CASE REPORT

Fluctuating nature of an orbital venous-lymphatic anomaly in association with intracranial vascular malformations: a classical presentation

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SUMMARY

Venous-lymphatic anomalies (VLA) are rare and benign congenital lesions of the lymphatic system, composed of endothelial-lined lymphatic cysts. They are most frequently located in the region of the head and neck, and represent 4% of all orbital masses. In those patients with extensive orbital VLAs, a strong association with intracranial vascular anomalies has been reported. Factors known to suddenly increase the size of these lesions include upper respiratory tract infections or intralesional haemorrhage; however, complete spontaneous regression is rare. We report on the classic presentation of a patient with a fluctuating right orbital VLA in association with an intracranial cavernous malformation and intracranial developmental venous anomaly.

BACKGROUND

Venous-lymphatic anomalies (VLAs) are rare and benign congenital lesions of the lymphatic system, occurring in approximately 2.8 of every 100 000 births,¹ with a slight female predisposition (female: male ratio of 1.4:1).² They are composed of endothelial-lined lymphatic cysts, supported by a matrix of fibrous connective tissue.^{3–4} Lesions vary in size from a few millimetres to several centimetres in diameter.⁵ They are most frequently located in the region of the head and neck (48%), followed by truncal and extremity locations (42%), and intrathoracic or intra-abdominal locations (10%).⁶ Orbital VLAs represent 4% of all orbital masses⁷ and are unencapsulated, with a tendency to violate normal anatomical boundaries by infiltrating both intraconal and extraconal spaces in the orbit. They can enlarge suddenly due to intralesional haemorrhage or infection, with resultant lymphoid hyperplasia.⁸ Other common symptoms include eyelid swelling and/or ptosis, proptosis and chemosis. Visual disturbances, such as astigmatism, strabismus and amblyopia can occur.⁹ Notably, complete spontaneous regression is rare. We report on the classic presentation of the fluctuating nature of a right orbital VLA in a patient with an associated intracranial cavernous malformation and intracranial developmental venous anomaly.

CASE PRESENTATION

A 14-year-old girl presented to our institution in 2002 for evaluation of right upper eyelid ptosis. Her medical history was significant for a history of congenital malformation of the anterior segment of

her right eye, and glaucoma, for which she had undergone surgery as a young child. She also had a history of a right orbital VLA, discovered shortly after birth. She had been experiencing episodes of intermittent pain, proptosis and worsening ptosis of the right upper eyelid, associated with upper respiratory and sinus infections. On examination, visual acuity was 20/50 in the right eye and 20/20 in the left eye. She had no relative afferent pupillary defect or visual field defect suggestive of an optic neuropathy. Other pertinent findings on the right included 3 mm of right upper eyelid ptosis, 1 mm of proptosis and 5 mm of hypoglobus (figure 1A). A firm and mobile mass was palpable at the nasal aspect of the right superior orbital rim.

MRI of the brain and orbits showed areas of T2 hyperintensity in the intraconal space of the right orbit. A distinct, T2 hyperintense-enhancing mass located superior and medial to the right globe was also noted. Findings were consistent with a VLA. Much of the venous component was located anterior and superior to the orbit with a small portion invading the anterior right orbit (figure 2A). MRI of the brain also showed a non-contiguous right basal ganglia cavernous malformation and an associated developmental venous anomaly (figure 3A, D). Treatment options were discussed, but the patient was lost to follow-up.

Figure 1 Clinical photographs from 2002 (A) and 2011 (B) demonstrating right upper eyelid ptosis and significant right hypoglobus. The superficial extraconal venous malformation (arrow in (B)) visibly increases in size from 2002 to 2011.

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Figure 2 MRI of the orbits. Axial T2-weighted images at the level of the orbits from 2002 (A), 2009 (B) and 2011 (C) showing stability of the superficial extraconal venous malformation (arrowheads). The intraconal lymphatic malformation (arrows) significantly increases in size in 2009 (B) and spontaneously regresses in 2011 (C). Note the characteristic fluid-fluid levels of the lymphatic malformation in (B).

In 2009, the patient returned with a 1-week history of pain in her right eye, particularly on movement of the eye, and double vision in up and lateral right-gaze. Visual acuity in the right eye was unchanged although she had increased right proptosis. She was taking clindamycin for a wisdom tooth infection.

MRI of the orbits and brain showed enlargement of the T2 hyperintense right intraconal mass, with new fluid-fluid levels characteristic of intralesional haemorrhage into the VLA. The venous component superior and medial to the orbit remained relatively unchanged (figure 2B), while the right basal ganglia cavernous malformation had decreased in size (figure 3B).

The patient was seen twice in 2010, with her examination unchanged, and, in 2011, she wanted to pursue surgical resection of the superficial component. The only notable change in her medical history was the inclusion of NuvaRing hormonal therapy for contraception.

MRI of the orbits and brain showed a significant decrease in size of the VLA, consistent with resorption of the intralesional haemorrhage, a classic pattern. In contrast, the more superficial component was larger (figures 1B and 2C), and the right cavernous malformation continued to evolve by decreasing in size and developing a well-formed haemosiderin ring (figure 3C).

TREATMENT

The patient underwent preoperative percutaneous glue embolisation of the right superficial component by direct puncture using a 20% *N*-butyl cyanoacrylate glue concentration (figure 4). She tolerated the procedure well and there were no complications. The following day, the patient underwent a right anterior orbitotomy to surgically resect the superficial, extraconal aspect of the VLA. A right eyebrow incision was made with subsequent dissection carried out medially to the level of the nasal bridge. The lesion was noted to be highly vascular and was dissected out carefully using bipolar electrocautery. Once adequate debulking of the lesion was safely achieved, the eyebrow incision was closed and the orbital tissue sent for pathology. The patient did well post-operatively, with stable visual findings and significant debulking noted in the medial aspect of her orbit. Pathology of the lesion was consistent with VLA.

DISCUSSION

VLAs have been described as a type of hamartoma, with sequestration of primary lymphatics that fail to establish a normal connection with the central collecting lymphatic system.^{10 11} They

Figure 3 MRI of the brain. Axial T2-weighted images at the level of the third ventricle from 2002 (A), 2009 (B) and 2011 (C), demonstrating the evolution of a right basal ganglia cavernous malformation (single arrow in A–C). The characteristic 'popcorn ball' appearance with fluid levels and a complete haemosiderin rim are noted in all images. (D). Axial T2-weighted image at the level of the lateral ventricles showing the associated draining vein (double arrows) of the developmental venous anomaly.

Figure 4 Ultrasound and fluoroscopic images obtained during percutaneous glue embolisation of the extraconal venous malformation. Ultrasound is utilised to visualise the globe (asterisk in (A)) and guide needle placement into the venous malformation (white arrow in (B)). The venous malformation (white arrow in (B)) is seen on ultrasound as multiple mixed hyperechoic and hypoechoic areas, corresponding to the multiple small venous sacs. Subtracted (C) and unsubtracted (D) frontal views after injection of contrast into the venous malformation (black arrows) are performed to confirm accurate needle placement and opacification of the venous malformation prior to glue embolisation.

are thought to develop during the sixth to seventh week of embryogenesis. While there has been no clear inheritance pattern detected, it is thought that these benign neoplasms may be driven by somatic mutations in one or more of the vascular endothelial growth factor genes.^{12–14}

A strong association between periorbital VLAs and intracranial vascular anomalies exists^{15 16} and was seen in our patient, who had a right basal ganglia developmental venous anomaly and cavernous malformation. Throughout her imaging studies from 2002 to 2011, the characteristic appearance and evolution of the cavernous malformation as described above, which had undergone previous haemorrhage, are seen as well as the stability of her intracranial developmental venous anomaly. This association highlights the importance of excluding a concomitant intracranial vascular malformation, which is usually asymptomatic and incidentally discovered but may be present with haemorrhage, headaches or other neurological symptoms.¹⁵ For this reason, evaluation with contrast-enhanced MRI of the brain and orbits is recommended soon after clinical diagnosis of periorbital lymphatic malformations.¹⁵

Complete spontaneous regression of VLAs has been reported to occur in <2% of documented cases,¹⁷ and is extremely rare. Rather, most cases, as in our own, demonstrate the classic fluctuating nature of acute intralesional haemorrhage followed by resorption of the blood products. While the exact mechanism of

regression is unknown, one hypothesis is that a localised inflammatory response in the VLA may result in regression due to endothelial damage such as that resulting from the use of therapeutic sclerosant compounds.¹⁸ Spontaneous involution of a facial VLA in a patient following local infection of the malformation has been reported.¹⁹ As a result, the possibility of an underlying infection, either known or unknown to the clinician, may lead to spontaneous regression of VLA.

A novel hypothesis for the spontaneous regression of VLA is the potential effect of hormonal contraception, specifically progesterone receptor agonists, on the vascular endothelium of the VLA. Progesterone has inhibitory effects on endothelial growth. Vazquez *et al*²⁰ demonstrated that cell signalling via the progesterone receptor can cause cell cycle and suppression of endothelial proliferation. Recent studies have shown that progesterone receptors are present on the endothelial cells of VLAs.²¹ Given that our patient began NuvaRing hormonal contraception between 2009 and 2011, this therapy may have contributed to the regression of the VLA, as the principal compounds of the NuvaRing contraceptive device are etonogestrel and ethinyl oestradiol, which are progesterone and oestrogen receptor agonists, respectively.

VLAs are rare, benign congenital lesions that are typically treated by interventional techniques similar to other slow-flow vascular malformations (eg, venous malformations). Their

complete spontaneous regression is rare, with proposed theories including a localised inflammatory response and inhibitory hormonal effects; however, a definitive causative factor has not been identified. Most cases, however, as in our own, do not reflect complete regression, but rather a fluctuating cycle of intralesional haemorrhage and resorption. In the absence of visual compromise, conservative management of an orbital VLA may be considered in addition to traditional sclerotherapy techniques. Furthermore, an MRI of the brain should be performed to exclude the presence of associated non-contiguous intracranial vascular anomalies (cavernous malformations and developmental venous anomalies) in patients with complex orbital VLAs.

Learning points

- ▶ Complete spontaneous regression of venous-lymphatic anomalies (VLAs) is rare.
- ▶ The classic presentation of orbital VLAs involves a fluctuating cycle of intralesional haemorrhage and resorption.
- ▶ The possibility of concomitant intracranial vascular malformations should be considered and evaluated by MRI of the brain in patients with superficial vascular malformations.

Competing interests None declared.

Patient consent Obtained.

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