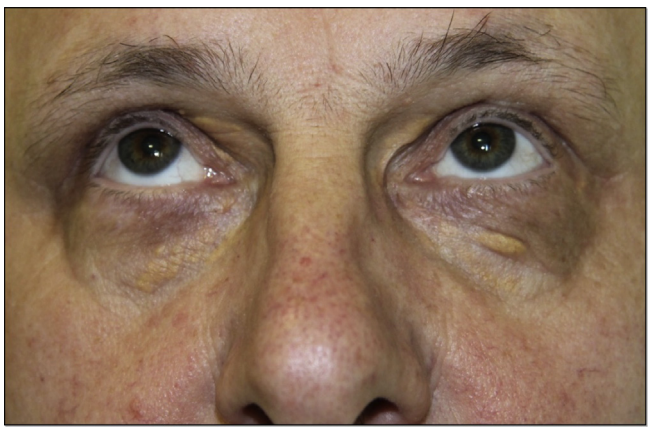

Fig. 18. Patient 3. Orbital Venous Malformation Type 2 (OVM2). Postoperative view. No residual exophthalmos.

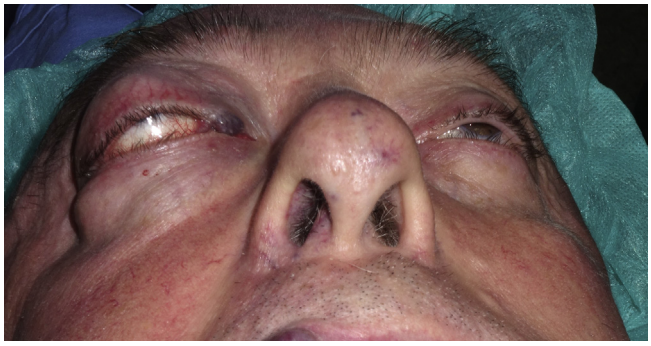

Fig. 19. Patient 4. Orbital Venous Malformation Type 3 (OVM3). Frontal view. Severe exophthalmos and dystopia are evident.

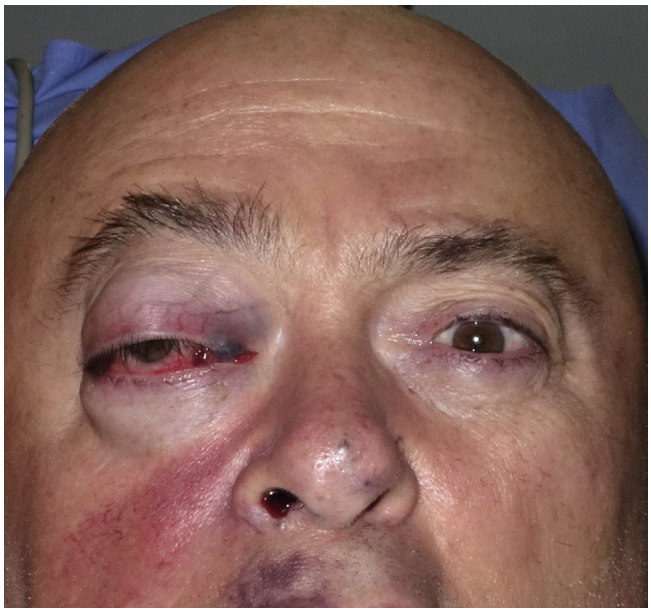

Fig. 20. Patient 4. Orbital Venous Malformation Type 3 (OVM3). Severe exophthalmos threatens vision.

syndrome that may lead to amaurosis (Colletti et al., 2017). Moreover, some sclerosing agents (pure ethanol in particular) can produce necrosis in the surrounding tissues (Benoiton et al., 2017), thus making sclerotherapy far from being the first line of treatment in these diseases. Treatment of OVM2 and OVM3 should be dictated by functional disturbances only. Only in very selected cases may simple proptosis with esthetic relevance suffice as an indication to treat.

4.4. Lymphatic malformations

These are composed by a plexus of lymphatic channels, lined by D2-40 (podoplanin) positive endothelium, that can inflate and form chambers that can be small (<2 cm, or microcysts) or large (>2 cm, or macrocysts) (Hamoir et al., 2001). Although this division is generally accepted and serves for indication for treatment, we believe that, in the orbit, a diameter of 1 cm is a better threshold for discriminating between micro- and macrocysts, as suggested by other authors as well (Poldervaart et al., 2009) (see later here). Lymphatic malformations can have a vascular component owing to two mechanisms: (1) the lymphatic channels can be linked to the

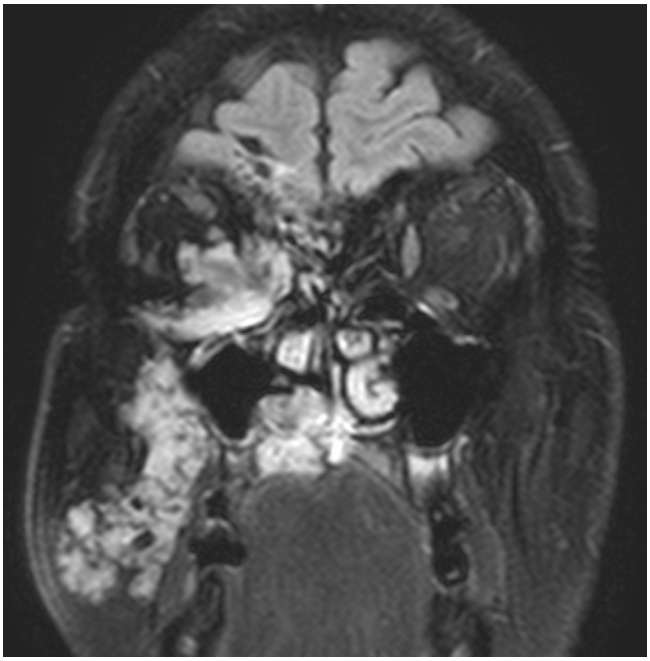

Fig. 21. Patient 4. Orbital Venous Malformation Type 3 (OVM3). Coronal MRI. A diffuse VM involves with an infiltrative behavior the right orbit.

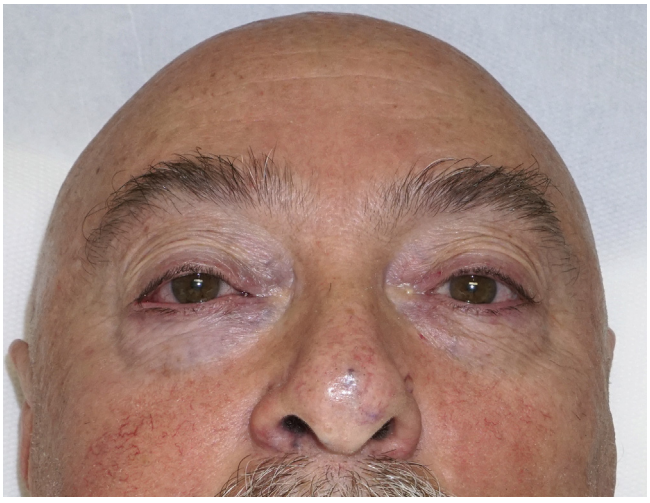

Fig. 22. Patient 4. Orbital Venous Malformation Type 3 (OVM3). Postoperative frontal appearance after bony decompression and sclerotherapy with 3% STS. Good symmetry has been achieved.

venous system, and (2) small arterioles and venule can run within the intercystic septae.

The diagnosis is based on clinical and MRI features.

Clinically, lymphatic malformations cause a stable proptosis with some degree of bulbar dystopia, depending on the site of the malformation. The microcystic component usually infiltrates surrounding tissues, producing bulky malfunctioning lids. Infection within the lymphatic chambers is common, and this causes acute inflammation with redness, pain and worsening of the clinical signs.

On MRI, just like OVM 2 and 3, they appear isointense on T1w and hyperintense on T2w. Not infrequently, a liquid-to-liquid level is detectable inside major chambers. This is due to deposits of debris or intracystic hemorrhage. After contrast, they remain

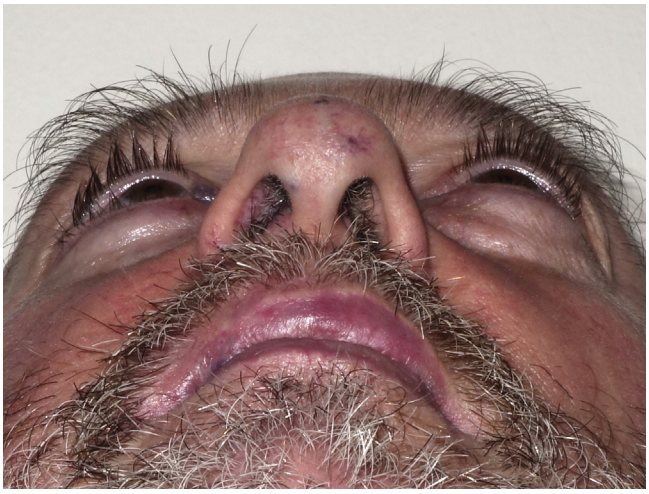

Fig. 23. Patient 4. Orbital Venous Malformation Type 3 (OVM3). Postoperative worm's eye view. No residual exophthalmos is evident on dependence.

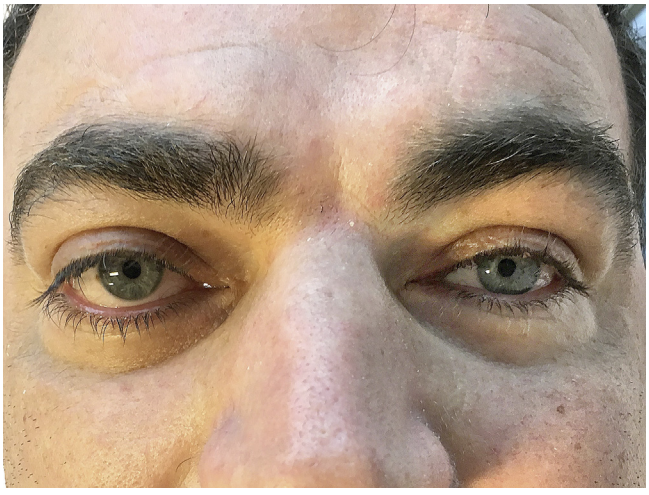

Fig. 24. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Preoperative frontal view. The right eye is proptotic and dislocated. The patient is diplopic.

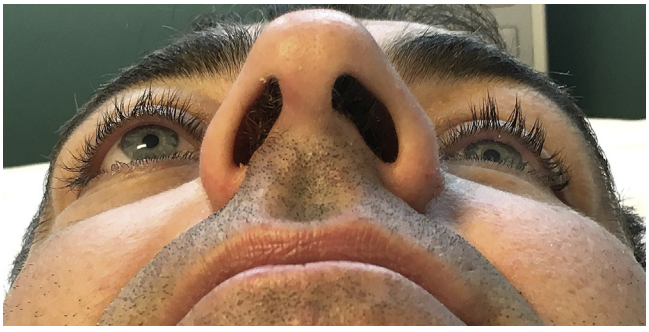

Fig. 25. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Preoperative worm's eye view. A right exophthalmos is evident.

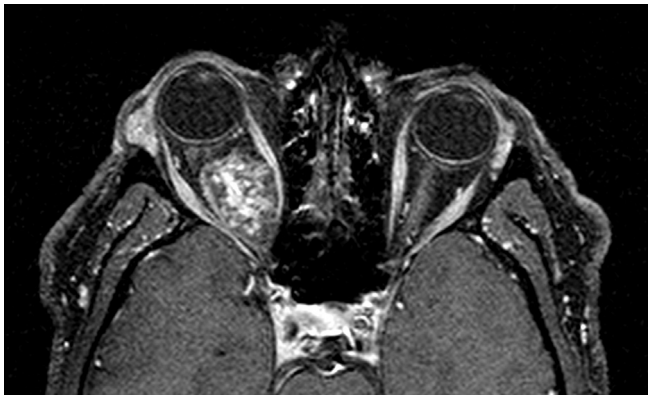

Fig. 26. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Preoperative Axial MRI. A retrobulbar intraconal OVM is present.

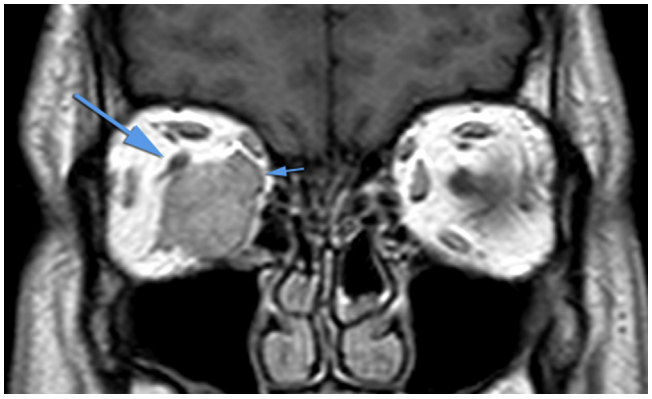

Fig. 27. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Preoperative Coronal MRI. The Intraconal OVM displaces the optic nerve superolaterally (large arrow) and the medial rectus muscle superomedially (small arrow). The position of the mass makes a transnasal approach ideal for the surgical treatment.

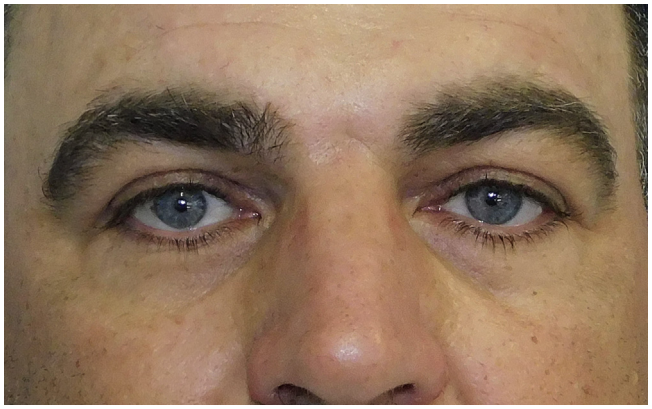

Fig. 28. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Postoperative frontal view. A radical ethmoidectomy with removal of the papyracea has been carried out. The mass was then removed and the medial wall reconstructed with a polyethylene sheet. No residual exophthalmos is present.

unenhanced, while the intercystic septae usually become more intense. On ADC, a high value is typical (>2.8 mm/s), and this might create confusion with OVM2-3. This is, however, easily solved by looking at contrast-enhanced T1w sequences: here LM remain iso-hypointense, while OVM2-3 become higly hyperintense. The distinction between micro- and macrocystic lymphatic malformation is of the utmost relevance in general: macrocysts will respond very well to sclerotherapy (Figs. 32–38), while microcysts usually will not. However, almost all sclerosants will cause some degree of swelling. Pure ethanol will generate the most intense swelling and

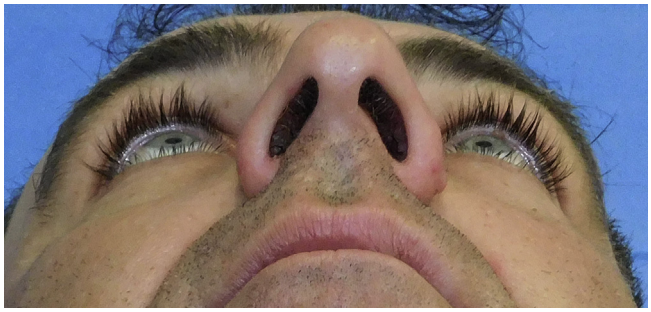

Fig. 29. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Postoperative worm's eye view. The eyeballs are now symmetrically projected.

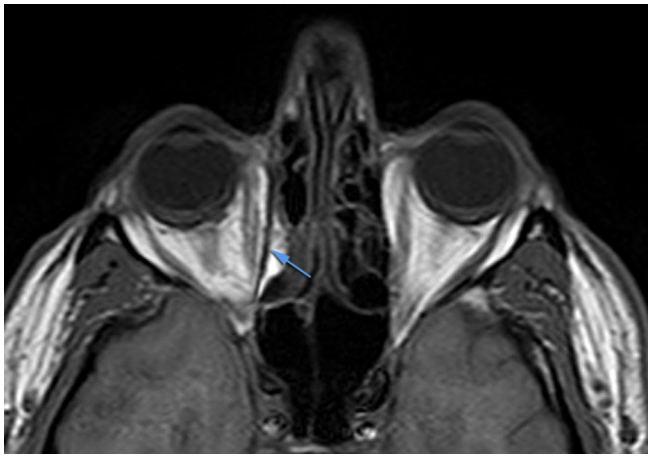

Fig. 30. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Postoperative Axial MRI. No remnants of the mass are left. The polyethylene sheet is visible (arrow).

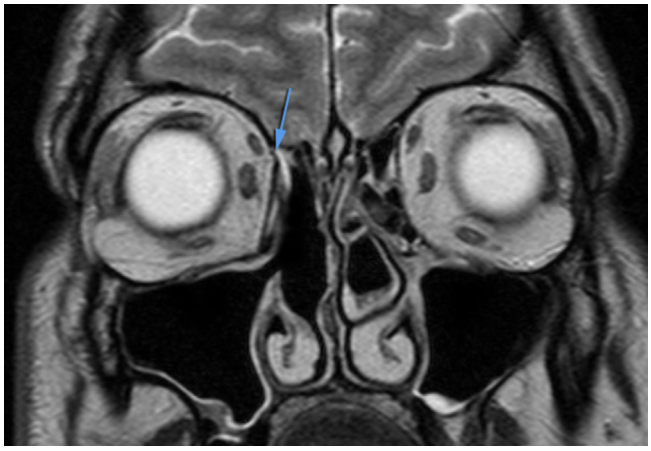

Fig. 31. Patient 5. Orbital Venous Malformation Type 1 (OVM1). Postoperative Coronal MRI. No remnants of the mass are left. The polyethylene sheet is visible (arrow).

bleomycin the smallest. Even mild edema in the orbit can cause a compartmental syndrome and thus sclerotherapy, which is the first choice in LMs located elsewhere but might not be the first choice to treat orbital LMs. In the present case series, even major LMs of the orbit that were treated surgically were not jeopardized by long-term complications. On the other hand, one patient with LMs who underwent sclerosing with bleomycin had an orbital compartment syndrome that, despite early decompression,

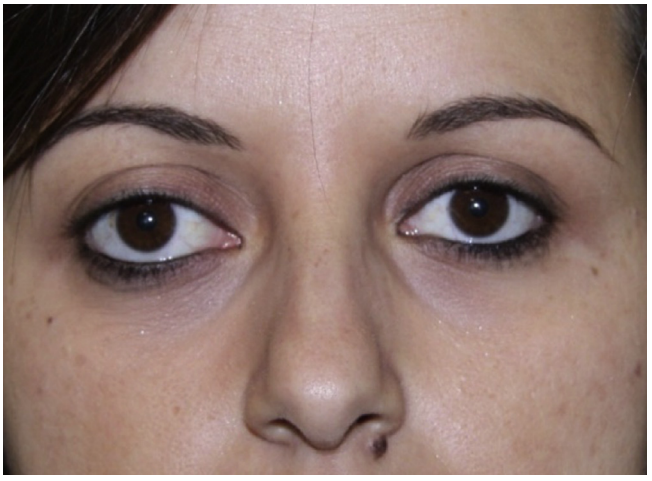

Fig. 32. Patient 6. Mixed lymphatic malformation of the right orbit. Frontal view. The eyeball is dislocated inferolaterally, causing diplopia.

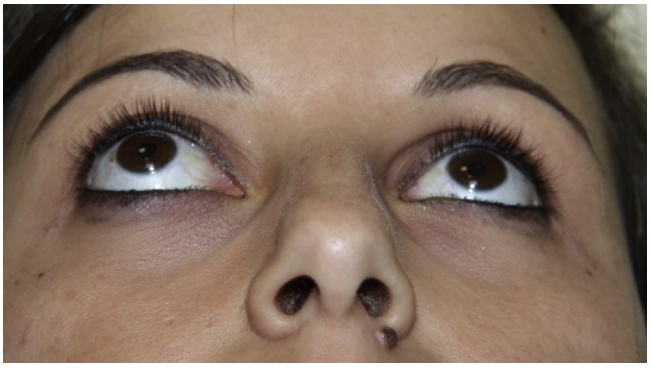

Fig. 33. Patient 6. Mixed lymphatic malformation of the right orbit. Worm's eye view. Moderate exophthalmos is clearly apparent.

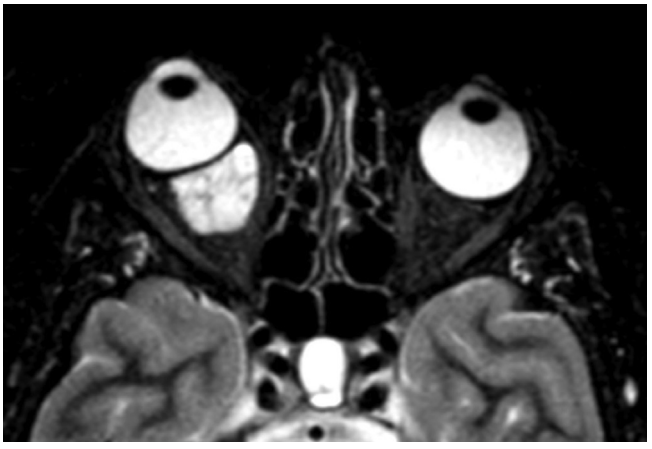

Fig. 34. Patient 7. Mixed lymphatic malformation of the right orbit. Axial MRI. The macrocystic component is intraconal.

produced amaurosis. Other authors, however, report very good results with a very low overall complication rate (Barnacle et al., 2016). Other studies report the need for early decompression to resolve compartment syndrome after sclerotherapy of orbital LMs (MacIntosh et al., 2014).

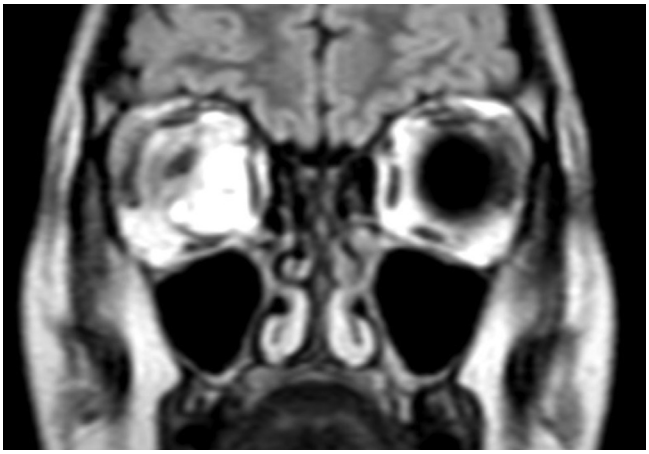

Fig. 35. Patient 7. Mixed lymphatic malformation of the right orbit. Coronal MRI. The LM conspicuously involved the orbital content.

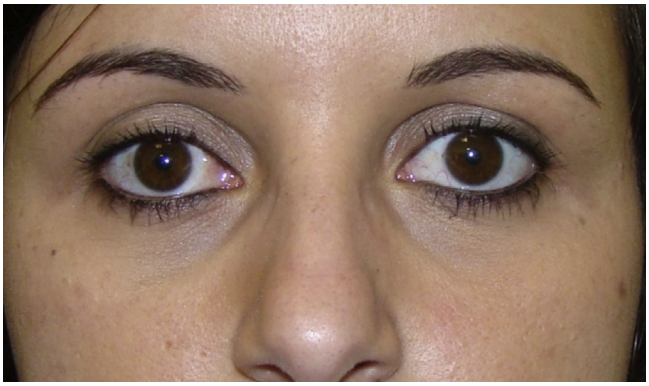

Fig. 36. Patient 7. Mixed lymphatic malformation of the right orbit. Postoperative frontal appearance after 1 session of sclerotherapy with bleomycin. The eyeballs are now symmetric.

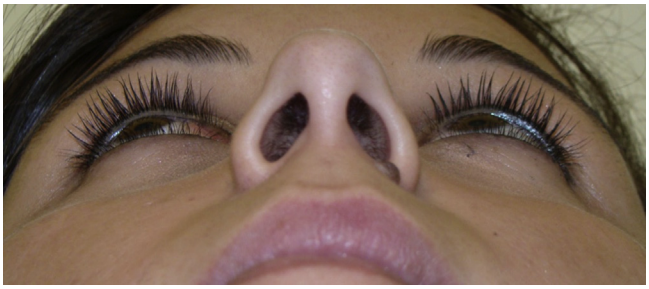

Fig. 37. Patient 7. Mixed lymphatic malformation of the right orbit. Postoperative worm's eye view. No residual exophthalmos is detectable.

The microcystic component of a LM is always infiltrative by nature and thus a clear cleavage with the surrounding orbital structures is lacking. Any surgical approach must take into account this aspect and must be aimed either at partial removal or at orbital decompression (Figs. 39–46). Relapses, as a direct consequence, are common. For these reasons, we believe that orbital LMs should have absolute indications for treatment in the presence of vision disturbances only, and that treatments with cosmetic purposes should be clearly discussed with the patient.

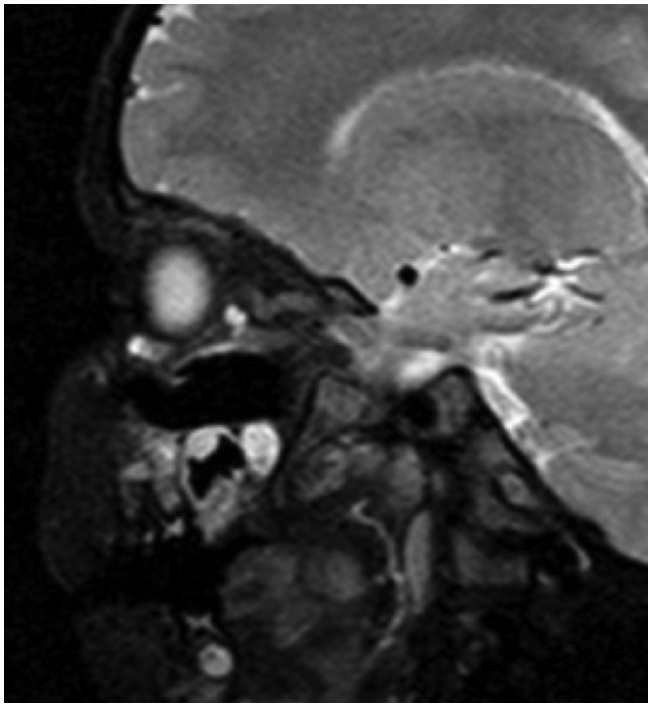

Fig. 38. Patient 7. Mixed lymphatic malformation of the right orbit. Postoperative sagittal MRI. No residual disease.

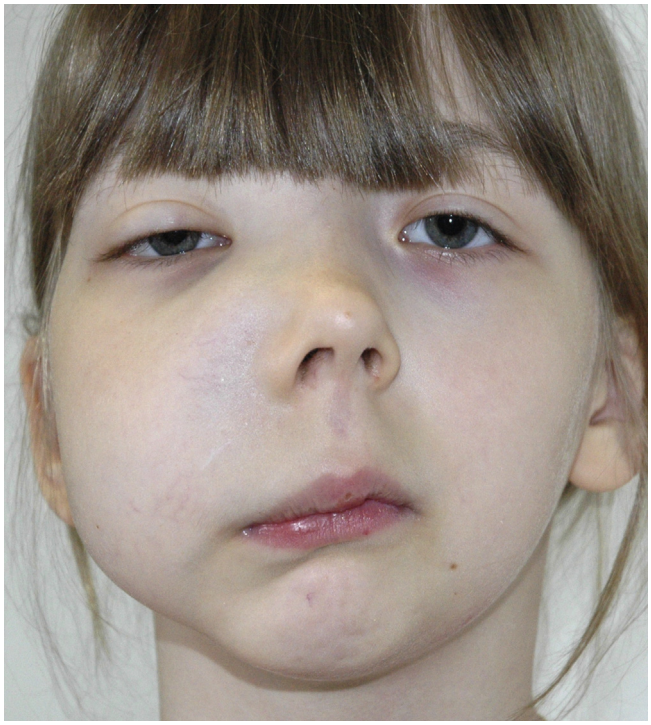

Fig. 39. Patient 8. Microcystic lymphatic malformation of the right orbit. Preoperative frontal appearance. The malformation infolves almost all the middle and lower third of the face of this patient. The eyeball is dislocated inferolaterally.

4.5. Arteriovenous malformations

AVMs of the orbit are very critical. Different from all other vascular malformations, AVM possess an invasive behavior, tend to

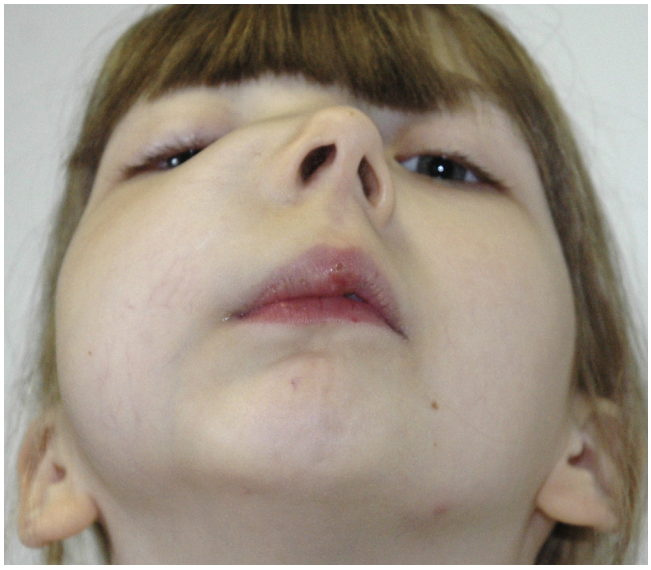

Fig. 40. Patient 8. Microcystic lymphatic malformation of the right orbit. Preoperative worm's eye view. A complex deformity is produced on the soft tissues as well as on the bone.

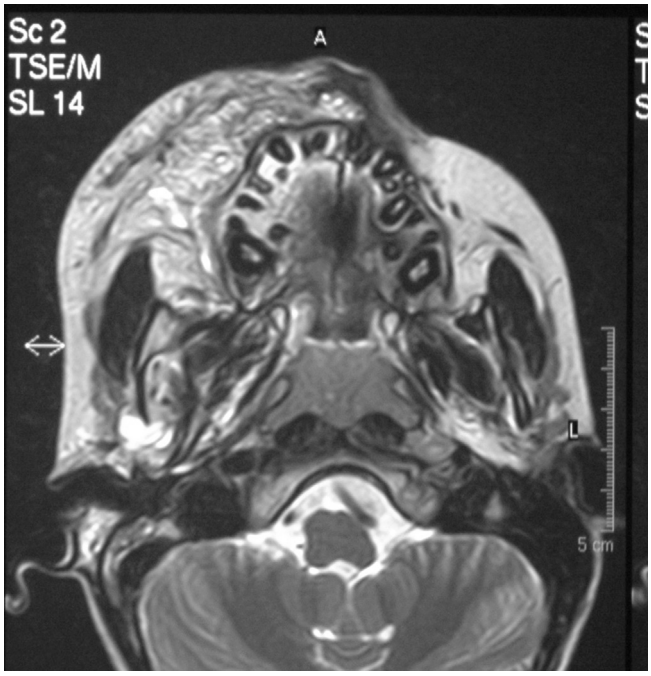

Fig. 41. Patient 8. Microcystic lymphatic malformation of the right orbit. Preoperative Axial MRI. A diffuse infiltration of the soft tissues by the small chambers of the malformation is seen.

progress in size and to be complicated by ulceration, bleeding, infection and, although rarely, they can cause heart failure. Moreover, when AVMs are approached incorrectly (either with surgery or endovascular treatment), they may react with an explosive growth, leading to a much worse clinical situation (Liu et al., 2010).

Clinically, AVMs appear as lesions with indistinct margins and signs and symptoms that are relative to the stage of the disease. Schœbinger Stage I AVMs may appear as simple skin staining with redness and warmth. With time they will progressively grow, and, as a Stage II is reached, then pulsations, bruits and tortuous dilated

Fig. 42. Patient 8. Microcystic lymphatic malformation of the right orbit. Intraoperative detail. Through a blepharoplasty incision the malformation involving the lid is removed.

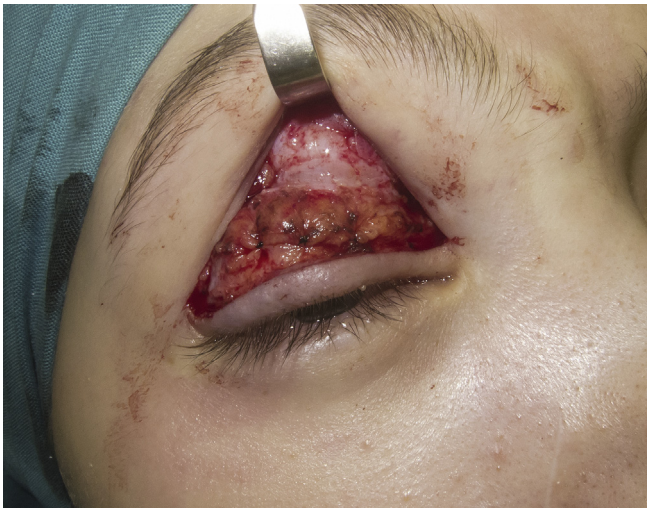

Fig. 43. Patient 8. Microcystic lymphatic malformation of the right orbit. Intraoperative detail. The tarsus is suspended with non adsorbable stitches.

Fig. 44. Patient 8. Microcystic lymphatic malformation of the right orbit. Intraoperative detail after a second surgery. The remaining medial part of the malformation is removed through a direct access.

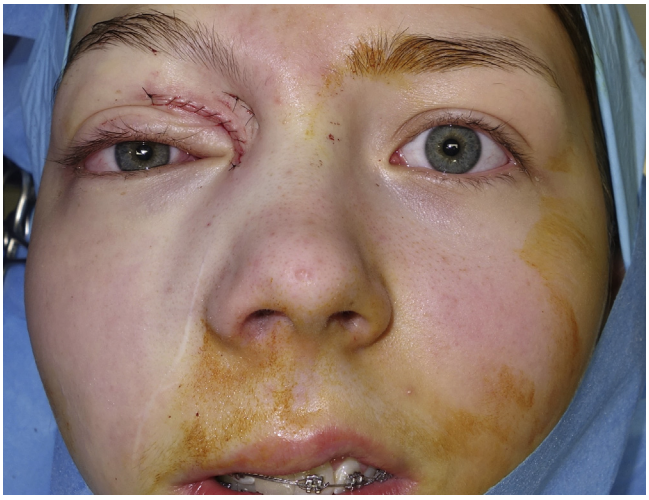

Fig. 45. Patient 8. Microcystic lymphatic malformation of the right orbit. Appearance at the end of the second surgery. A repositioning of the medial canthal tendon has been carried out at the end of the procedure.

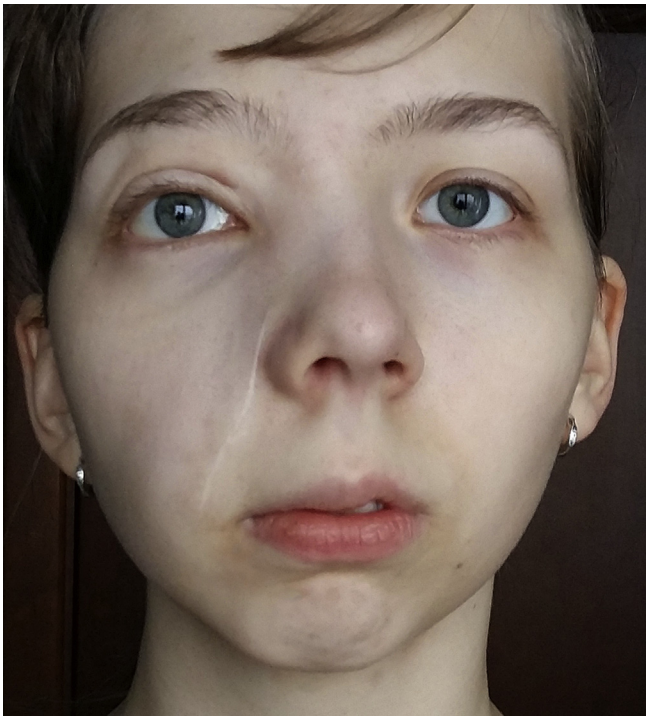

Fig. 46. Patient 8. Microcystic lymphatic malformation of the right orbit. Postoperative appearance. A good symmetry of the eyeball was obtained.

veins become apparent. Stage III is characterized by local complications such as ulceration, bleeding, infection and pain. Vast AVMs may reach Stage IV, with general complications. The AVM will produce a flow-steal syndrome with chronic fatigue and heart failure that may eventually be fatal.

On conventional MRI with or without contrast, AVMs are characterized by flow voids as the high-flow vessel that nourish them are visualized as voids. TRICKS MRI is particularly useful because it can give a precise topography, mapped in time, of arterial afferents and venous drainage.

Conceptually, AVMs should receive therapeutic planning closely resembling an oncological approach: that is, every effort should be

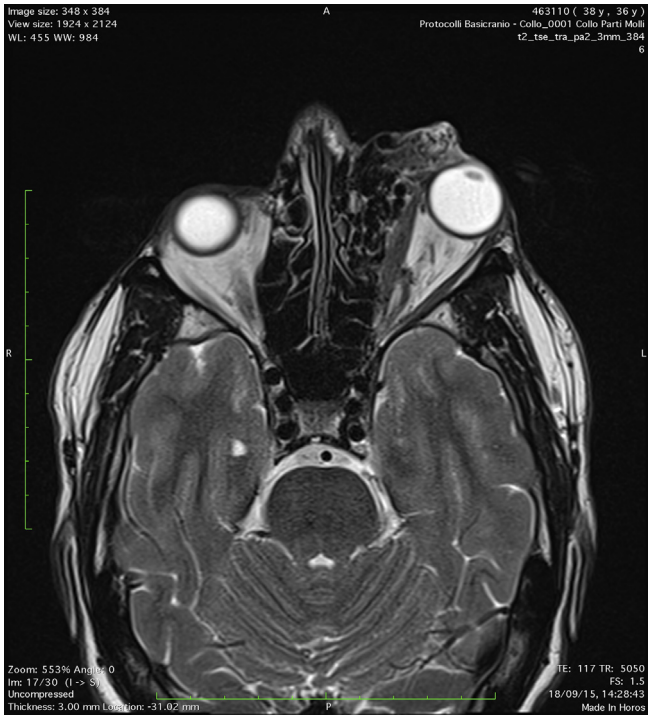

Fig. 47. Patient 9. AVM of the left orbit. Preoperative MRI Axial view. A plethora of tortuous and dilated vessels infiltrate the orbit.

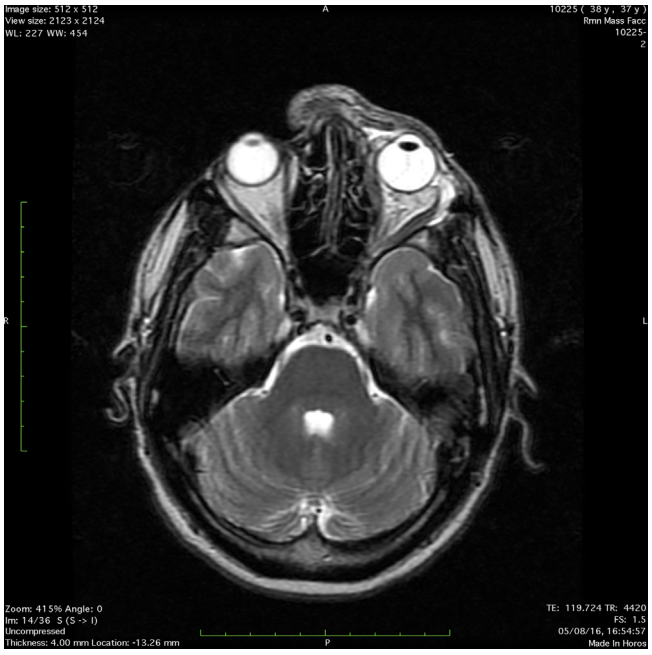

Fig. 48. Patient 9. AVM of the left orbit. Postoperative MRI Axial view. No residual disease is detected after surgical removal of the malformation.

made to remove them entirely (Liu et al., 2010). This may be achieved with relative ease in other parts of the body. However, it very rarely is the case when dealing with orbital AVMs. Orbital AVMs then present with two more crucial aspects. The first one is the significant risk of intraoperative bleeding. This could be reduced by preoperative embolization. However, in all of our patients this was not doable, since they were treated with endovascular approaches

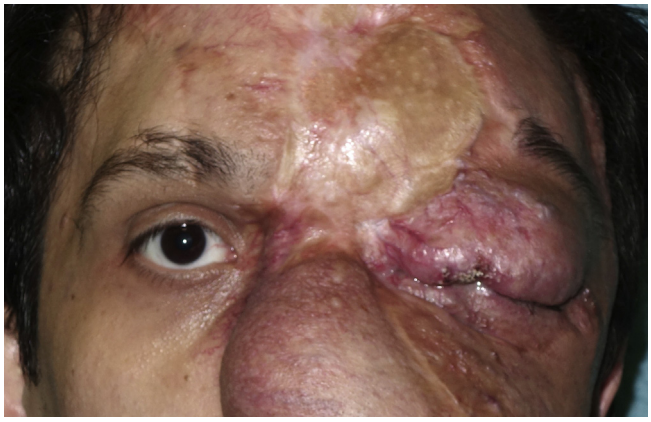

Fig. 49. Patient 10. An Arteriovenous Malformation of the left hemiface involves the orbit and causes a subtotal obliteration of the orbital rim.

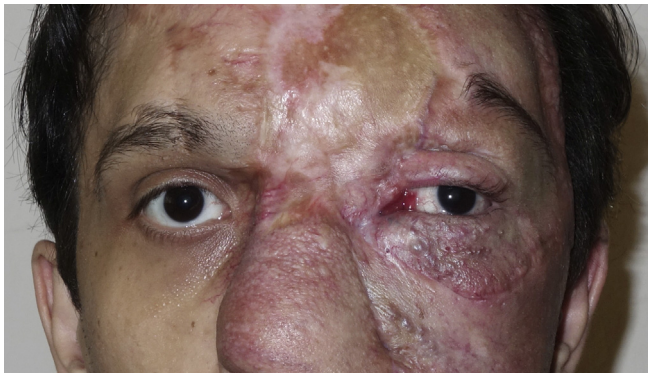

Fig. 50. Patient 10. Arteriovenous Malformation of the left hemiface. Postoperative appearance after debulking the lids and medial and lateral canthal repositioning. An acceptable symmetry was achieved.

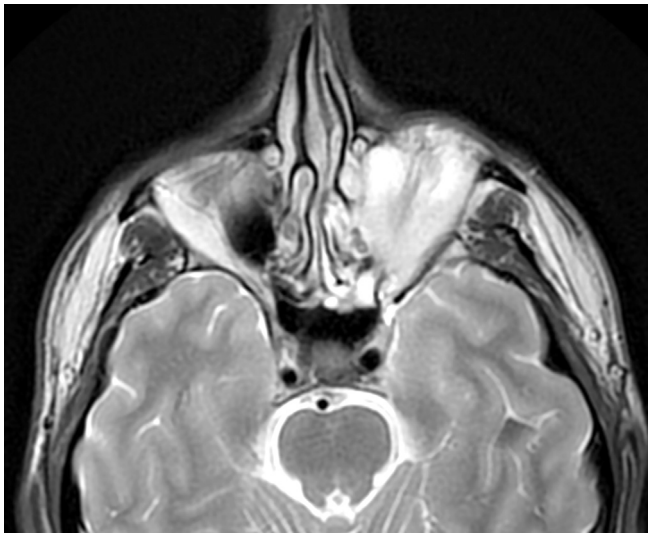

Fig. 51. Patient 11. Valsalva augmented T2w Axial MRI: an OVM3 is occupying the left orbit and pushing the orbital content out.

elsewhere before and there was no room for re-treatment. The second, intuitive aspect is the need (or at least the purpose) to preserve vision and extrinsic movements of the eye. Considering all

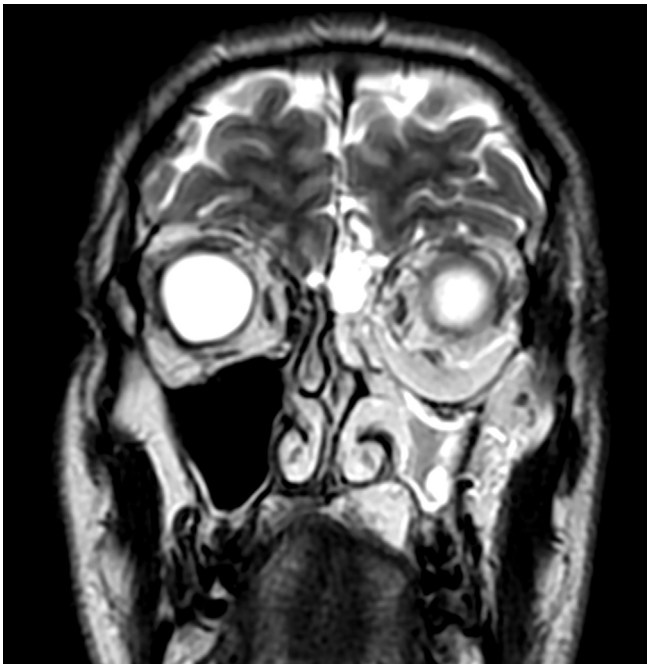

Fig. 52. Patient 11. Valsalva augmented T2w Coronal MRI: the OVM3 involves the left orbit, maxilla, palate and infratemporal space.

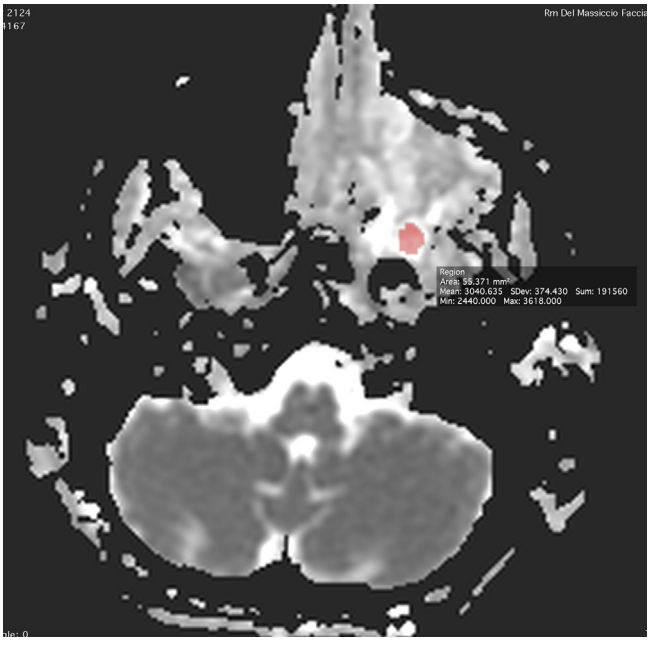

Fig. 53. Patient 11. DWI-ADC. ROI has been drawn in the area affected by the OVM3. A value of 3.04 mm/s2 is measured. A diagnosis of VM is 100% sensible and specific.

these aspects together, as far as indications to treatment are concerned, orbital AVMs can be divided into two groups: (1) potentially curable AVMs, and (2) AVMs for which a cure will never be achieved. Group 1 AVMs fall then two distinct settings: those AVMs that can be cured without impairing functionally and esthetically relevant structures; and AVMs that can be cured only by sacrificing relevant structures (Figs. 47 and 48). This must be clearly discussed with the patient who may choose the radical treatment or to let the disease fall into group 2.

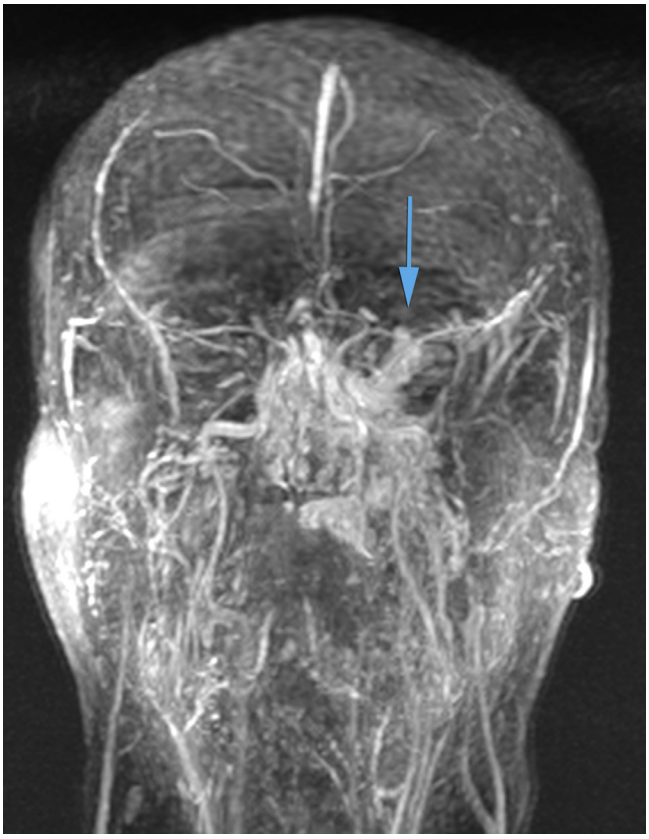

Fig. 54. Patient 11. Late phase TRICKS MRI. A venous flow into the cavernous and sigmoid sinus becomes evident (arrow).

Group 2 orbital AVMs are ab initio not curable because they involve vital structures that cannot be sacrificed or they can comprise group 1 AVMs where a non-radical treatment has been chosen. A non-radical approach has few indications (Figs. 49 and 50). Hemorrhages, pain and visual disturbances usually require treatment. On the other hand, bare morphological (esthetic) impairments are usually not an indication for surgery. Indeed, the risk of triggering an explosive growth spur after surgery is significant.

5. Conclusion

Virtually any kind of vascular malformation can take place inside the orbit. A profound knowledge of the different features that characterize them is essential for an appropriate diagnosis.

Distinguishing between LM, VM and AVM is crucial for a correct treatment.

Moreover, venous malformations of the orbit (OVM) have to be further differentiated into OVM1, OVM2 and OVM3, since each type has to be treated differently. Overall the results of this large case series seem to confirm that vascular malformations of the orbit should be treated in highly specialized centers where a multidisciplinary discussion and planning of the single case can be obtained; this is a prerequisite for lower morbidity and better outcomes.

Conflict of interest

The authors have no conflict of interest to declare. This work received no support in form of grants.

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