

Percutaneous Sclerotherapy for Low-flow Vascular Malformations in Paediatric Patients: 6-Year Experience of a Multidisciplinary Team

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ABSTRACT

Objectives: The Vascular Anomalies Multidisciplinary Team at the Queen Elizabeth Hospital, Hong Kong, delivers one-stop integrated care by a comprehensive team of specialists and nurses to paediatric patients with vascular anomalies. This study aimed to review the efficacy, safety, and outcomes of percutaneous sclerotherapy performed at our centre for low-flow vascular malformations in paediatric patients.

Methods: A retrospective study of 49 paediatric patients who underwent sclerotherapy from 1 June 2009 to 30 June 2015 was performed. Of the patients, 25 were male and 24 were female, with a mean age of 6.3 years (range, 2 months to 17 years). In all, 29 (59%) patients had venous malformation and 20 (41%) had lymphatic malformation. The location of lesions included 25 (51%) in the head and neck, 11 (22%) in the trunk, and 13 (27%) in the extremities. The outcomes of treatment were reviewed from electronic patient records.

Results: A total of 98 sclerotherapy sessions were performed (mean, 2.0 sessions per patient; range, 1-8 sessions) by an interventional radiologist. Some procedures were performed in collaboration with paediatric surgeons, head and neck surgeons or ophthalmologists. The mean follow-up duration was 39.7 months (range, 1-75 months). The most commonly used sclerosants were sodium tetradecyl sulphate alone in 28 (39%) sessions, alcohol (ethanol) and lipiodol mixture in 24 (34%) sessions, and ethanolamine oleate in 10 (14%) sessions. For lymphatic malformations, doxycycline was used as the sclerosant in 27 (100%) sessions. General anaesthesia was administered in 85 (87%) sessions and local anaesthesia in 13 (13%). Among 46 patients, 35 (76%) reported a decrease in swelling and eight (17%) had complete resolution of symptoms. There were no major complications; 10 minor complications, including skin blistering and pneumonia, subsequently resolved.

Conclusion: A multidisciplinary approach in treating low-flow vascular malformations can offer patients an optimal and individualised treatment plan. Percutaneous sclerotherapy is an effective and safe therapy for certain vascular malformation lesions in paediatric patients.

Key Words: Lymphatic abnormalities; Sclerotherapy; Vascular malformations

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中文摘要

經皮硬化劑治療小兒低流量脈管畸形：一個多學科小組的六年經驗

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目的：香港伊利沙白醫院的血管異常診治多學科小組由多名專科醫生和護士組成，為血管異常的兒科患者提供一站式綜合處理。本研究旨在評估本中心以經皮硬化劑治療小兒低流量脈管畸形的有效性和安全性。

方法：納入2009年6月1日至2015年6月30日期間接受硬化劑治療的49名兒科患者為回溯研究對象，其中男性25例、女性24例，平均年齡6.3歲（介於2個月至17歲）。29例（59%）為靜脈畸形、20例（41%）為淋巴管畸形。病變部位包括頭頸部25例（51%）、軀幹11例（22%）和四肢13例（27%），並從患者電子病歷記錄中核對治療效果。

結果：由一位介入放射科醫生進行98次硬化劑治療（平均每名患者2.0次，介於1-8次），部分聯同小兒外科、頭頸外科或眼科醫生完成。平均隨訪期為39.7個月（介於1-75個月）。用於治療靜脈畸形的硬化劑包括十四烷基硫酸鈉（STS；28次〔39%〕）、酒精/碘油混合液24次（34%），以及乙醇胺油酸酯10次（14%）。用於淋巴管畸形的硬化劑為強力黴素27次（100%）。進行全身麻醉共85例（87%），局部麻醉13例（13%）。46例中，35例（76%）腫脹減輕、8例（17%）完全緩解。所有患者均未出現嚴重併發症，只有10例出現包括皮膚起泡和肺炎的輕微併發症，及後全部消退。

結論：多學科方法治療低流量脈管畸形為患者提供最佳個性化治療方案。經皮硬化治療對某些脈管畸形病變的兒科患者來說是有效和安全的。

INTRODUCTION

Low-flow vascular malformations are deformities that involve the venous or lymphatic system. They commonly present in infancy before the age of 2 years. Patients with low-flow vascular malformations often experience pain, bleeding, disfigurement, or loss of function. Percutaneous sclerotherapy is the mainstay of treatment for symptomatic low-flow vascular malformations. The Vascular Anomalies Multidisciplinary Team at the Queen Elizabeth Hospital, Hong Kong, was established in 2009 to deliver one-stop integrated care to these patients by a comprehensive team of specialists and nurses. The purpose of this study was to review the technical efficacy, safety, and outcomes at our centre for paediatric patients who underwent percutaneous sclerotherapy for a low-flow vascular malformation.

METHODS

Patient Population

This study was approved by Kowloon Central / Kowloon East Cluster Research Ethics Committee;

patient/guardian informed consent was not required for this anonymous retrospective study. Between 1 June 2009 and 30 June 2015, 49 paediatric patients underwent percutaneous sclerotherapy at our centre. Retrospective review of patient clinical records was performed to assess the lesion characteristics, preoperative and postoperative imaging findings, angiographic findings, procedure-related complications, and patient outcomes. The patients comprised 25 males and 24 females, with a mean age of 6.3 years (range, 2 months to 17 years). Among them, 29 (59%) had a venous malformation and 20 (41%) had a lymphatic malformation. The location of lesions included 25 (51%) in the head and neck, 11 (22%) in the trunk, and 13 (27%) in the extremities.

Patient Assessment

Patients with suspected vascular malformations who are referred to the Vascular Anomalies Multidisciplinary Team are assessed at the Joint Vascular Anomalies Clinic, which is held every 2 weeks. Patients are concurrently assessed by the paediatric surgeon and interventional radiologist, when a detailed clinical history, physical

examination, and physical measurements are obtained and medical photographs can be taken. A portable ultrasound machine is available for real-time ultrasound and Doppler examinations.

Preoperative Imaging

Ultrasonography

Ultrasonography is helpful in differentiating vascular malformations from other pathologies. It can also allow differentiation between low-flow lesions (venous malformations [VMs] or lymphatic malformations [LMs]) and high-flow lesions (arteriovenous malformations). Among low-flow VMs, 98% of cases demonstrate a heterogeneous echotexture, of which 82% are predominantly hypoechoic, 10% hyperechoic, and 8% isoechoic.¹ Sometimes, anechoic tubular structures (4%-50%) and pathognomonic phleboliths that are hyperechoic with posterior shadowing (16%) can be seen in low-flow VMs.^{1,2} Most VMs demonstrate monophasic (78%) or biphasic (6%) flow on Doppler ultrasonograms. However, in some cases there may be no detectable flow.³ Macrocystic LMs are usually enlarged anechoic spaces without detectable Doppler flow, whereas microcystic LMs may mimic VMs because they may appear hyperechoic in echotexture.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is useful in confirming the diagnosis of vascular malformation and excluding pathologies that may mimic vascular malformation clinically. It is also helpful in treatment planning. On MRI, VMs usually demonstrate a lobulated, serpentine, or infiltrative appearance. They are usually hypointense on T1-weighted images, and hyperintense on T2-weighted and T2-weighted short-tau-inversion recovery images. Intralesional signal voids indicate the presence of phleboliths or thrombosed vessels.² On contrast imaging, they usually show homogeneous or heterogeneous enhancement. Macrocystic LMs are usually lobulated and septated in appearance, hypointense on T1-weighted images, and hyperintense on T2-weighted and T2-weighted short-tau-inversion recovery images. They show no enhancement, except in the wall or septae.³⁻⁵ Microcystic LMs show fewer cystic components and also do not enhance.

Percutaneous Sclerotherapy Techniques

All sclerotherapy procedures are performed in our angiographic suite or in the endovascular operating room, which are both equipped with digital subtraction

and real-time ultrasound facilities. Procedures are usually performed under general anaesthesia, except for those performed in older children who have peripherally located lesions. Written informed consent is obtained from the patient's parent or guardian before procedures.

After the surgical skin site is prepared and sterile drapes have been applied, a safe puncture route to access the lesion is selected with the aid of ultrasound. Under ultrasound guidance, the lesion is punctured with a 23- to 25-G butterfly needle attached via a low-volume connection tube to a syringe of iodinated contrast diluted with saline. Occasionally, when lesions are superficial and small, puncture by direct visualisation or palpation is sufficient. After placement of the needle, back-flow or a 'flash' of blood is visualised. Contrast agent is then injected under fluoroscopic guidance to delineate the size and distribution of the lesion, visualise drainage veins, determine the flow rate and volume, and confirm the intraluminal position throughout the contrast injection process.

After anatomical delineation, the syringe of sclerosant is connected to the connection tubing, and sclerosant is injected at the appropriate rate and pressure. The contrast within the vascular malformation can be seen to be displaced by the sclerosant under the roadmap technique.^{6,7} For VMs, we most commonly use alcohol (ethanol) and iodinated contrast mixture (Omnipaque; GE Healthcare, Pittsburgh [PA], USA), as well as an alcohol and lipiodol mixture as sclerosants. Sodium tetradecyl sulphate (STS) foam and ethanolamine oleate were used in some of the earlier cases. Puncture of other sites of the lesion can be performed to optimise treatment results. The puncture needles are left in place for several minutes, followed by application of a compression dressing. Skin and neurovascular assessment is performed before the patient leaves the angiographic suite.

For LMs, especially macrocystic lesions, a needle or pigtail catheter is inserted into the dominant cystic space under ultrasound guidance, followed by contrast injection to delineate the lesion. The fluid contained within the lesion is then aspirated until the lesion is mostly collapsed. Afterwards, sclerosant is injected within the safe volume limits. Doxycycline is used as the sclerosant of choice in our centre. To minimise the radiation dose to patients, ultrasound visualisation during sclerosant injection is used. The injected sclerosant is allowed to dwell for about 4 hours before

being withdrawn via the pigtail catheter. Further rounds of sclerotherapy via the same pigtail catheter may be considered in sizeable lesions. The catheter is then removed after the procedure is complete.

Post-procedural Management

Patients are closely monitored in the paediatric intensive care unit until they are extubated and stabilised. Frequent skin and neurovascular assessment are mandatory immediately post-sclerotherapy. Adequate analgesia with oral acetaminophen and an opioid are given based on the anticipated level of pain. Non-steroidal anti-inflammatory drugs and steroids are routinely given for expected post-procedural swelling.

RESULTS

A total of 98 sclerotherapy sessions were performed (mean, 2.0 sessions per patient; range, 1-8 sessions). The mean follow-up duration was 39.7 months (range, 1-75 months). Sclerosants used for VMs included STS in 28 (39%) sessions; STS, alcohol and lipiodol mixture in three (4%) sessions; alcohol and lipiodol mixture in 24 (34%) sessions; alcohol and Omnipaque iodinated contrast mixture in six (8%) sessions, and ethanolamine oleate in 10 (14%) sessions. For LMs, doxycycline was used in 27 (100%) sessions. General anaesthetic was administered in 85 (87%) sessions and local anaesthetic in 13 (13%).

Currently, there is no established objective international standard for quantifying treatment outcome for vascular malformations. The definition of an adequate response varies among studies. It is widely accepted that the determining factor of treatment success and future therapy should be patient satisfaction and symptomatic improvement, rather than imaging findings.⁸ Therefore, in our study, treatment success was considered a subjective reduction of symptoms or complete resolution of a lesion as reported by the patient on follow-up. All electronic patient records were reviewed and recorded.

After treatment, among 46 patients who predominantly presented with swelling, 35 (76%) reported decreased swelling and eight (17%) had complete resolution of symptoms. Among three patients who presented mainly with pain, two (67%) reported significant pain reduction.

Post-treatment MRI was performed in 11 patients who had been scheduled for further intervention. Compared

with the MRI findings before treatment, lesion size was seen to decrease in five (45%) patients, to be similar in four (36%) patients, and to increase in two (18%).

Complications were defined according to the Classification System of Complications by Outcome in Society of Interventional Radiology Standards of Practice Guideline.⁹ There were no major complications directly related to sclerotherapy, such as permanent nerve injury, thrombophlebitis or deep venous thrombosis, pulmonary embolism, haemolysis, renal toxicity, anaphylaxis, bradycardia, or cardiovascular collapse. Ten minor complications were observed and included skin blistering or ulceration (after 7 sessions; 7%) and pneumonia (after 3 sessions; 3%). All resolved subsequently. No surgical intervention was required for the skin blistering or ulceration.

The imaging findings, digital subtraction angiography images from the sclerotherapy sessions, and clinical outcomes of selected cases are illustrated in Figures 1 to 4.

DISCUSSION

Percutaneous sclerotherapy is an established independent therapy for low-flow vascular malformations. Sclerosants that are introduced intraluminally will cause death of the adjacent endothelial lining and initiate a cascade of thrombosis and fibrosis within the lumen.¹⁰⁻¹² Different sclerosants exert their effect by different mechanisms. Ethanol is a potent agent; it causes endothelial damage and denatures blood proteins, leading to thrombus formation, and vascular occlusion.¹¹ Potential local complications include skin blisters or necrosis, transient pain, muscle contracture and motor or sensory nerve injury. It is therefore less useful for superficial cutaneous or mucosal VMs and those that are close to major nerves.¹³ Ethanol that escapes into the deep venous outflow may result in deep-vein thrombosis, pulmonary artery hypertension, pulmonary embolism, cardiopulmonary collapse and death. Careful injection to prevent extravasation or over-injection is vital, and the dose should not exceed 1 mL/kg.¹²

In contrast, STS is an ionic surfactant with a soapy consistency that induces endothelial cell inflammation and fibrosis. It is associated with a lower risk of local injury or systemic complications than ethanol but is not as potent. In earlier cases, STS was more frequently used by our interventionists, owing to its lower risk of potential complications should extravasation occur. As

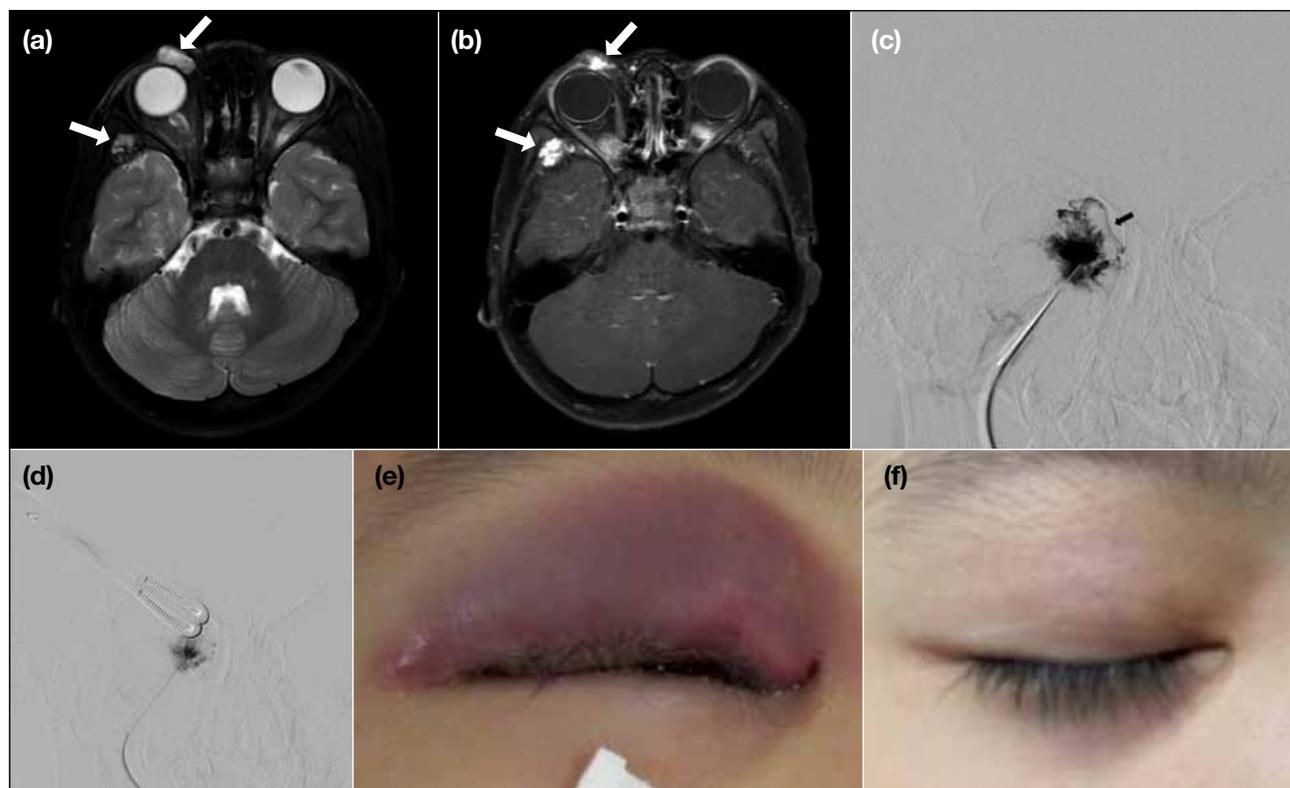


Figure 1. An 8-year-old patient with venous malformation on the right eyelid causing mass effect, with concerns of cosmesis and potential future visual complications. T2-weighted magnetic resonance image with fat-saturation (a) and T1-weighted image with fat-saturation following gadolinium administration (b) demonstrated a T2-hyperintense lesion at the medial aspect of the right upper eyelid, with homogeneous contrast enhancement. These features were compatible with a venous malformation. An incidental finding of another similar lesion in the right temporal region was noted. Percutaneous sclerotherapy was performed for the right upper eyelid venous malformation. After puncturing the lesion with a butterfly needle, a contrast venogram (c) was obtained to delineate the size of lesion, visualise drainage veins, determine the flow rate and volume, and confirm intraluminal position throughout the injection process. An intracranial draining vein was seen (arrow). Manual compression was applied to the draining vein with the aid of a clamp during the injection of ethanolamine oleate sclerosant (d). Immediately post-sclerotherapy, more swelling of the treated lesion was an expected finding (e). Follow-up clinical photograph (f) showed shrinkage of the lesion after sclerotherapy.

our interventional radiologists gained more experience in treating VMs, ethanol became the sclerosant of choice because of its superior potency, except for superficial lesions or lesions that were close to major nerves. They also used ethanolamine oleate—a salt of an unsaturated fatty acid with good thrombosing properties that has fewer neurological side effects,¹⁴ but is less penetrative, than ethanol. For treating LMs in children, the use of doxycycline as the sclerosant has been shown to be safe and effective, with a low complication rate.¹⁵ Potential systemic complications include haemolytic anaemia, hypoglycaemia, and metabolic acidosis.¹⁶

During injection of sclerosants, great care must be taken to identify any extravasation, non-target migration of sclerosant, or venous reflux.¹⁷ Skin colour should

be monitored for signs of blanching, duskiness, or induration to prevent skin necrosis.^{6,18} It is also important to avoid over-distension of the lesion. For lesions with rapid venous outflow, temporary downstream occlusion using a tourniquet, pneumatic cuff, or focal compression with a vascular clamp may be effective in reducing sclerosant outflow and maximising endothelial contact time. However, caution must be taken, as a tourniquet may over-distend the VM. Moreover, on tourniquet release, there may be sudden uncontrolled release of a bolus of sclerosant into the draining veins.¹³

When a sufficient amount of sclerosant is injected, it is allowed to remain in place by leaving the puncture needles in situ for several minutes. After removal of the puncture needles, mild compression is applied to

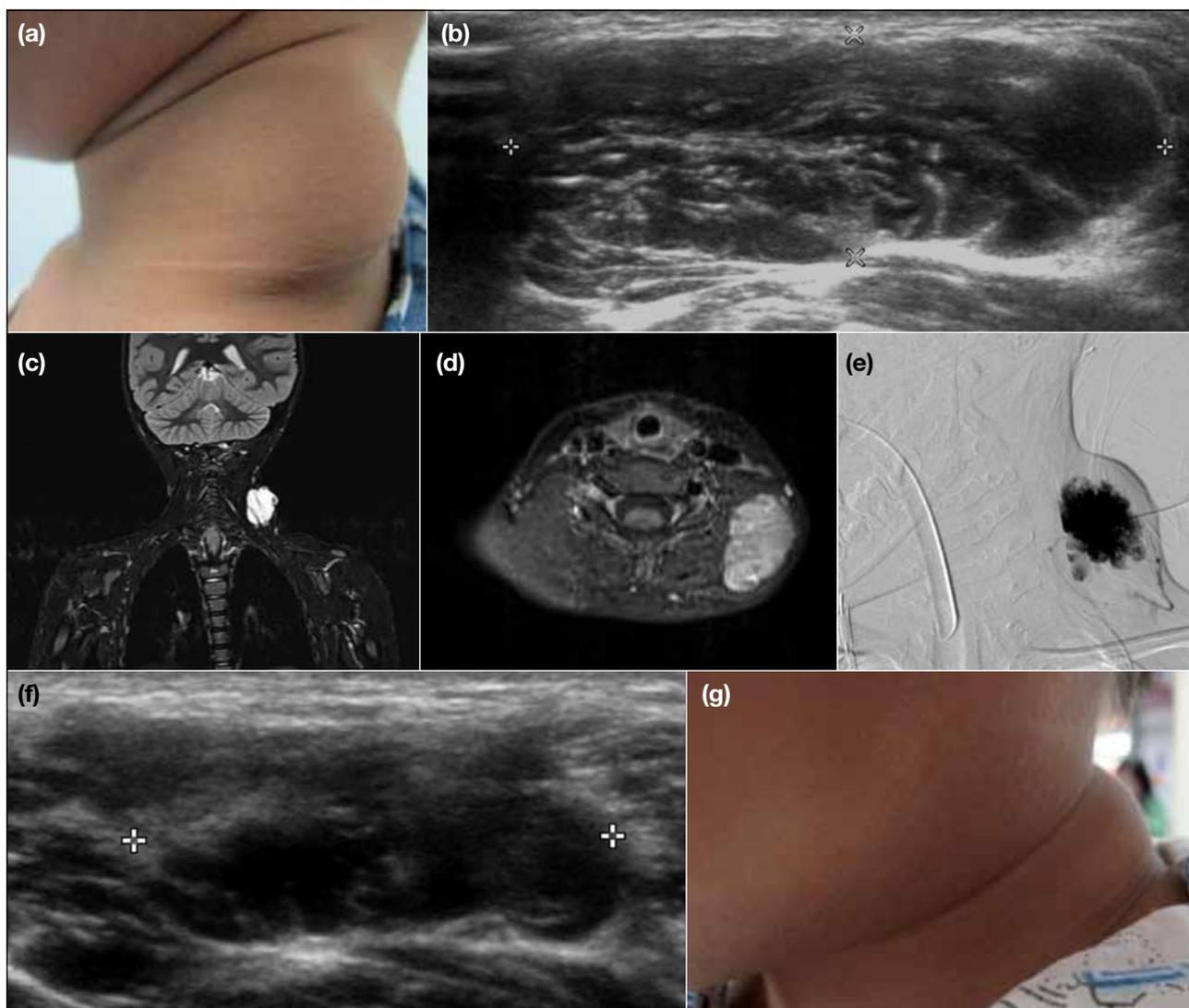


Figure 2. Clinical photograph (a) of a 4-year-old patient with right neck venous malformation. Ultrasonogram (b) showed a hypoechoic heterogeneous lesion with slight compressibility. On magnetic resonance imaging, T2-weighted short-tau-inversion recovery image (c) and T1-weighted image with fat-saturation following gadolinium administration (d) demonstrated a T2-hyperintense lesion in the left neck, containing thin septations and homogeneous post-contrast enhancement. These features were compatible with venous malformation. Percutaneous sclerotherapy was performed, using alcohol and lipiodol mixture as sclerosant (e). Post-sclerotherapy ultrasonogram showed shrinkage of the lesion (f). There was significant reduction in mass effect on follow-up (g).

augment wall apposition and healing of the lesion. It is important not to apply excessive pressure, as doing so may inadvertently cause the displacement of contrast to the outflow veins into the deep venous system.

In our opinion, the decision to repeat treatment should be based on the clinical response and persistence of symptoms during clinical follow-up. Follow-up ultrasonography or MRI should be used as an adjunct modality to assess treatment response. Follow-up MRI

evaluation of treated VMs is recommended preferably at 6 months post-procedure, because inflammatory changes can be slow to resolve.^{2,6,7} Nonetheless, caution must be exercised in interpretation, especially in paediatric patients, as their physique is growing continuously. Comparison of lesion size alone based on imaging measurements may be misleading, as a treated lesion may appear similar in size or even enlarged in a growing child, whereas the child could be experiencing much-improved symptoms.

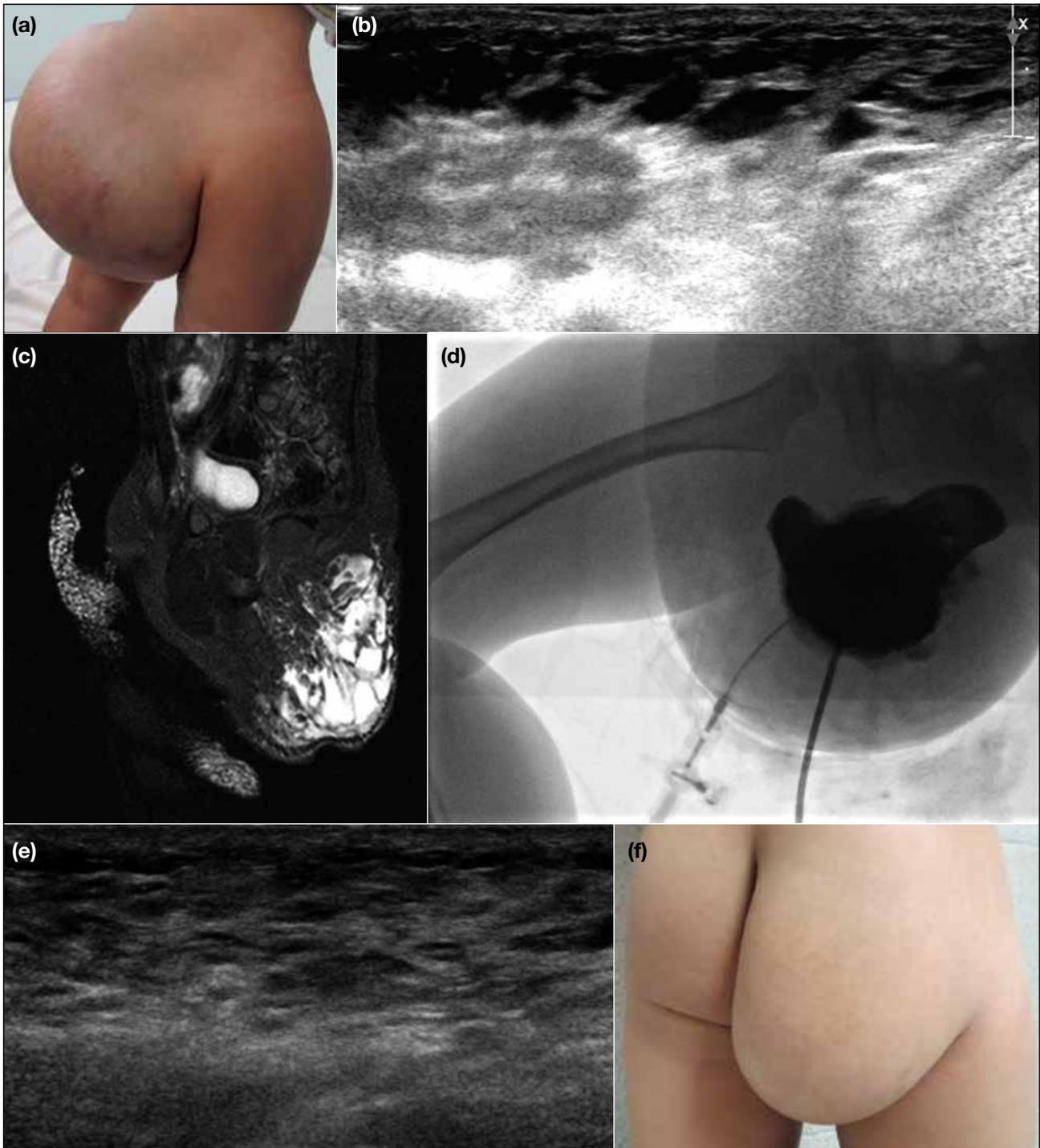


Figure 3. A 1-year-old patient with a massive right buttock lymphatic malformation (a). Ultrasonogram showed a large lesion with anechoic spaces (b). No Doppler flow was detected. T2-weighted with fat-saturation magnetic resonance image (c) demonstrated a large cystic mass without enhancement, consistent with lymphatic malformation. Percutaneous puncture and insertion of a pigtail catheter was performed. The lesion was outlined after contrast injection (d). After the position of catheter was confirmed, the fluid within the lesion was aspirated. Afterwards, doxycycline was administered via the pigtail under ultrasound visualisation, and the sclerosant was left within the lesion for about 4 hours before being withdrawn. A second sclerotherapy session was performed using the same pigtail owing to the large lesion size. Post-sclerotherapy ultrasonogram showed shrinkage of the lesion with smaller anechoic spaces (e). Three years after sclerotherapy, the lesion was significantly smaller in proportion to the patient's growing body (f).

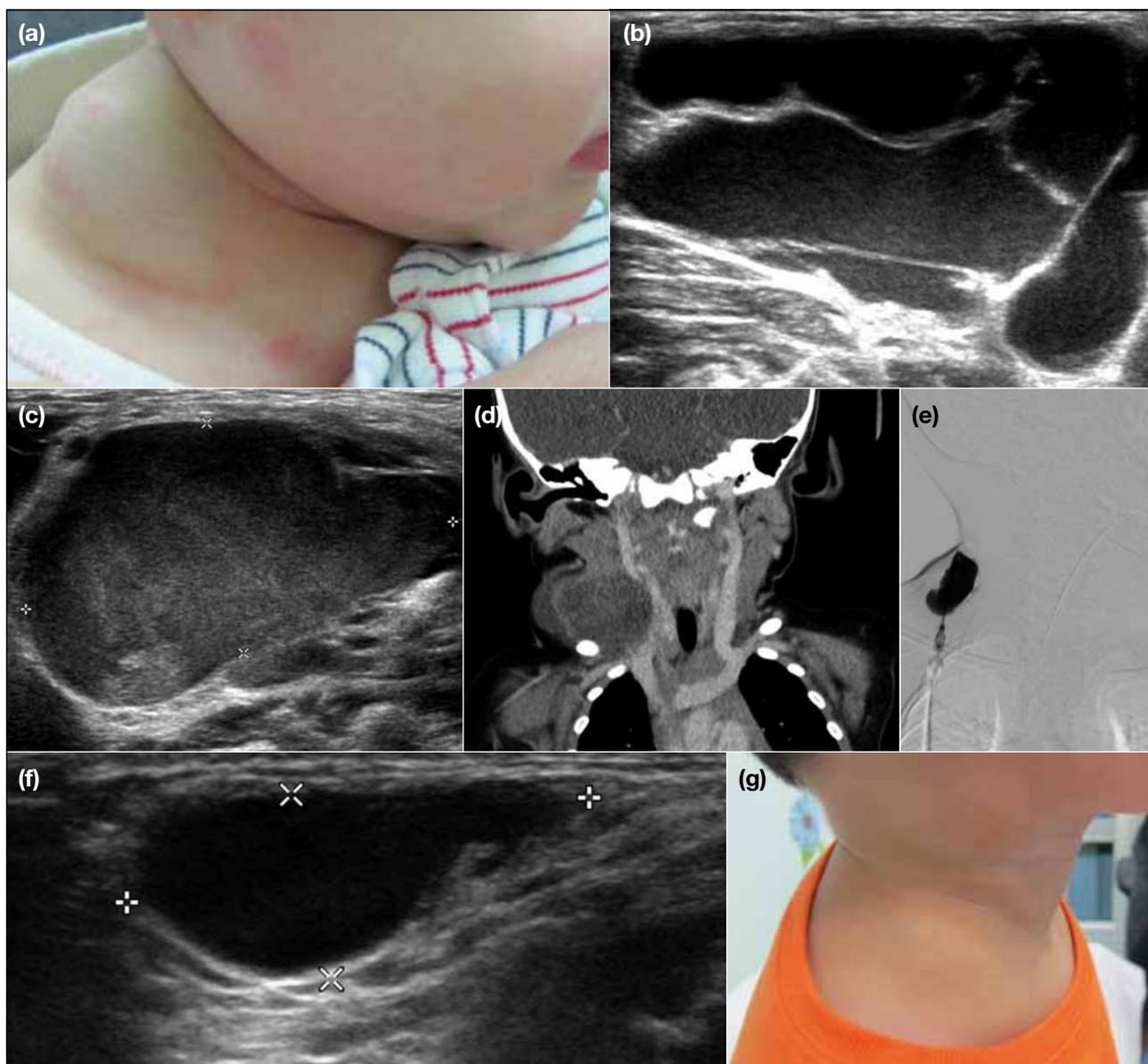


Figure 4. A patient with right neck lymphatic malformation who presented with a right neck mass at the age of 1 year (a). Ultrasonograms showed an anechoic lesion with septations (b), and areas containing low-level echogenicities suggestive of prior haemorrhage (c). No internal Doppler signal was seen. Computed tomogram demonstrated a well-defined hypodense lesion without enhancement (d). Percutaneous puncture of the lesion was performed with an angiocatheter; the lesion was opacified after contrast injection (e). Doxycycline was injected after aspiration of lymphatic malformation fluid. Follow-up ultrasonogram showed a reduction in lesion size (f), and the lesion became much less noticeable (g).

There are several limitations to our study. First, there is currently no internationally recognised grading system for the symptoms that arise from vascular malformations. The clinical response after treatment as reported by patients is subjective. In future studies, more objective pain scores would be helpful to evaluate the reduction in pain symptoms. Second, there is no

standardised follow-up imaging protocol for treated VMs and LMs, so the radiological response could not be analysed in this study. Moreover, since VMs and LMs can sometimes be extensive and infiltrative in morphology, the task of accurately documenting lesion size radiologically would pose a difficult challenge to the radiologist.

CONCLUSION

This study demonstrates that a multidisciplinary approach in treating low-flow vascular malformations can offer patients an optimal and individualised treatment plan. In addition, image-guided percutaneous sclerotherapy is an effective and safe treatment modality for low-flow venous and LMs in paediatric patients.

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