Preoperative embolization of nasopharyngeal angiofibromas: The role of direct percutaneous injection of cyanoacrylate glue in conjunction with particulate endovascular approach

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ABSTRACT

Purpose: The aim of this study was to assess the clinical application, extent of tumour devascularization and surgical outcome after embolization of nasopharyngeal angiofibromas prior to surgery by using percutaneous cyanoacrylate glue and endovascular particulate material. We discuss our primary experience, and describe technical considerations and potential complications of the procedure.

Subjects and methods: This study reports 29 patients with juvenile nasopharyngeal angiofibromas; that were embolized prior to surgical resection with percutaneous cyanoacrylate glue and endovascular particulate material; with surgery performed 24–72 h later. Preoperative and postoperative imaging studies were reviewed. Documented intraoperative blood loss was obtained and analysed.

Results: Almost complete radiographic devascularization was encountered in 26 of 29 tumours. An average of 3.2 spinal needles was placed in the tumours. An average of 4.2 mL of cyanoacrylate glue was injected into each tumour. The estimated mean of the blood transfused during the operations was 150 mL. The embolization procedure proved to be safe and effective with no major or serious complications.

Conclusion: The embolization of nasopharyngeal angiofibromas before surgery using percutaneous cyanoacrylate glue with endovascular particulate material proved to efficiently devascularize these tumours with lower blood loss during surgery and no major procedural complications.

1. Introduction

Nasopharyngeal angiofibromas are highly vascular benign tumours that occur exclusively in adolescent males and in most instances manifest with recurrent epistaxis [1]. They are centred on the sphenopalatine foramen and extend into the neighbouring structures causing bone erosive changes [2]. Several grading systems of nasopharyngeal angiofibromas are available with the Fisch grading system being the most common one used (Table 1). Nasopharyngeal angiofibromas receive very rich blood supply mainly from the branches of the external carotid...
artery on the same side. Large tumours receive arterial feeders from the internal carotid artery and from branches of the external carotid artery on the other side. This raises significantly the risk for massive blood loss during the surgical removal of such tumours. Therefore, endovascular embolization nowadays is very crucial and necessary to devascularize nasopharyngeal angiofibromas prior to surgical resection to minimize intraoperative bleeding and thus reduce morbidity and mortality rates [3].

Despite the widespread of endovascular embolization, great challenges are limiting this technique and preventing it from being effective in complete obliteration and devascularization of nasopharyngeal angiofibromas before surgery. The most encountered problems are technical and related to catheter navigation, arterial selection and particle injection. The interventionist might find it difficult to super select a small tortuous arterial feeder during the procedure; this may lead to arterial dissection or spasm and failure of arterial catheterization. The size of particles is also a crucial during embolization as large sized particles may clump and obstruct the catheter. In addition, the complex angioarchitecture of the tumour bed and the existence of dangerous intracranial anastomosis can cause distal migration of particles increasing the rate of stoke and neurological defects [4].

The increasing role of direct percutaneous injection of cyanoacrylate glue has become apparent as an effective and successful solution to overcome the aforementioned limitations of particulate endovascular embolization [5].

### 2. Subjects and methods

We obtained approval from the institutional ethical committee of our hospital for review and analysis of the medical and imaging records of 29 patients with pathologically proven juvenile nasopharyngeal angiofibromas, who performed preoperative combined percutaneous and endovascular embolization between May 2013 and April 2015. The procedures were carried out using a Siemens Axiom Artis monoplan, Germany.

Preoperative multislice post contrast CT and MRI scans were obtained to precisely assess the location, size, and thus classification of juvenile nasopharyngeal angiofibromas. The following protocols were used: multislice post contrast CT scans of the nasopharynx in soft tissue and bone windows with multiplanar reformating and MRI scans of the nasopharynx in pre and post contrast T1WIs and T2WIs sequences taken in axial, coronal and sagittal planes.

Pre procedure assessment of the general clinical condition of patients and an informed consent were taken acknowledging that the interventionist and anaesthetist had explained the procedure and the possible risks and complications from the proposed procedure and general anaesthesia. The risks and complications of the procedure include minor pain, bruising and/or infection at the puncture site. Post embolization syndrome was damage to surrounding structures such as nerves, blood vessels and muscles. The blockage of nontarget arteries results in potential irreversible damage to other organs and tissue.

All patients are subject to general anaesthesia during the procedure. Diagnostic cerebral angiography (four vessels angiography) was performed with selective catheterization of the internal and external carotid arteries on both sides using a diagnostic catheter (braided Berenstein or Headhunter 5 F) over a guidewire (Terumo Glidewire® hydrophilic coated 0.035”). The system had to be continuously flushed with saline, and road-map technique was performed, to visualize the feeding vessel to be catheterized.

The results of the diagnostic angiogram were used to assess the feasibility of endovascular or direct percutaneous embolization, to establish the arterial blood supply to the tumour and to evaluate for dangerous collaterals to the intracranial circulation. The most common pathways of external to internal carotid anastomoses are in the orbital region via the ophthalmic artery that is the interface between the internal maxillary and internal carotid territories: the petrous-cavernous region via the inferolateral trunk, the petrous branches of the internal carotid artery, and the meningohypophyseal trunk to the external carotid artery; the upper cervical region via the ascending pharyngeal, the occipital, and the ascending and deep cervical arteries to the vertebral artery.

Microcatheter was then introduced into the guiding catheter with a coaxial microcatheter technique. The microcatheter used was (Renegade Boston Scientific); superselective micro-catheterization of the feeding artery was performed, until reaching the most distal point of the feeding artery to avoid reflux of the embolizing material. The most common encountered feeding artery was the internal maxillary artery and its branches namely the sphenopalatine and descending palatine arteries.

We start by using small sized particles (150–250 μm) in diameter to allow distal embolization, homogenous penetration and obliteration of the fine arterioles and venules within tumour vascular bed. When we start encountering stagnation of flow and reflux we shift to larger particles to occlude the feeders using larger sized particles (250–355 μm) in diameter. Sometimes if the tumour bed is so large or if there is a dangerous intracranial anastomosis/collateral we start by using large sized particles (355–500 μm) in diameter to facilitate faster tumour bed occlusion and avoid the potential risk of inadvertent intracranial reflux of embolizing material.

In all instances residual tumoural blush is encountered being supplied by arterial feeders that cannot be catheterized due to their narrow calibre or tortuous course or due to the presence of hazardous intracranial anastomoses that make it very risky to embolize as it may result in distal migration of the particles causing stoke. In many cases a small deep component of the tumour is supplied by the ipsilateral internal carotid artery and cannot be targeted.
through endovascular route and therefore direct percutaneous embolization is used.

Direct puncture of the residual tumour bed is done by 18 or 20 gauge spinal needles under fluoroscopic guidance with road mapping to avoid injury of major arteries using either the subzygomatic and/or paramaxillary approaches (Figs. 1 and 2).

In the subzygomatic approach, the needle is introduced inferior to zygomatic arch and passed through the mandibular sigmoid notch (lying posterior to coronoid process, anterior to condyle of mandible and superior to ramus of mandible). The needle is passed through the masticator and parapharyngeal spaces. The superficial position of the mandibular sigmoid notch permits easy manipulation of the needle in many directions, allowing easy access to multiple target areas.

In the paramaxillary approach, the needle is introduced through the cheek (buccal space) below the maxillary zygomatic process and passed posteriorly between the maxilla and mandible. It is critical to avoid the facial artery, which is identified using road mapping of the ipsilateral external carotid artery. The needle passes through the buccinators, masseter, lateral and medial pterygoid muscles.

After puncturing the lesion the stylet is pulled out to look for blood reflux. If no blood is seen the needle position is changed till blood flow is slow and persistent. After making sure of the adequate position of the needle we start gentle injection of non-ionic contrast agent through the needle to confirm contrast opacification of the tumour bed and that there is no contrast extravasation into surrounding tissues or opacification of any important artery or vein that supplies vital structures. We thereafter start embolizing the tumour bed by injecting liquid embolizing material containing mixture of cyanoacrylate glue (Histoacryl; Braun, Aesculap AG, Germany) and Lipiodol (Guerbet; Aulnay-Sous-Bois, France).

The glue mixture concentration was variable according to the size of the lesion targeted and depending on the rate of flow. The injection should be very slow and cautious under continuous road mapping. If any amount of glue escaped into arterial feeders or into a vein or into a dangerous anastomosis, injection should be paused for a while and then resumed repeatedly for several times as required. We may need additional punctures to completely cast the tumour by glue and to reach near-total devascularization on final control angiogram.

In direct percutaneous approach, cyanoacrylate glue: lipiodol mixture with concentrations ranging between 1:3 and 1:4 was injected via single or multiple spinal needle placements. The average amount of cyanoacrylate glue: lipiodol injected in different cases was 4.2 ml with a range of 2–8 ml. The average number of punctures needed to achieve complete embolization of tumoural bed was in the range of 2–6 needles.

The therapeutic response was assessed by the percentage of residual tumoural blush on control angiograms and the results were divided into three main categories: mild to moderate (30–70%), suboptimal (70–90%) and near complete (90–99%) radiographic devascularization, by estimating the volume of residual tumoural blush on final control angiogram in relation to the whole tumour bed volume in the pre-embolization angiograms. The volume of intraoperative blood lost was quantified and recorded by the operating surgeon.

3. Results

A total of 29 male patients (mean age, 14.1 years; range, 8–20 years) presenting with 29 juvenile nasopharyngeal angiofibromas underwent particulate endovascular embolization in conjunction with direct percutaneous embolization with cyanoacrylate glue. All patients’ data, procedural details and results are listed in Table 2. Nine
patients (31%) were classified as Fisch I, fifteen patients (52%) as Fisch II, four patients (14%) as Fisch III, and one patient (3%) as Fisch IV (Fig. 3).

All the 29 nasopharyngeal angiofibroma cases (100%) had arterial feeders from the internal maxillary artery branches (sphenopalatine and descending palatine arteries); 17 cases (58.6%) from the right, 8 cases (27.6%) from the left and 4 cases (13.8%) from both internal maxillary arteries. The ascending pharyngeal artery was also shared in the arterial supply of 10 cases (34.5%). Selective internal carotid angiography showed that 19 cases (65.5%) were supplied from branches of the internal carotid artery (pterygoid branches and inferolateral trunk).

Initial angiograms revealed that all tumours in the study had dense capillary blush and fast flow with feeding arteries from the ECA branches and small component directly supplied from the ICA (Figs. 6, 7 and 10A and B). Injection of 250–355 um PVA particles over 40–60 min resulted in total occlusion of the tumour compartment supplied by the ECA (Figs. 8, 7 and 10C and D). Direct percutaneous embolization of the residual tumour component supplied from the ICA was done by introducing multiple spinal needles into the tumour bed. Histoacryl:lipiodol mixture was injected till complete occlusion of the residual tumour bed (Figs. 6, 7 and 10D–G). The estimated procedural times ranged from 90 to 180 min. Post embolization CT and microscopic images showed the cyanoacrylate glue within the tumour bed (Figs. 4 and 9 B, Fig. 5). Post-surgical resection gross pathology of one of the cases is illustrated (Fig. 8).

The surgeons reported near-complete obliteration of the vascular bed of most of the tumours they surgically removed after embolization. The average blood transfusion required in the operative theatre was 150 ml (50–500 ml). Of the 29 tumours treated, 89.7% (n=26) showed near complete devascularization, while 10.3% (n=3) showed suboptimal devascularization.

The average duration of surgery after embolization was 2.5 h (1–3 h). Transnasal endoscopic approach was used in removal of all cases of nasopharyngeal angiofibroma with minimal blood loss, shorter operative times and better demarcation of the tumour outline facilitating easier resection from the surrounding structures. No clinical or technical complications were encountered in any of the cases in our study. None of these cases suffered from neurological defects or stroke after the embolization procedure which was technically successful.

### Table 2

All patients’ data, procedural details, extent of angiographic devascularization and IBL.

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<th>Amount of glue (cc)</th>
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4. Discussion

The standard endovascular approach using particles is the most widely used approach for preoperative embolization of nasopharyngeal angiofibromas. It can be used solely to target small sized tumours with no intracranial extensions and in tumours having single or few arterial feeders. Different-sized particles used are associated with different penetration characteristics into the capillary bed of the tumour, with a range from larger (355–500 μm) to smaller (50–150 μm) particles. Smaller particles result in obliteration of the fine arterioles within tumour vascular
Larger particles are believed to provide the best agreement between safety (collaterals) and efficient devascularization.

However, this approach faced several limitations such as technical difficulties to catheterize small tortuous arterial pedicles and the high risk of inadvertent intracranial migration of particulate material due to the presence of dangerous intracranial anastomoses [6]. Given these limitations direct percutaneous injection of nasopharyngeal angiofibromas has shown to be beneficial in many ways.

The direct percutaneous approach using liquid embolic materials such as glue or onyx is the most widely used approach. However direct percutaneous embolization can be also done using particulate embolic agents. The use of particulate material is more time consuming and not practical when compared to liquid agents, because particles are radiolucent and require contrast solution to indirectly determine the extent of tumour embolization adding to the overall contrast load during the procedure. Furthermore, the particles dissipate over time allowing revascularization of the tumour if tumour resection is not achieved in a timely fashion.

The embolic material that we injected percutaneously was cyanoacrylate glue diluted by oily based contrast medium lipiodol. It stays in liquid form until exposed to blood where it solidifies instantly and thus reducing the risk of inadvertent distal migration during injection.

Despite its instant solidification, the hazard of distal embolization still remains with highly diluted glue mixture. This can be avoided by adjusting the dilution of

Fig. 6. Case 1: (A and B) Right external and internal carotid angiograms with lateral projections showing intense tumoural blush within the right nasopharyngeal region with arterial feeders from the branches of right ECA and ICA. (C) Post endovascular embolization by PVA particles showing complete occlusion of arterial feeders from ECA branches. (D) Residual tumoural blush supplied from ICA. (E) Direct percutaneous embolization of the residual tumoural blush by spinal needle. (F) Control angiogram showing total occlusion of the tumoural feeders from both ICA and ECA branches.
the cyanoacrylate glue in the mixture. In small lesions we injected a less diluted mixture (1:2–1:3). As opposed to large lesions we injected a more diluted mixture (1:4) in a very slow controlled manner that facilitated more distal penetration of the glue with complete obliteration of the tumour bed. We were forced to use multiple punctures in all of the lesions we injected because of the rapid solidification nature of the glue mixture hindering the homogeneous penetration of the tumour vascular bed through single puncture. So each compartment of the lesion was punctured by a separate spinal needle ensuring complete devascularization.

Another liquid embolic agent commonly used in practice is Onyx. The benefits of Onyx over glue are primarily due to the slower rate of polymerization which allows deeper penetration within the tumour vasculature, in contrast to the instant polymerization of glue on contact with blood that prevents uniform and controlled penetration of the tumour vasculature. Onyx is also more favourable than glue due to its properties of decreased fragmentation, ability to be injected slowly over longer periods of time, and its decreased tendency to occlude the needle quickly. However if the parenchymogram of the tumour displayed fast flow or a quick venous shunt, then the use of the more viscous glue...
with instant solidification properties will be of advantage to prevent the risk of migration of the embolic material through high flow shunt or dangerous anastomosis.

Structures that could be injured with these approaches include the mandibular and maxillary nerves in the masticator space, the pterygoid venous plexus, the internal maxillary artery and its branches in the masticator and parapharyngeal spaces. However, such potential risks are of little concern in practice and are significantly low in incidence with small calibre needles and gentle manipulation. Injury to cranial nerves and branches in this region with subsequent sensory or motor loss remains a theoretical concern; however, many large series have failed to demonstrate any such risk [7].

In large tumours with complex arterial feeders and possible dangerous intracranial anastomoses, direct percutaneous approach can be used solely to target the whole tumour or can be used as an adjuvant to particulate endovascular approach to reach complete obliteration of the tumour bed. The authors suggesting the use of direct percutaneous approach solely believed that particulate endovascular approach in such tumours will be a lengthy and time consuming procedure as they will need to inject very large amount particles to start reaching adequate devascularization rates. Additionally, they suggested that targeting the whole tumour will be easier and more feasi-

Fig. 8. Case 2: Post-surgical resection gross pathology.

Fig. 9. Case 3: (A) Contrast enhanced axial CT scan of the nasopharynx showing a right nasopharyngeal angiofibroma extending into the posterior nares with no intracranial extension. (B) Post embolization CT of the right nasopharynx showing hyper dense histoacryl:lipiodol droplets within the tumoural bed.
ble than targeting a small component that will need precise needle placement and carries higher risk of non-target embolization. On the contrary, the authors suggesting the use of direct percutaneous glue as an adjuvant to particulate endovascular approach believed that direct percutaneous approach needs great experience and high skills with needle handling and placement and therefore should minimize the number of needles and amount of glue delivered as much as possible by targeting only the residual tumour. Moreover, the operating surgeons experienced more difficulties in surgical resection of tumours where large amounts of glue were injected directly in terms of tumour being very hard in consistency with the liability of extravasation of larger amounts of glue within the surrounding tissues.

The mean intraoperative blood loss was 150 ml of the 29 tumours treated, 89.7% of the cases had near total devascularization, while 10.3% had subtotal devascularization. The cases with suboptimal devascularization were due to the presence of dangerous intracranial anastomosis at the orbital region between the ophthalmic artery and middle meningeal artery that resulted in early termination of the embolization procedure before complete tumoural bed obliteration. Because as we get close to the end the intratumoural pressure increases and possibility of inadvertent intracranial reflux is increased.

These results match with a big study that involved 22 cases presented with nasopharyngeal angiofibromas and were embolized before surgical resection with endovascular particulate material and direct percutaneous

Fig. 10. Case 3: (A and B) Right external carotid angiograms with lateral projections showing intense tumoural blush within the right nasopharyngeal region with arterial feeders from the right internal maxillary and ascending pharyngeal artery. (C) Post endovascular embolization by PVA particles showing complete occlusion of arterial feeders from ECA branches. (D) Direct percutaneous embolization of the residual tumoural blush by four spinal needles. (E) Post percutaneous embolization showing complete residual tumor bed occlusion by histoacryl:lipiodol mixture. (F) Control angiogram showing total occlusion of the tumoural feeders from both ICA and ECA branches.
cyanoacrylate glue. This series reported a range of intraoperative blood loss between 0 and 600 ml with the devascularization rates between 80% and 100% [6]. One study have reported effective devascularization of fifteen hypervascular head and neck tumours after preoperative embolization by using percutaneous injection of onyx in combination with particulate endovascular embolization [8].

Two new case reports describe preoperative direct percutaneous embolization with onyx of nasopharyngeal angiofibromas prior to surgery. Total radiographic devascularization was obtained in the two cases, with average blood loss of 200 and 400 ml [9,10]. Another study reported direct injection of onyx into nasopharyngeal angiofibromas through endoscopy. The mean intraoperative time was 230 min and estimated blood loss was 410 ml [11].

Furthermore, another study reported fifteen angiofibromas that underwent preoperative endovascular embolization using particulate material only without the need to use the direct percutaneous approach. All cases were removed by endoscopy and revealed average blood loss of 370 ml. Our results are compared favorably with these former studies [12].

According to the surgeons in our study, tumour surgical resection was easy due to the effective tumour vascular bed obliteration turning the tumour into a solid hard mass with clear demarcation of the plane between normal adjacent tissues and the embolized tumour. This relies on the proper injection of glue into the tumour compartment with no glue reaching the normal surrounding soft tissues resulting in extensive adhesions that make surgical extraction of the lesions more difficult.

In our narrow practice, we have experienced reflux of cyanoacrylate glue into arterial and venous tributaries supplying the tumour during the procedure. The instance we notice any reflux of glue we immediately pause the injection for a couple of minutes and then continue. The injection is then resumed slowly and cautiously with the necessity to identify these vessels on road maps to avoid inadvertent migration of glue into the intracranial circulation.

Nineteen cases received blood supply from the internal carotid artery branches which were not possible to catheterize using a micro catheter due to their tiny size. We were able to effectively devascularize the deep component of the tumour receiving blood supply from the internal carotid artery by the direct percutaneous injection of cyanoacrylate glue. Large tumours involving the skull base with intracranial extension always show blood supply from the internal carotid artery which can only be targeted by direct puncture which can be challenging and requires high skills and experience, but is very crucial to avoid uncontrollable bleeding during surgical excision. This helped the surgeons to completely excise the lesions with no residual deep components and therefore minimize the recurrence rates. Consequently, all tumours were resected by endoscopy without the need for open surgery. Some studies have compared nasopharyngeal angiofibroma endoscopic resection versus open surgical resection and have found that endoscopic resection is safer and more effective with less complications rate [13].

There are a number of limitations to our study. In the first place, the number of cases included in this study is relatively small which makes generalization of results not possible. Furthermore, this study lacks a control group. Moreover, all nasopharyngeal angiofibromas were embolized with combined endovascular and direct percutaneous approach using cyanoacrylate glue; thus, the estimated intraoperative blood loss is a result of the combined use of both approaches and both embolic agents. Therefore a conclusion cannot be made on which approach or embolic agent was more effective.

Finally, the surgical skills of the operating surgeons are variable affecting the amount of intraoperative blood loss, with larger tumours having intracranial extensions being more difficult for the surgeon to excise showing higher amounts of intraoperative blood loss and higher recurrence rates. There is also some minor inaccuracy in estimated intraoperative blood loss due to the fact that adjustment is made for the surgical effluent containing both fresh blood and operative irrigation fluid.

5. Conclusion

The preoperative embolization of nasopharyngeal angiofibromas by direct percutaneous injection of cyanoacrylate glue in addition to particulate endovascular embolization appeared to be safe and effective, increasing the extent of angiographic devascularization prior to surgical resection, consequently minimizing intraoperative blood loss and improving the chance to total surgical resection with decreased incidence of residual or recurrence. The initial results of this study as regards the extent of angiographic devascularization, intraoperative blood loss volume and surgical outcomes motivate us to use the direct percutaneous approach more frequently in treatment of these lesions.

Conflict of interest

The authors declare that there are no conflict of interests.

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