ORIGINAL ARTICLE

An institutional review of paediatric haemangiomas: prevalence, imaging features, and outcomes

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Objective To review the demographic data, imaging features, and outcomes of paediatric haemangiomas.

Design Retrospective study.

Setting University teaching hospital, Hong Kong.

Patients A total of 58 children diagnosed with haemangioma between 1998 and 2007.

Main outcome measures Demographic data, imaging features, type of treatment received, and outcomes.

Results In all, 19 (33%) of these patients were males and 39 (67%) were females. Most of the lesions (64%) were in the head and neck region. Three (5%) of the patients were complicated by the Kasabach-Merritt syndrome; 21 underwent no imaging, and 37 had ultrasound and/or magnetic resonance imaging. In the majority (85%), ultrasound of the lesions revealed mixed echogenicity and/or phleboliths with variable colour Doppler patterns. On magnetic resonance imaging, most (87%) of the lesions were T1 iso- to hypo-intense and T2 hyperintense with slight heterogeneous signalling and revealed presence of central flow voids (vascular channels) or low-signal areas (fibrous tissue or calcification). In all, 85% appeared homogeneous while 15% showed heterogeneous enhancement. Of 58 patients, 39 (67%) patients received conservative treatment; the lesions resolved spontaneously in 34 (87%) patients, enlarged in 2 (5%), and remained static in 3 (8%). Interventions were directed at the lesions in 19 patients. These entailed surgical excision (n=7), argon laser therapy (n=3), and medical treatment (n=9). Of the latter patients, treatment included: systemic steroids (n=5), interferon (n=1), steroids and interferon (n=1), vincristine (n=1), and sclerotherapy (n=1). Partial or complete resolution of the lesions ensued in 15 (79%) of the patients, while their size remained static in four (21%).

Conclusion Though ultrasound and magnetic resonance imaging features varied, the diagnosis of most haemangiomas could be confidently made by imaging. About 33% of haemangiomas underwent surgical/medical interventions, for which imaging was useful to monitor post-treatment progress.

Key words
Child; Hemangioma; Magnetic resonance Imaging; Soft tissue neoplasms; Ultrasonography, Doppler, color

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Introduction

According to the International Workshop for the Study of Vascular Anomalies,[1,2] based on their biological behaviour, haemangiomas are classified as a subset of vascular tumours as distinct from other vascular malformations. They are considered tumours of infancy that undergo a phase of rapid growth and expansion followed by a period of slow, but steady, regression during childhood.[3] Females are more often affected than males. Mulliken et al[1,2] also separated haemangiomas from vascular malformations: capillary, lymphatic, venous, arterial, or combined (capillary venous, lymphaticovenous, arteriovenous malformation). This classification has been clinically useful[2] and has facilitated correlation with angiography,[4] and was recently adopted for interventional radiology.[5] By and large, haemangiomas exhibit three phases which include proliferation, involution, and the involuted phase, with distinct histological, radiographical, and molecular findings. Rarely, haemangiomas may present atypically and can have life-threatening sequelae. In contrast,

vascular malformations consist of abnormal vascular channels which grow proportionately with the child, and do not undergo regression.

Although haemangiomas can occur anywhere, the head and neck is the site of predilection as noted in our series. Sporadic onset of haemangiomas is well known, is usually single, and autosomal dominant familial transmission has been reported.[6] Approximately 20% of affected children develop more than one lesion.

In this review, we described the demographics, imaging features, and treatment outcomes of paediatric patients presenting with haemangioma based on a 10-year experience at our hospital, which is a tertiary paediatric referral centre in Hong Kong.

Methods

Subjects were retrospectively identified from institutional records from 1998 to 2007 using the key word "vascular anomalies" for all patients aged up to 18 years, who referred for consultation under the specific team of Paediatric Haematology and Oncology. Electronic patient records were retrieved and from each record, the following information was specifically looked for: type of vascular malformation (eg haemangioma, lymphangioma), age at the manifestations, gender, presenting complaints, type of imaging investigations (X-ray, ultrasound, or magnetic resonance imaging [MRI]), location of haemangioma, initial size, treatment given (which included both medical or surgical treatment), follow-up imaging study to document progression, outcomes, and complications.

With respect to imaging, the following features were specifically evaluated: (a) ultrasound: echogenicity, margin, presence of phleboliths, colour Doppler pattern; and (b) MRI: signal intensity, homogeneity, presence of flow voids (representing vascular channels), low-signal areas (representing fibrous tissue or foci of calcifications), patterns of enhancement (which depended upon vascular angiomatous components of the lesion).

All the imaging findings were reviewed by two experienced radiologists by consensus reading. The study was approved by our institutional review board.

Results

From the database, a total of 77 patients with vascular anomalies were found, of whom 58 (75%) had haemangiomas. Relevant demographic data and locations of the lesions are given in Table 1. The majority (64%) of haemangiomas were subcutaneous and they were predominantly located in the head

小兒血管瘤的病發率、放射影像的特徵及結果：一所機構的資料回顧

目的 探討有關小兒血管瘤的病發率、放射影像的特徵及結果。

設計 回顧研究。

安排 香港一所大學教學醫院。

患者 1998至2007年期間共58名患有血管瘤的兒童。

主要結果測量 人口學資料、放射影像特徵、療法及結果。

結果 病人包括19（33%）名男童及39（67%）名女童。大部分（64%）病灶出現在頭及頸部；有3例（5%）併發卡－梅綜合徵（Kasabach-Merritt syndrome）。21例未進行放射檢、37例曾接受超聲檢及／或磁共振影像。超聲檢發現大部分（85%）病人的病灶呈混合性及／或靜脈石呈不同影像的彩色多普勒。磁共振影像上，很多（87%）病灶呈同等至低訊號及有輕微異類高訊號，顯示中間無訊號區（血管溝）或低訊號區（纖維組織或鈣化）的存在；85%呈均勻增強，15%呈不均勻增強。58例中，39例（67%）接受保守治療，結果34例（87%）的病灶自行緩解、2例（5%）病灶增大及3例（8%）病灶無變。19例接受介入治療，包括7例外科切除、3例氬激光治療及9例藥物治療。接受藥物治療的包括5例全身性類固醇、1例干擾素、1例類固醇及干擾素、1例長春新鹼、及1例靜脈曲張注射。接受介入治療的病人中，15例（79%）部分或整個病灶消失，4例（21%）的病灶則沒有消退跡象。

結論 雖然超聲及磁共振影像得出的影像特徵不同，放射影像肯定可以用來診斷血管瘤。約有33%血管瘤患者接受外科或藥物治療，用放射影像鑑察這些病人治療後的情況很有用。

TABLE 1. Demographic data and locations of haemangiomas

Demographics/location of haemangioma	Data*
Median age (range)	15 months (2 months-18 years)
Gender	
Male	19
Female	39
Locations	
Head and neck (including face, cheek, palate, orbit, maxilla, scalp, brain)	37
Axilla	1
Abdominal wall	2
Upper limb (including shoulder, scapula, arm, forearm, hand)	7
Lower limb (gluteus, thigh, calf)	8
Back	1
Thorax	1
Gastro-intestinal tract	1

* Data are shown as No. of patients, except otherwise indicated

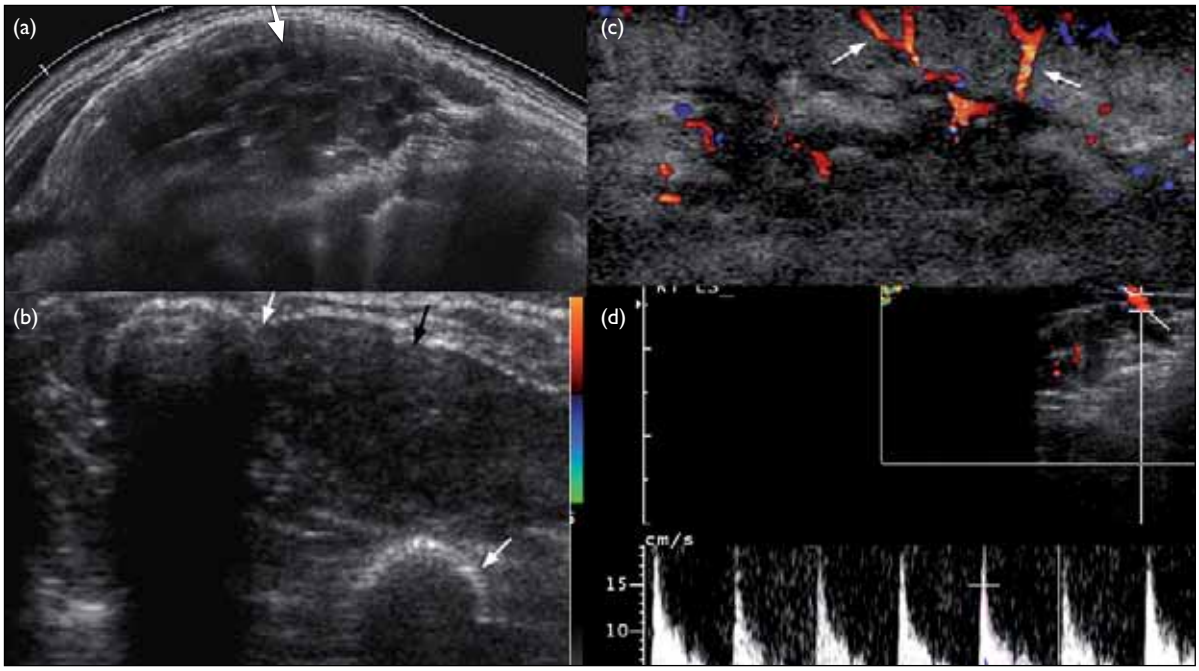

FIG 1. A 7-year-old girl presenting with painless forearm swelling since birth
(a) High-resolution grey scale ultrasound panoramic view of the forearm showing the heterogeneous predominantly hypoechoic haemangioma (arrow); (b) haemangioma (black arrow) and phleboliths (white arrows) are present with posterior acoustic shadows; (c) colour Doppler ultrasound shows fine vascular channels (arrows), the red and blue colours represent arterial and venous flow, respectively; and (d) Doppler spectrum: note the high spectral waveform denoting arterial flow

and neck region (Table 1).

In this cohort, 41 patients presented with a local swelling or mass, with or without associated skin discolouration, nine were asymptomatic and discovered incidentally (skin discolouration and/or mild swelling) during a health check, and eight had constitutional symptoms related to the lesion, including: anaemia (gastro-intestinal involvement), malaise, lethargy (left frontal cerebral involvement), sudden loss of consciousness and seizures (right frontal lobe involvement), visual deterioration (eyelid involvement), nasal growth (due to intranasal mass), dyspnoea (maxillary sinus involvement), right flank tenderness (extension of right thigh haemangioma into flank region), vulval bruising and sore buttock (left gluteal involvement). Three (5%) of the 58 patients were complicated with Kasabach-Merritt syndrome (purpura and bleeding) on presentation. These three patients had subsequent histological confirmation that they had a haemangioma.

Imaging findings

Of the 58 patients, 21 had no imaging (diagnosis was clinical based on characteristic bluish skin discolouration). These patients also represented milder cases. Of 15 patients with haemangiomas over the extremities, six underwent plain radiograph. In 37 patients, the lesions underwent imaging by ultrasound and/or MRI. On plain radiographs, the haemangiomas could always be identified as soft tissue masses. Phleboliths were seen occasionally.

On ultrasound, haemangiomas manifested as mixed echogenicity but predominantly hypoechoic. Characteristic small echogenic shadowing phleboliths were seen in a small portion of cases (20%) [Fig 1a and 1b]. Colour Doppler performed for 82% of the lesions showed variable flow patterns, depending on the phase of the haemangioma (proliferating or involuting). In all, 40% showed arterial, 45% showed venous, and 15% showed combined arteriovenous flow (Fig 1c and 1d).

On MRI, the majority (87%) of the lesions were T1 iso- to hypo-intense (Fig 2a) and T2 hyperintense with mild internal heterogeneous signals due to the presence of internal flow voids representing vascular channels and interspersed low-signal-intensity areas (corresponding to fibrous tissue, calcification, or areas of thrombosis) [Fig 2b]. Depending on the vascular angiomatous components, variable enhancement patterns were observed; 85% of lesions were homogeneously enhanced (Fig 2c), while 15% were heterogeneously enhanced. In four (7%) of the cases, there were atypical MRI features, including: large size, bizarre signal patterns with mixed intensities on both T1-weighted and T2-weighted sequences, irregular margins and local infiltration into the adjacent muscles and bones. In

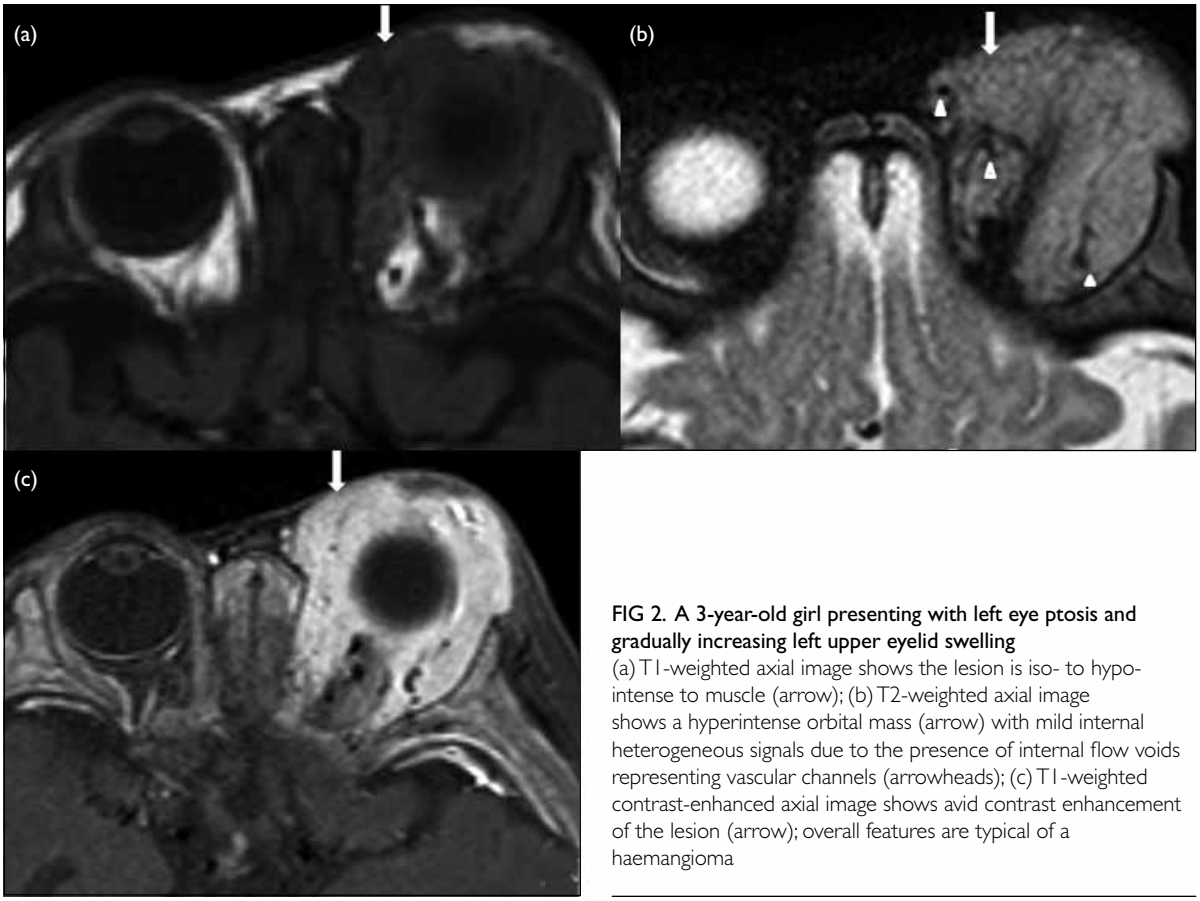

FIG 2. A 3-year-old girl presenting with left eye ptosis and gradually increasing left upper eyelid swelling
(a) T1-weighted axial image shows the lesion is iso- to hypointense to muscle (arrow); (b) T2-weighted axial image shows a hyperintense orbital mass (arrow) with mild internal heterogeneous signals due to the presence of internal flow voids representing vascular channels (arrowheads); (c) T1-weighted contrast-enhanced axial image shows avid contrast enhancement of the lesion (arrow); overall features are typical of a haemangioma

these cases, differentiation from other malignant soft tissue neoplasm was difficult based on imaging alone, in which case biopsy was crucial for making the ultimate diagnosis.

Treatment outcome

Of the 58 patients, 39 (67%) were asymptomatic and therefore they were treated conservatively (observation only). The remaining 19 (33%) patients received medical or surgical therapy. Reasons for interventions are: two had their haemangiomas excised during the proliferating phase due to recurrent bleeding (gastro-intestinal involvement) and airway obstruction (an intra-nasal mass); two others had intracranial haemangiomas, which were therefore excised; two underwent argon laser treatment because of visual impairment (eyelid lesion) and dyspnoea (maxillary sinus involvement); the remaining 13 lesions were treated because of poor cosmetic results even after involution; interventions included surgical excision (n=3), argon laser therapy (n=1), and medical treatment (n=9).

In the treatment group of 19 patients, 7 (37%) underwent surgical excision; 3 (16%) received argon laser therapy; 9 (47%) received medical treatment, including systemic steroids (n=5), interferon (n=1), steroids and interferon (n=1), vincristine (n=1), sclerotherapy (n=1) [Table 2]. All the patients who received treatment and a few under observations underwent serial imaging to monitor the size of their lesions. Of 39 patients on conservative treatment, 34 (87%) showed partial or complete resolution of their haemangioma during clinical follow-up, which was consistent with the natural course of this pathology. In three (8%) patients, the haemangiomas showed no change. Two patients (5%) manifested enlarging lesions during follow-up; one is a boy currently 14 years old with a congenital haemangioma over right scapula with extension into the chest wall and mediastinum. In the absence of definite feeding artery and its proximity to mediastinal structures, he was not deemed a candidate for surgical excision or vascular surgery, and is currently under consideration for injection sclerotherapy. Another boy is currently 7 years old, and presented with a congenital left facial haemangioma. His lesion was initially static but has increased in size recently, for which the option of sclerotherapy is also under consideration.

Regarding the 19 actively treated patients, 15 (79%) have had partial or complete regression of their lesions, and in 4 (21%) the lesions have remained static. Three received treatment at presentation due to complicating Kasabach-Merritt syndrome. Details of treatment type and outcome are summarised in Table 2.

TABLE 2. Treatment type and outcome in 58 patients with haemangiomas

Patients	Conservative treatment (n=39; 67%)	Active treatment (n=19; 33%)						
		Steroids (n=5; 9%)	Interferon (n=1; 2%)	Steroids + interferon (n=1; 2%)	Vincristine (n=1; 2%)	Sclerotherapy (n=1; 2%)	Surgical excision or vascular surgery (n=7; 12%)	Argon laser (n=3; 5%)
Group A (n=49; 84%) Decreasing size or completely resolved	34 (87%)	4 (80%)	1 (100%)	1 (100%)	1 (100%)	1(100%)	6 (86%)	1 (33%)
Group B (n=2; 3%) Increasing size	2 (5%)	0	0	0	0	0	0	0
Group C (n=7; 12%) Static size	3 (8%)	1 (20%)	0	0	0	0	1 (14%)	2 (67%)
Complicated by Kasabach-Merritt syndrome (n=3; 5%)	0	2 (40%)*†	1 (100%)‡	0	0	0	0	0

* A neonatal boy presenting with congenital left thigh haemangioma infiltrating into the pelvis, subsequently complicated by Kasabach-Merritt syndrome (platelet count, 17 x 10^9 /mm). He was put on platelet transfusion and high-dose steroid. His platelet counts returned to normal but the overall lesion remained static in size on imaging 4 years after treatment

† A 1-year-old girl presenting with rapidly increasing swelling of the left forearm complicated by Kasabach-Merritt syndrome. She was given prednisolone treatment. The haemangioma has decreased in size

‡ A 14-year-old boy presenting with huge left thigh swelling, complicated by Kasabach-Merritt syndrome and diplegia. He was put on interferon. The haemangioma has decreased in size

Discussion

In the majority of classical (infantile) haemangiomas, a clinical diagnosis can be accurately made based on history of timing and physical characteristics of the lesions (such as size, colour, surface characteristics, and tactile qualities).[3] In haemangiomas with atypical presenting features (dermal location, fully formed non-involuting or rapidly involuting varieties), imaging provides additional helpful information.[3] Plain films usually give no additional information for a clinically palpable soft tissue mass, except infrequently when phleboliths are found. Ultrasound is an imaging modality which is readily available, of relatively low cost, does not entail radiation, and is ideal for superficially located haemangiomas. As shown in this cohort, the grey-scale ultrasound appearance of haemangiomas is fairly typical (Fig 1). Using colour Doppler, by applying the criteria of high vessel density (>5/cm^2) and high Doppler shift (>2 kHz), the diagnostic sensitivity and specificity have been reported to be 84% and 98%, respectively.[7] In this cohort, we have detected vascularity in over 80% of our lesions.

Computed tomography can be used for imaging a proliferating haemangioma, which usually reveals a homogeneous mass with uniform enhancement after intravenous contrast. However, during involution, a haemangioma's fibro-fatty infiltration may give rise to a heterogeneous mass with decreased enhancement. In our institution, magnetic resonance rather than computed tomography is the preferred imaging modality for paediatric haemangiomas, as the former does not involve radiation and the lesion's relationship to adjacent structures can be better delineated.[8] Most cases in our cohort had classical magnetic resonance signals as described in the literature (Fig 2). As a rule haemangiomas can be differentiated from malignant soft tissue masses, based on morphology, signal intensity, and gadolinium enhancement patterns.[9] Some lesions, however, present atypical features with mixed intensities on both T1-weighted and T2-weighted sequences, irregular margins, extensive areas of necrosis and local infiltration into adjacent muscles and bones. Under such circumstances, the definitive diagnosis and differentiation from other soft tissue neoplasms can only be made histologically.

In general, 80 to 90% of all haemangiomas resolve without sequelae.[10] About 10% become complicated and predispose to ulceration, obstruction, bleeding, infection, congestive heart failure, and skeletal or aesthetic deformity.[11] According to other series, the risk of complications is greatest during the early to mid-proliferating phase when the haemangiomas are growing rapidly.[12] Complications including obstruction of the airway and coagulopathies have been reported. Involvement of bone and cartilage may lead to regional gigantism resulting in a detrimental psychological impact.[13] Kasabach-Merritt syndrome is a life-threatening uncommon complication of large haemangiomas, which is a kind of coagulopathy consisting of intravascular coagulation, clotting and fibrinolysis within the lesion manifesting as thrombocytopenic purpura.[14] In our cohort, only 5% of the patients had this complication, but had an uneventful recovery after treatment, although on follow-up they all had a residual haemangiomatous lesion.

There might have been selection bias in our cohort, as all the subjects had been referred from a special unit of Paediatric Haematology and Oncology

for consultation. At presentation, most of the patients had clinically alarming lesion (in terms of size or symptoms), though initially most were treated conservatively. The treatment decision for each case was discussed during regular meetings between paediatric oncologists, surgeons, and radiologists.

Aggressive treatment is subject to debate. In our institution, during the proliferative stage of most haemangiomas, intervention is only offered to patients with large lesions causing adverse systemic (Kasabach-Merritt syndrome) or local effects. The latter include obstruction of airways or vision, deformation (cranial, corneal, retroauricular), and gastro-intestinal bleeding. For Kasabach-Merritt syndrome or cardiovascular adverse effects, systemic steroids, interferon alone or in combination are used; steroids are regarded as the first-line treatment. For lesions in the face or upper eyelid, local injection therapy (with steroids or vincristine) is used, since both surgery and laser therapy are not helpful in the 'acute' stage. In the involuting phase, intervention is reserved for haemangiomas with poor cosmetic outcomes, such as those causing redundant skin. Laser therapy is considered for persistent superficial lesions, particularly for ulcerated lesions and those with post-involution residual.

In general, medical treatment including systemic steroids, interferon, vincristine, and sclerotherapy (alone or in combination), as well as laser therapy offer less invasive alternatives. Systemic steroid use should be short-term, so as to avoid longer-term complications, including childhood growth retardation. Interferon is now seldom given, since in young children it may be associated with cerebral diplegia; one of our patients also developed this complication. Vincristine may be tried in resistant cases but this chemotherapy involves intravenous injections. Laser and surgical therapies have a relatively limited role in large-sized problematic haemangiomas.[15] The feasibility of surgery and a planned approach depends on accurate delineation of the extent, size, and location of the lesion,[8,16] for which preoperative MRI is the imaging of choice. An important predictor for the success of argon laser therapy is the percentage of any affected area occupied by vessels. Cohen et al[8] have suggested that areas occupied by large vessels can be clearly identified with MRI, which may be valuable in predicting the success of laser therapy. Embolisation has been reported to have beneficial effects in infantile hepatic haemangiomas, but may be associated with life-threatening complications (heart failure, consumptive coagulopathy, and hepatic rupture). However, embolisation can save these very sick infants from undergoing hazardous procedures such as hepatic artery ligation or surgical resection.[17]

Recently, propranolol has been used for patients who have failed standard therapy. Léauté-Labrèze et al[18] have reported a remarkable therapeutic innovation for problematic haemangioma using propranolol at 2.0 mg/kg/day. Explanations for the therapeutic potential of propranolol (a non-selective beta-blocker) for treating infantile capillary haemangiomas include vasoconstriction. This becomes immediately evident as a change in colour, associated with a palpable softening of the haemangioma; decreased expression of vascular endothelial growth factor and basic fibroblast growth factor genes through the down-regulation of the RAF-mitogen-activated protein kinase pathway.[19] These two major proangiogenic factors are involved in the growth phase, which could explain the progressive improvement of such lesions, and the triggering of apoptosis of capillary endothelial cells[20] simulating the involution.[15] Careful monitoring is mandatory during early treatment, to mitigate adversity from potential side-effects (hypoglycaemia and hypotension). As the treatment is relatively safe and easily administered, it is now commonly started as first-line treatment. Our recent experience in few patients recently (after completion of this study period) has been encouraging.

In conclusion, we have described our institutional experience on the prevalence, imaging features, and treatment outcomes of patients with paediatric haemangiomas. About 64% underwent imaging to aid clinical diagnosis at presentation. Though ultrasound or MRI features are variable, about 90% of the haemangioma could be confidently diagnosed by imaging. About 40% of the patients underwent surgical/medical interventions, for which imaging was useful as a means of monitoring treatment response.

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