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Large parotid and cheek infantile hemangiomas refractory to medical treatment: Is there a role for embolization?

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ABSTRACT

Objectives: The aim of this study was to evaluate the results of transarterial embolization (TAE) as a stand-alone treatment for large parotid and cheek infantile hemangiomas (IHs) that are refractory to medical treatment.

Material and Methods: We retrospectively reviewed patients with head and neck IHs who underwent TAE at two single tertiary centers. We then analyzed the clinical and angiographic data of those patients with IHs located in the parotid and/or cheek regions.

Results: A total of 38 patients with head and neck IHs were treated with TAE. Sixteen patients had a follow-up 2 months or more after treatment; from these patients, 6 IHs were located in the parotid or cheek regions. Four of the six tumors were in the proliferative phase. After TAE, almost 100% of angiographic obliteration of the IHs was attained. There was a complete shrinking of the tumor mass in all patients within a period of 2–5 months. One partially reversible complication occurred.

Conclusion: Our preliminary results showed that TAE may be a useful therapeutic treatment not only before surgery but also as upfront and definitive therapy for parotid and cheek IHs.

Keywords: Embolization, Head and neck, Hemangioma, Parotid, Treatment

INTRODUCTION

Infantile hemangiomas (IHs) are the most common tumors of childhood. There are three types of IHs: Superficial, deep, or mixed. Superficial and mixed IHs appear in the first few weeks of life and grow rapidly, reaching their maximum size when the child is between 6 months and 8 months of age. The proliferative phase of deep IHs, however, could last up to 2 years. Deep IHs may proliferate for 12–14 months, although some cases have lasted up to 2 years. The onset of involution has not been clearly established, but it is usually signaled by a change in color from bright red to purple or gray.[1] Involution may begin by about 1 year of age and continue for 5–10 years.[2] At the end of the involutive phase, superficial and mixed IHs often leave disfiguring scars.[3] Rarely, a congenital hemangioma is seen fully developed at the time of birth.[4]

Most patients with IHs do not require any treatment because the IHs enters the involution phase and disappear. Only 10% of all patients will need therapy. Corticosteroid therapy was

traditionally used, but since 2008, propranolol has become the first-line treatment for IHs. Studies have shown that propranolol stops the growth and triggers remission in most parotid IHs.[5,6] However, 2–20% of patients with IHs may be resistant to propranolol or show contraindications.[7] Surgery may be prescribed to treat IHs that are in critical locations such as those that obstruct the airway or the visual axis, that are bleeding, or that are associated with Kasabach–Merritt syndrome. Large facial IHs that cause an aesthetic deformity also warrant excision to avoid psychological sequelae, although there is a risk of leaving a post-operative disfiguring scar.[8,9] To avoid excessive blood loss during the excision of large IHs, pre-operative transarterial embolization (TAE) may be prescribed.[4] Laser therapy can also be used to treat ulcers and scars from involuted IHs.[10] Radiation therapy is not used to treat patients with IHs because of its unclear correlation with long-term tumorigenesis.[11]

It can be challenging to assemble experienced head and neck, vascular, esthetic, and reconstructive surgeons to treat patients with IHs while ensuring that the necessary equipment for an embolization procedure is available. Since 1996, we have performed pre-operative TAE for selected patients with head and neck IHs that were found to be refractory to medical treatment or were prone to significant intraoperative bleeding. From our first cases, parents and surgeons noticed a rapid and remarkable shrinkage of the tumors after the TAE was performed, which caused the surgery to be deferred; for these patients, a wait-and-see strategy was adopted as surgery was not required and embolization remained as the sole treatment for IHs.

There is a scarcity of papers on the effectiveness of pre-operative TAE and even fewer reports on treating IHs only with TAE. Thus, the aim of this paper was to report on our experience with TAE as an upfront and definitive treatment of parotid and cheek IHs after failed medical treatment.

MATERIAL AND METHODS

Study population

We performed pre-operative TAE on 38 patients with IHs who were ≤12 years old between 1996 and 2019. Surgery had been prescribed for these patients because of the size of the IH, the location of the IH in functional areas or the IH presented as a significant aesthetic deformity for which treatment with corticosteroids or propranolol had failed. For the purpose of this study, we define an IH to be refractory to conventional medical treatment when there is no tumor shrinking after at least 2 months of receiving corticosteroid therapy using escalating doses of prednisone or prednisolone 2–4 mg/kg/day and or propranolol 1–3 mg/kg/day. The parents had provided consent for each patient. From the 38 patients, 6 had parotid and or cheek IHs. They received follow-up care for 2 months up to 2 years after TAE and constituted the population of this study. Their clinical files, photographs, and angiographies were studied and the findings described (table, and figure).

Embolization technique

The children were given general anesthesia, and a 5 French 10-cm introducer sheath was installed in the right femoral artery and a 5F guiding catheter was navigated into the right external carotid artery of the side of the IH. Angiograms were used to assess the dominant feeders, to verify the characteristic multilobulated, cotton wool angiographic aspect, and the flow pattern of the tumor. Using a road map and the coaxial technique, 2.4–2.8 French microcatheters with an inner diameter of 0.021'–0.02' inch and a 0.014' inch microguidewire were advanced distally in each feeder(s) to avoid reflux to the normal proximal branches. Polyvinyl alcohol (PVA) foam embolization particles (PVA-300®, Cook Medical, Bloomington, IN, USA), 300–500 microns in size, were injected in flux libre until the arterial supply of the tumor was obliterated. Our fluoroscopic rate was set to 1–2 images/s and we used the lowest radiation exposure possible. Once maximal embolization was reached or reflux was obtained, we performed angiograms, removed the catheters, and achieved hemostasis using manual compression of the puncture site in the groin. Once the patient was alert, he/she was sent to a recovery unit for clinical and neurologically monitoring for 2 h and then transferred back to the pediatric ward. Embolization was only performed once for all patients. All 6 TAEs were performed by the first author (ARP) and the second author assisted him in 3 of them. Each one has more than 20 years of experience in endovascular interventions.

Clinical assessment after TAE

Patients were clinically assessed and managed for 1 or 2 days and then were discharged to home. Patients were prescribed analgesics for pain; no other medication was given. A clinical follow-up was carried out for all patients after 2 weeks and then monthly for up to 6 months. Afterward, an annual follow-up was prescribed whenever possible. During the follow-up, patient's photographs were taken. Clinical follow-up of all patients occurred between 2 months and 2 years after TAE.

RESULTS

Our six patients ranged in age from 4 months to 4 years (mean 16.33 months and median 8.5 months); all patients

Table 1: Patient demographics, clinical and angiographic features of the IHs, and results of embolization.

Patient number	Age (in months)/sex	Extent of IH in the hemiface	Prior treatment (s)	Symptoms	TAE obliteration rate	Tumor shrinkage/ time elapsed after TAE (months)	Complications
1	4 F	70%	C, P	AD, pain, fear of rupture	100%	100% 2 months	Left hemifacial hypesthesia
2	5 F	50%	C	AD	100%	100% 4 months	None
3	48 F	70%	C	AD	100%	100% 4 months	None
4	24 F	50%	C	AD	100%	100% 5 months	None
5	8 F	50%	C, P	AD	95%	100% 6 months	None
6	9 F	60%	C (+ILT) with necrosis	AD	100%	100% 6 months	None

P: Propranolol, C: Corticosteroids, ILT: Intralesional triamcinolone, AD: Aesthetic deformity, IHs: Infantile hemangiomas

were female. The extent of the tumor in relation to the hemiface ranged from 50% to 70% (mean 58.33%). Four of the IHs were in the proliferative phase (66.66%). Table 1 summarizes the patient demographics, the clinical and angiographic features of the IHs, and the embolization and clinical results [Figures 1-6].

Some patients had been previously treated with oral corticosteroids, while two patients had received oral corticosteroids and propranolol. One patient also received previously an intralesional injection of triamcinolone in another hospital and developed central necrosis of the tumor (Patient 6).

All six patients were treated for aesthetic deformities and tumor hypersensitivity; one patient was also treated for pain. The arterial supply of the tumors was the branches of the external carotid artery, mainly the facial artery and the transverse facial artery. The mean devascularization rate achieved after TAE was 99.17%. Follow-up at 2–6 months (mean 4.33 months) after TAE showed that the tumor volume had shrunk by 100%.

Each patient underwent a single TAE. In one patient, a post-procedural neurological examination showed moderate ipsilateral facial hypoesthesia, which may have corresponded to trigeminal ganglion ischemia [Figure 1]. Thus, in this study, there was an overall short-term partially reversible complication rate of 16.66%.

DISCUSSION

About 60% of all IHs are located in the maxillofacial region.[12] The management of IHs that causes disfigurement is very difficult, and the negative emotional effects of IHs on parents should not be underestimated.[1,4,6] Surgical excision of IHs in the head and neck is limited to small lesions due to the risks of scar deformities, as well as potential injury to the facial and trigeminal nerves or to the facial muscles. Surgery is mainly used for the management of residual deformities left after natural or drug-induced tumor involution to improve cosmesis and function. TAE before surgery is advisable in large and richly vascularized tumors to decrease the tumor size and intraoperative bleeding.[4,13-17] Occasionally, TAE has been used as a primary therapy to treat bleeding IHs, large cervical or peripheral IHs, those that are associated with Kasabach–Merritt syndrome, and as an urgent treatment for alarming IHs.[18-25]

Embolization has been suggested as an upfront treatment of maxillofacial IHs, although the supporting evidence has been limited to case reports and studies of a series of cases that involve direct puncture and bleomycin sclerotherapy.[25-27] Few studies have investigated the effects of TAE using different embolic materials on IHs.[23-25] For example, Demuth *et al*. treated three patients with maxillofacial IHs with isobutyl cyanoacrylate.[23] Two patients developed skin necrosis and required further surgery; one patient developed post-operative ipsilateral loss of vision. The third patient did not require surgery. Patel *et al*. performed TAE in 10 patients, most of them children, who had non-involuting congenital IHs.[24] The embolization involved the use of 4F catheters and a wide array of embolic materials, including 25% n-butyl cyanoacrylate (n-BCA) dissolved in lipiodol, ethylene-vinyl alcohol copolymer, or microparticles of an inert PVA foam. Most of the patients also received direct percutaneous sclerotherapy of sodium tetradecyl sulfate, 98% ethanol, microfibrillar collagen, thrombin hemostatic matrix, and n-BCA. To achieve 12 months without lesion recurrence or progression, most patients required 1–2 treatments. Eight patients (80%) did not

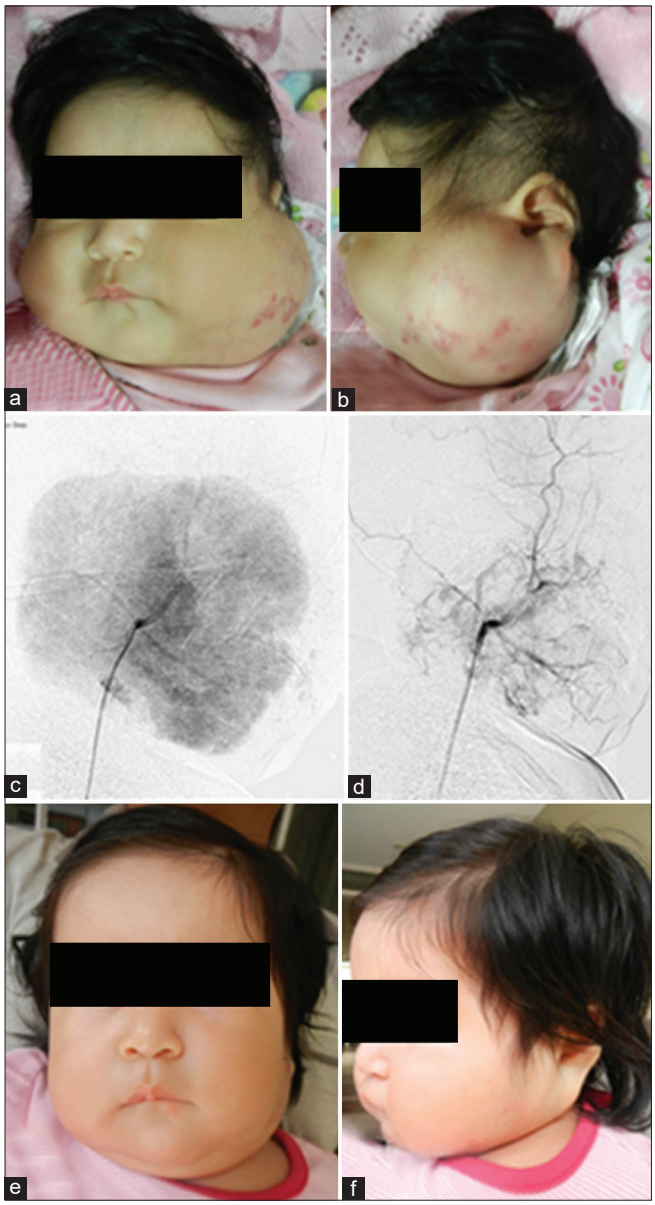

Figure 1: (Case 1): A 4-month-old baby girl with a large and rapidly growing, deep parotid/cheek IH. (a) and (b) Pre-embolization pictures. The tumor caused aesthetic disfiguring and pain. (c) and (d) The IH was embolized, notice the angiographic lobulated pattern of cotton wool appearance. (e) and (f) two months later the tumor was no longer visible, patients pain and irritability disappeared. The infant did develop a left facial hypoesthesia probably due to ipsilateral Gassers ganglion infarction with partial improvement over two years follow-up.

require surgery after treatment. Jianhong *et al.* treated 10 out of their series of 17 patients with IHs with TAE using both coils and the embolic mixture of n-BCA and lipiodol. Their other 7 patients had direct puncture and sclerotherapy with bleomycin.[25] During the follow-up period, their IHs that did not shrink to a satisfactory size

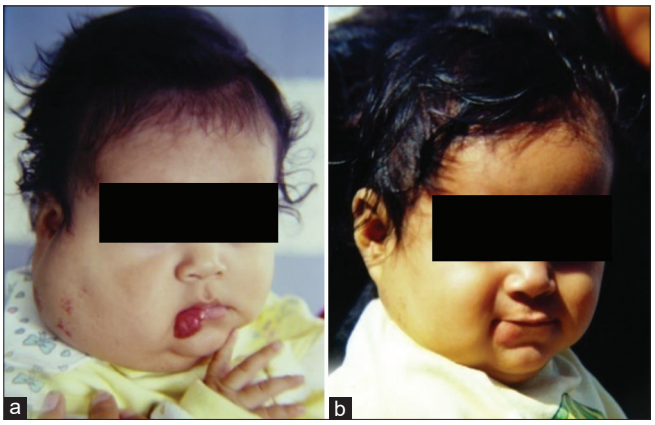

Figure 2: (Case 2): A 5-month-old baby girl with a right mixed parotid/cheek IH. (a) Pre and (b) 4 months post TAE. Surgical excision had been scheduled after embolization. The mother refused surgery due to the rapid and progressive shrinking of the tumor post TAE.

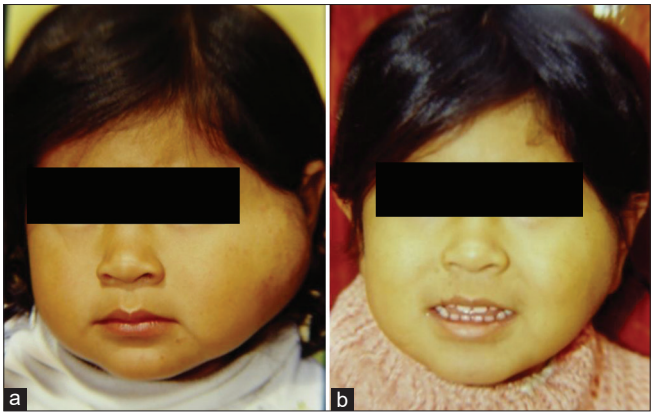

Figure 3: (Case 3): A 4-year-old girl with a deep left parotid/cheek IH with facial deformity. (a) Before, and (b) At 4 months' follow-up after 100% devascularization. The tumor regressed completely.

were additionally treated with intratumoral injections of bleomycin in lipiodol until the tumor reached a surgically manageable size. The mass of the tumors shrank ≥75%. Complications ranged from local pain to dyspnea that was associated with the migration of the embolic material to the lungs and was resolved after conservative treatment. There were no recurrences of the IHs during the follow-up period of 5–86 months, although five patients required surgery. The authors concluded that TAE plus bleomycin sclerotherapy is an effective therapy either alone or as a pre-operative adjunctive treatment for patients with extensive maxillofacial IHs.

In our study, we found that the tumor shrank 100% in six patients with deep or mixed IHs in the parotid or cheek region who were given TAE. Five of the patients did not require further treatment. Only one patient experienced complete involution after TAE; the patient had a mixed IH

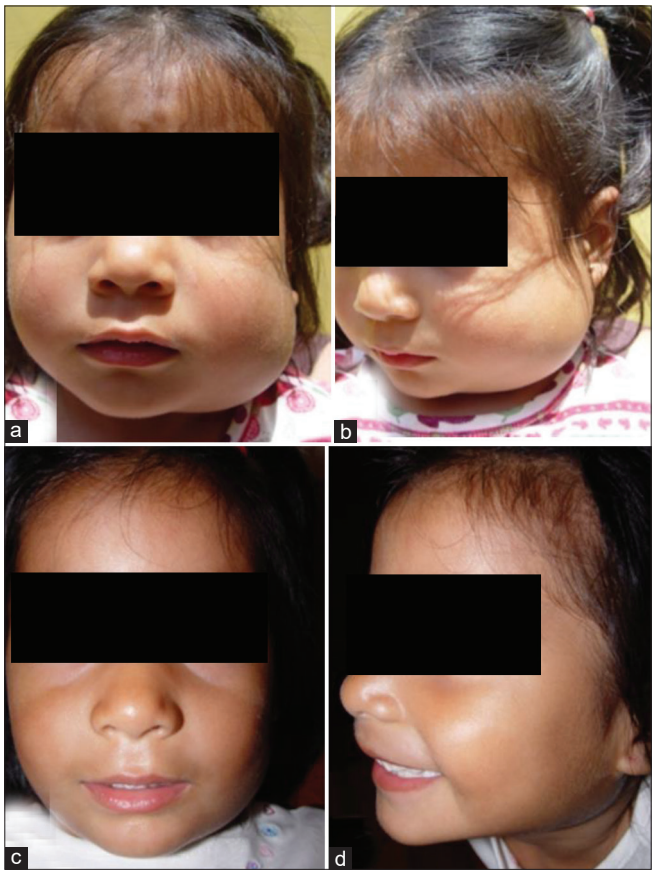

Figure 4: (Case 4): A 2-year-old little girl with a large left parotid/cheek IH. (a) and (b) Before, and (c) and (d) 5 months after TAE. Embolization had been scheduled previous to surgical excision. Patient's mother refused the surgery due to the rapid and progressive shrinkage of the tumor observed as early as 3 weeks after TAE.

and had developed central necrosis of the tumor after an intralesional triamcinolone injection. Since the patient had a superficial scar, a surgical skin graft was recommended [Patient 6 of the table and Figure 6].

TAE should be performed with extreme caution. Selective arteriography and superselective microcatheterization are difficult in infants because their vessels are short, thin, and prone to arterial spasm, dissection, and thrombosis. TAE in IHs may have serious and potentially fatal consequences and, therefore, should only be performed by trained teams.[28,29] Since the extracranial arterial anastomoses with the intracranial and ophthalmic circulation are wide open in babies and children, the embolic material may migrate and produce infarction of the brain or retina.[30] TAE can cause mild complications, such as transient local pain and fever, or major complications, such as skin necrosis, embolism and stroke, vision loss, and cranial nerve palsies. The main causes of complications include using the wrong embolic material, reflux of embolic particles, and failure to recognize dangerous anastomoses.[31] In this study, our

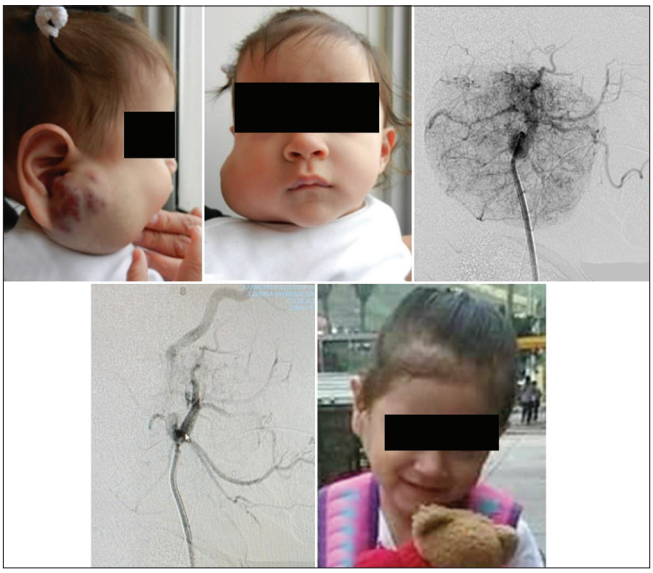

Figure 5: (Case 5): An 8-month-old baby girl with a large right mixed parotid/cheek IH. (a) and (b) Clinical pictures before TAE. (c) Lateral external carotid artery angiogram shows profuse arterial supply to the tumor. (d) Post-TAE angiogram shows ≥ 95 devascularization. (e) The tumor began to shrink one month later and disappeared after 6 months (photo not shown). The last picture was taken at 2 years' follow-up.

complication rate was 16.66% and consisted of a single case of facial hypoesthesia, which was probably due to trigeminal ganglion ischemia which partially improved after 1 year. It is worth noting that this was the only complication in our overall series of 38 embolized head and neck IHs; the readjusted complication rate for the total series was 2.6%. The complication probably occurred due to reflux of embolic particles and the occlusion of the trigeminal ganglion artery, which is an extracranial branch of the middle meningeal artery.[32] There are concerns about the long-term effects on the central nervous system, the optic apparatus, and the thyroid gland from radiation given to an infant or child during TAE. Thus, we limited our procedures to one whenever possible and minimized radiation exposure.[33]

We studied six patients with parotid and cheek IHs that were refractory to medical therapy. After the patients were treated with TAE, there was a rapid and complete response by the tumor and surgery was avoided. The responses occurred after a near 100% devascularization rate of the tumors, which were in the proliferating phase. Our results were similar to other experiences with TAE and/or sclerotherapy for maxillofacial IHs. It should be noted that we used inert non-bioactive embolic material (PVA particles), which means that ischemia itself may lead to IH involution regardless of the embolic agent used. Our results were contrary to the findings by Enjolras and Gelbert that TAE

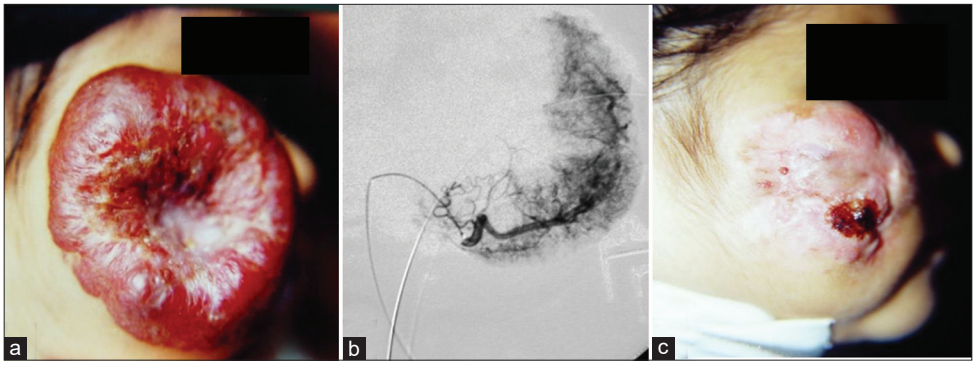

Figure 6: (Case 6): A 9-month-old girl with a large superficial non-involuting congenital cheek IH with a doughnut appearance. She had had intratumoral injections of triamcinolone in another institution, developing central tumor necrosis. (a) Before TAE. (b) Superselective endovascular PVA injection in the facial artery. (c) Clinical picture at 5 months' follow-up showed dramatic regression of the tumor. Patient was sent to Cosmetic Surgery for skin grafting.

gave inconstant results.[29] However, our results agreed with Patel *et al*. and Jianhong *et al*., who suggested that TAE alone may be an effective treatment for large proliferating and richly vascularized parotid and cheek IHs.[24,25] The results from our small series showed that TAE could be used to treat parotid and cheek IHs that were refractory to medical therapy.

CONCLUSION

Our early experience using TAE to treat parotid/cheek IHs that were resistant to medical treatment yielded good results with few complications. Complete tumor devascularization led to the termination of the proliferative phase and triggered a rapid involution in all of our patients without producing scars. Only one patient experienced a partially reversible complication. This paper contributes to the literature on TAE as an upfront therapy for IHs that could help avoid surgery. Larger studies on the effects of TAE on IHs should elucidate these preliminary findings.

Declaration of patient consent

Institutional Review Board permission obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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