Presurgical Embolization of Intracranial Extra-Axial Tumours Using Glubran 2®: Our Experience in 14 Patients

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SUMMARY – This study aimed to define the indications, technique and results of presurgical embolization of intracranial extra-axial tumours using Glubran 2® a new acrylic glue with the CE mark, suitable for permanent embolization of the pathological circulation of tumours. Embolization was performed prior to surgery in seven patients with benign tumours and three patients with malignant lesions. All the procedures were technically feasible and achieved partial or complete embolization of the vascularized lesion without periprocedural complications. Glubran 2® proved easy to use with excellent intravascular penetration achieving permanent embolization. The degree of presurgical embolization in terms of surgical field haemostasis was satisfactory in all cases and correlated to the degree of vascular occlusion achieved.

Introduction

The embolization of intracranial extra-axial tumours was most widely practised in the eighties in the wake of reports emphasizing the importance of reducing surgical morbidity and outlining the technical criteria for endovascular treatment [3,7,9-10,18,22-23]. These criteria remain largely valid, but the application of embolization varies: some centres undertake endovascular treatment routinely, whereas others seldom implement the technique. The reasons for this discrepancy on the usefulness of pre-operative embolization are the following [1,5,6,19,24]:

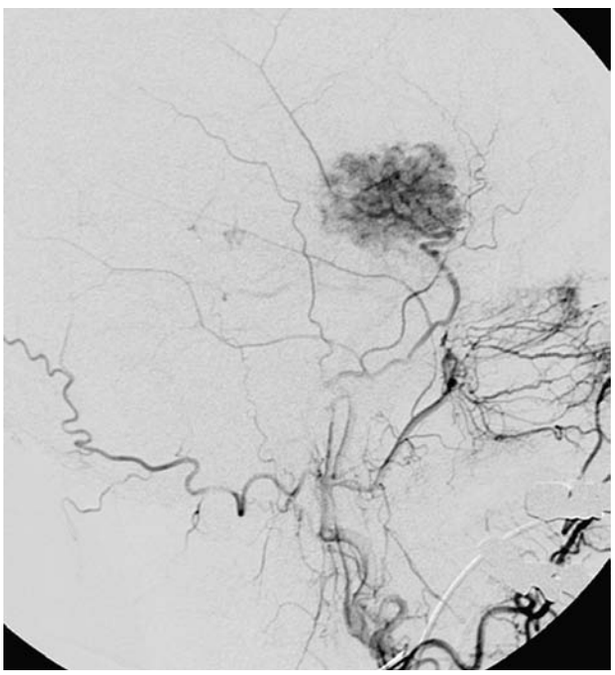
• Microsurgical techniques have evolved to the extent that in expert hands most intracranial extra-axial tumours can be surgically resected without difficulty to achieve prior closure of the main arterial afferents;

• Neuroradiologists sometimes undertake only proximal embolization of the feeding vessels without ensuring intralesional penetration of the embolization agent and hence achieving poor results in terms of stability and depth of devascularization;

• Particles are the material most widely used for presurgical embolization: despite being easy to insert with good intralesional penetration, they have the drawback of making the embolization unstable. This means that endovascular treatment must be closely coordinated with subsequent surgery which may be inconvenient.

Whereas the first two problems can be overcome by the neuroradiology and neurosurgery teams working together in patient selection and deciding on the most important vascular peduncles to embolize, the third issue can only be resolved by using permanent embolizing agents like acrylic glues.

Acrylic glue has long been advocated as an embolization agent for intracranial tumours [2-4], but has not been widely used for two main reasons. Firstly, acrylic glues are technically more difficult to use than particles, making them more hazardous in less expert hands and hence contraindicated for presurgical procedures which by definition must be low risk. Secondly, the overall cost of using glues (materials and procedure time) is higher than that of particles. For these reasons, glue has been confined to percutaneous use in tumours which cannot be reached or in extremely rare cases requiring the embolization of pial afferent branches [3].



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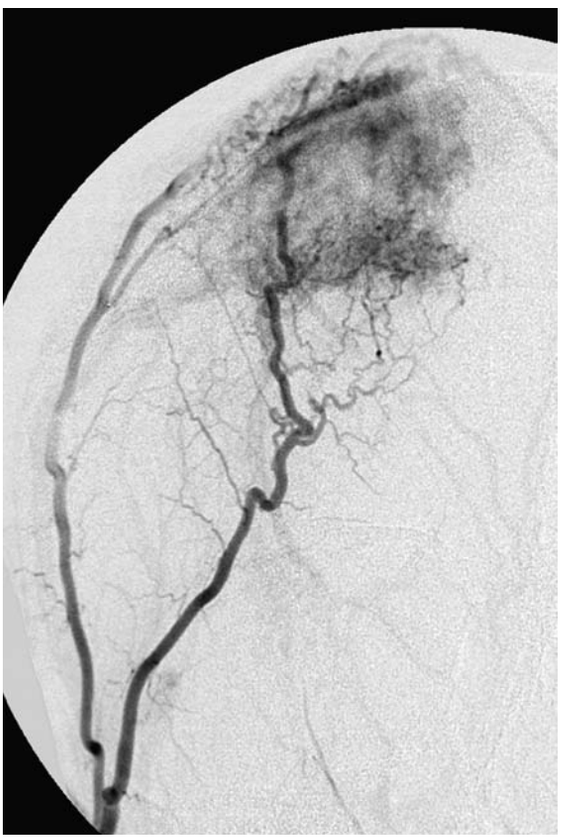

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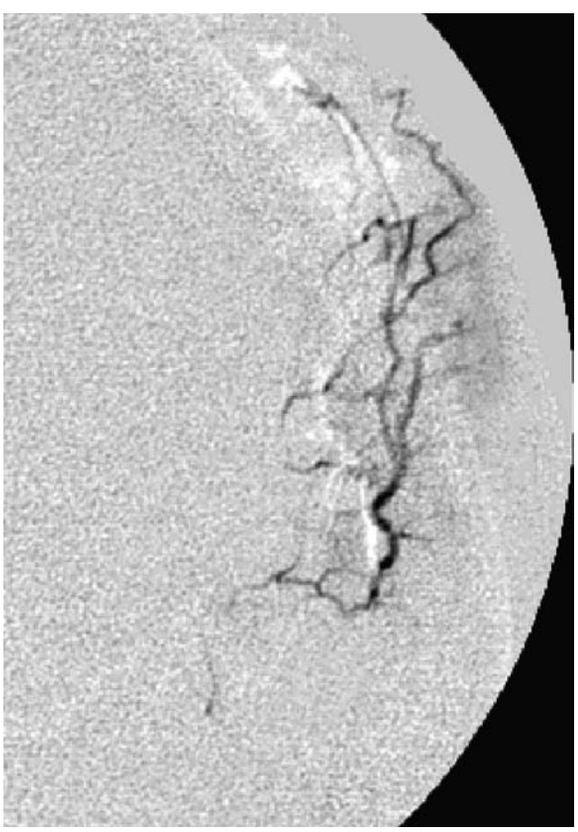

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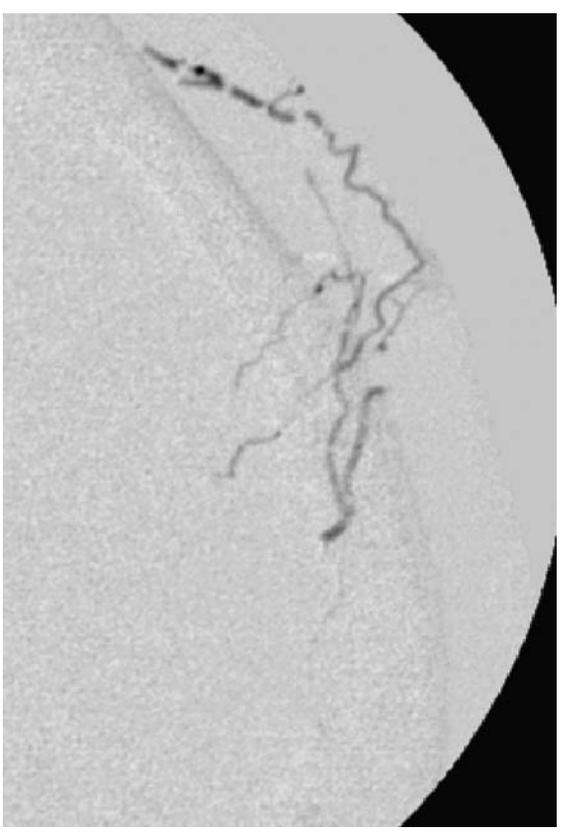

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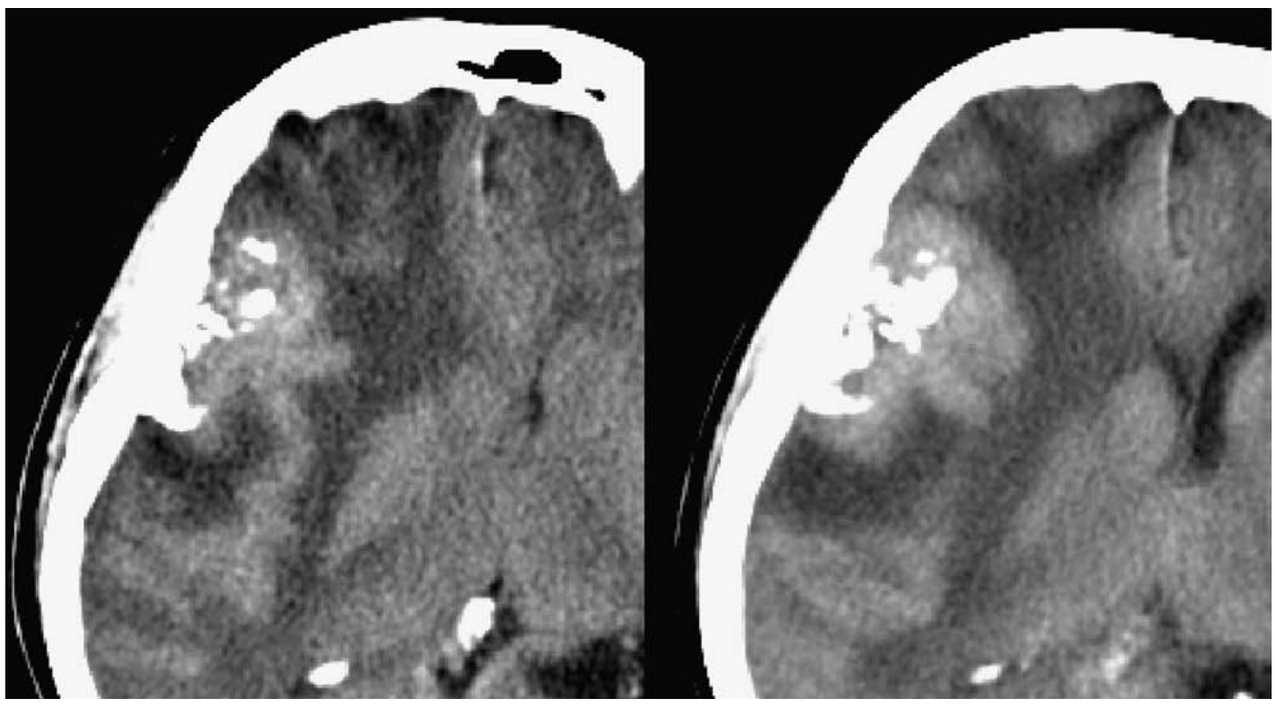

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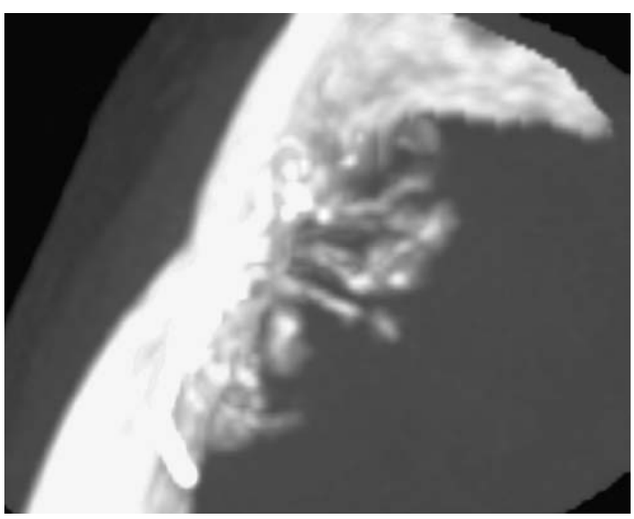

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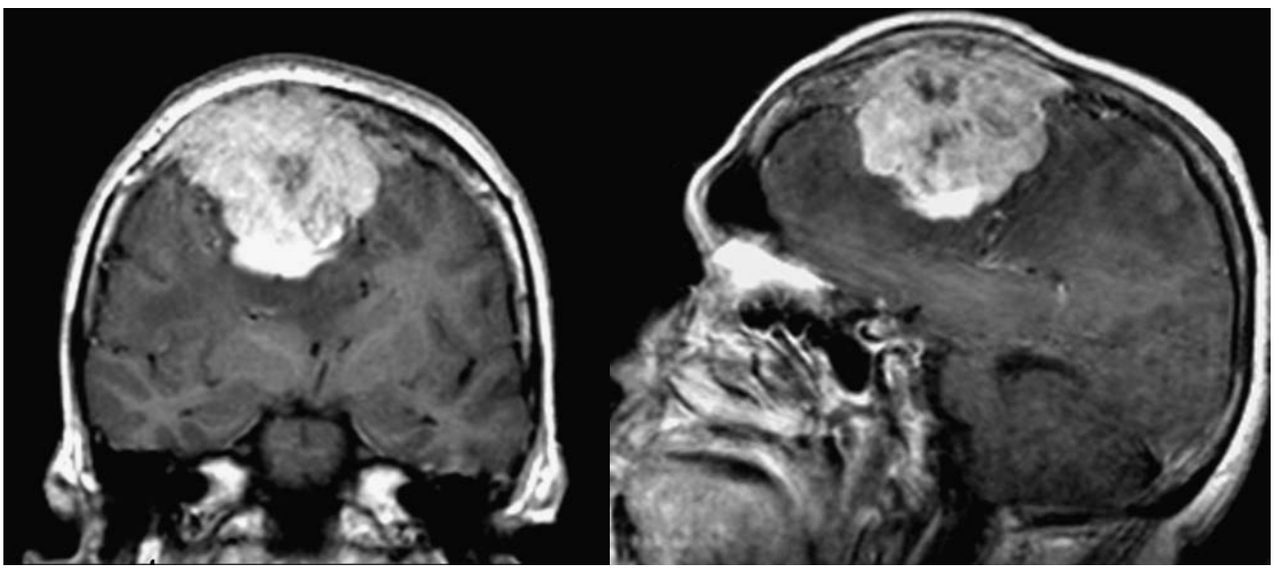
Figure 1 Right pterional meningioma. A) Right external carotid angiography, arterial phase, lateral view. Note the pathological circulation feeding the tumour from the middle meningeal artery. B) Right internal carotid angiography, arterial phase, lateral view. Note the pial pathological circulation of the tumour. C) Superselective angiography of the tumour's pathological circulation. D) Injection of Glubran 2® and its diffusion within the pathological circulation. E) and F) CT scan without contrast administration after embolization. The scans show intralesional penetration of the glue. G) CT- volumetric reconstruction of the glue cast within the tumour.

In the last three years, we used Glubran 2® for the permanent embolization of intracranial extra-axial tumours. Glubran 2® is a new acrylic glue bearing the CE mark and sold in Europe to replace Histoacryl which has been shown to spread in the pathological vascular network causing endothelial injury and necrosis. Glubran 2® diffuses in a very similar way to Histoacryl but has a more homogeneous fluidity and an excellent correspondence to the angiographic picture of superselective catheterization [11,12,15].

Prior to its clinical use, experimental studies were undertaken to test the featuresof Glubran 2® such as its fluidity at different concentrations and injection behaviour, and to study its tendency to adhere to the microcatheter and the short and long-term histological effects on animal models [13-14]. These experimental studies were followed by clinical administration of the



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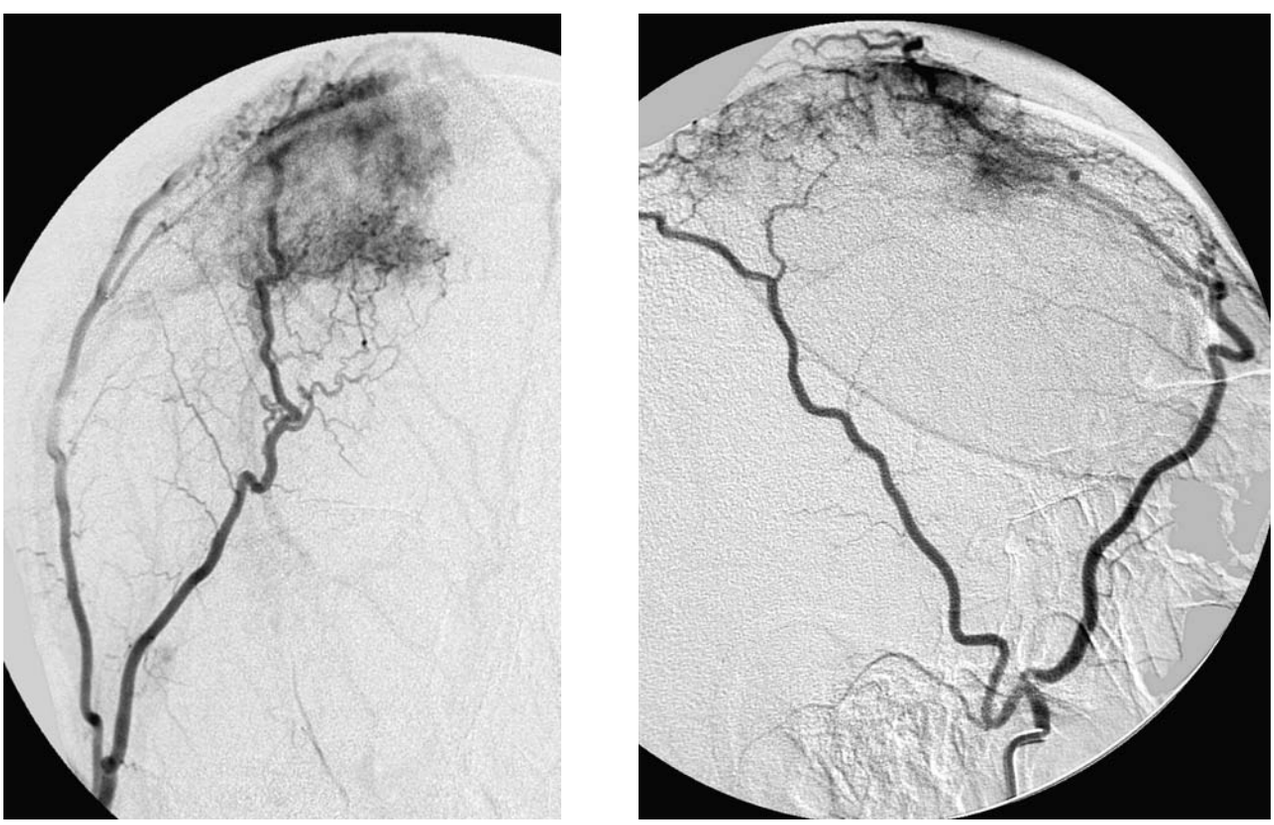

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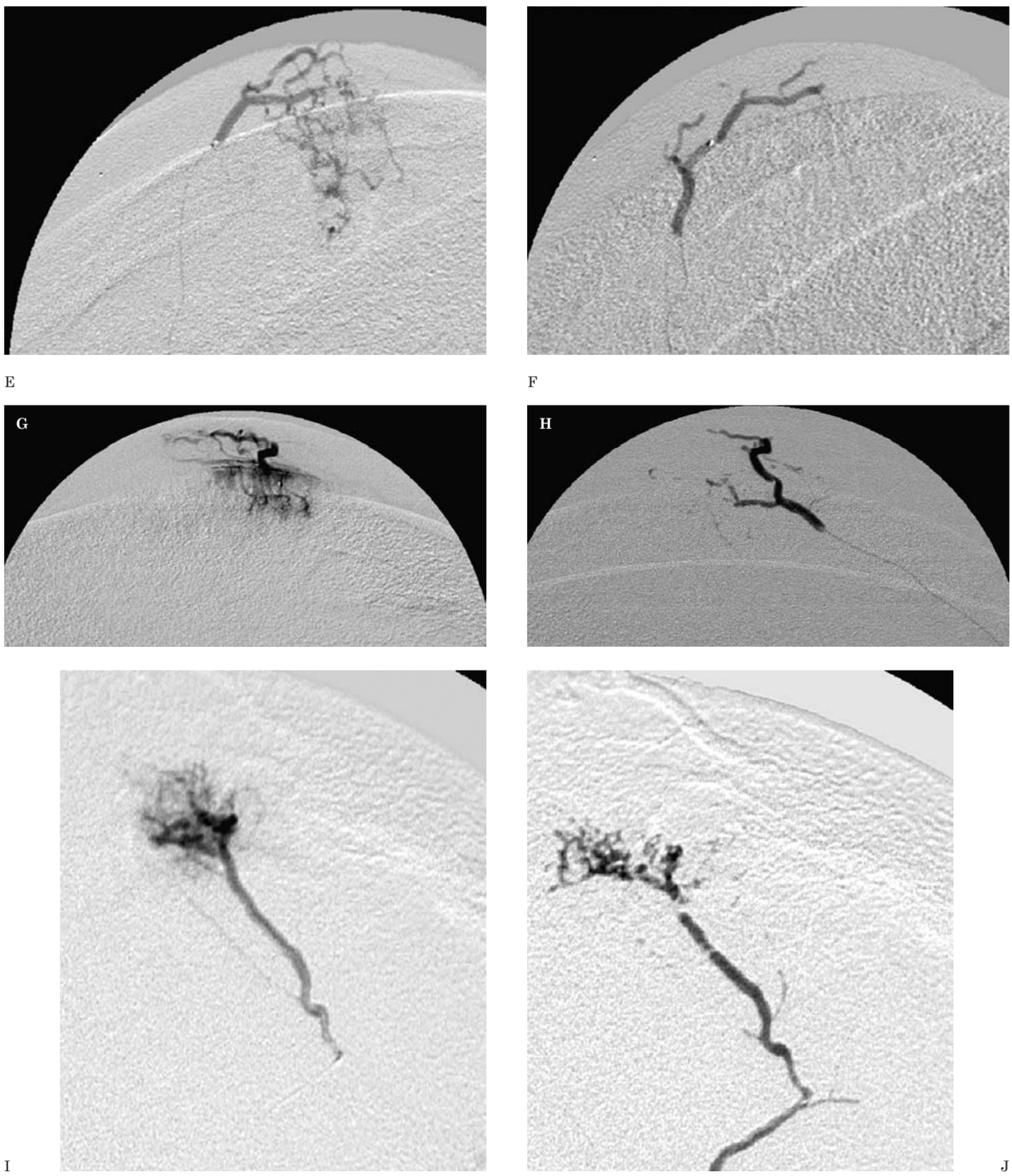


Figure 2 Bilateral parasagittal frontal sarcoma. A) Coronal MR scan after contrast administration. B) Sagittal MR scan after contrast administration. The tumour arises from the cranial theca and shows extensive intracranial development. C) Right external carotid angiography, arterial phase, anteroposterior view. D) Right external carotid angiography, arterial phase, lateral view. Note the pathological circulation feeding the tumour from the middle meningeal artery. E) Superselective angiography of the tumour's pathological circulation through one of the first peduncles. F) Injection of Glubran 2® and its diffusion within the pathological circulation shown in E). G) Superselective angiography of the tumour's pathological circulation through a second peduncle. H) Injection of Glubran 2® and its diffusion within the pathological circulation shown in G). I) Superselective angiography of the tumour's pathological circulation through a third peduncle. J) Injection of Glubran 2® and its diffusion within the pathological circulation shown in I).

glue in safe vascular areas such as the vertebrae and external carotid artery [16].

The rationale behind the use of Glubran 2® as an embolizing agent is the possibility of achieving a more extensive and uniform permanent occlusion of the pathological circulation thereby avoiding rigid planning for surgery after endovascular treatment [16].

This paper describes the indications, technique and results of presurgical embolization of intracranial extra-axial tumours in fourteen patients using Glubran 2® acrylic glue.

Material and Method

From December 2001 to December 2004, fourteen patients with intracranial extra-axial tumours underwent presurgical embolization. Patients were aged between 36 and 71 years and were equally divided by gender. Ten patients had benign tumours (eight meningioma, two paraganglioma) whereas three had malignant lesions (one sarcoma, one epidural metastasis, one chordoma and one epidural and intradural metastasis).

In all cases, diagnostic angiography included exploration of the internal and external carotid arteries and the vertebral artery. Catheterization was performed with Terumo 4F material (Terumo Corporation, Tokyo, Japan) in order to use the diagnostic catheter as the guiding catheter thanks to its wide internal lumen.

Embolization was carried out by co-axial catheterization using different microcatheters with calibres varying from 0.014" to 0.018" and the over-the-wire technique. The microcatheter was positioned as proximally as possible to the pathological circulation to embolize in compliance with general safety criteria for microcatheterization.

Glubran 2® (GEM Srl, Viareggio, Italy) was injected following the technical guidelines for cyanoacrylate preparations (the microcatheter was washed with a glucosate solution to remove the saline solution and blood), diluted and made radiopaque by mixing the glue with Lipiodol (Guerbet, Roissy CdG Cedex, France). The dilutions used varied from 1:2 to 1:3, confining the latter dilution for cases in which the microcatheter was relatively distal to the pathological circulation or the calibre of the afferent vessel and initial intralesional branches was particularly narrow. The injection was made using a continuous column of glue and the flow and placement of Glubran 2® was monitored by slow rate digital angiography, stopping the injection when retrograde flow was visible in the afferent vessel. In every case we had an excellent correspondence to the angiographic picture of superselective catheterization (figures 1 C-D, 3 C-D, 4 A-D)

In eleven out of fourteen patients, embolization of a single peduncle was sufficient whereas two or three peduncles were embolized during the same session in the remainder (figures 2 E-J).

CT scans were done in seven patients a few hours after embolization to visualize intralesional penetration of the glue. Surgery followed endovascular treatment after an interval of between 48 hours and ten days in twelve patients; the two patients affected by paraganglioma are still in treatment (figures 4, 6).

Table 1 Record of cases

N°	*Name*	*Sex*	*Age*	*Tumour type and location*
1	SR	M	55	Extradural metastasis
2	OE	F	65	Meningioma
3	RA	M	42	Intradural metastasis
4	AA	F	69	Meningioma
5	PR	F	36	Meningioma
6	BA	M	65	Meningioma
7	CD	F	56	Meningioma
8	AG	F	57	Sarcoma
9	MG	M	57	Meningioma
10	CF	M	65	Meningioma
11	MS	M	55	Paraganglioma
12	FD	F	61	Meningioma
13	MG	M	63	Chordoma
14	CM	F	71	Paraganglioma

Results

Embolization of the chosen portion of the pathological circulation was complete in all patients. There were no clinical or technical complications and the procedure was well-tolerated both during glue injection and after embolization.

The CT scans done after the procedure in

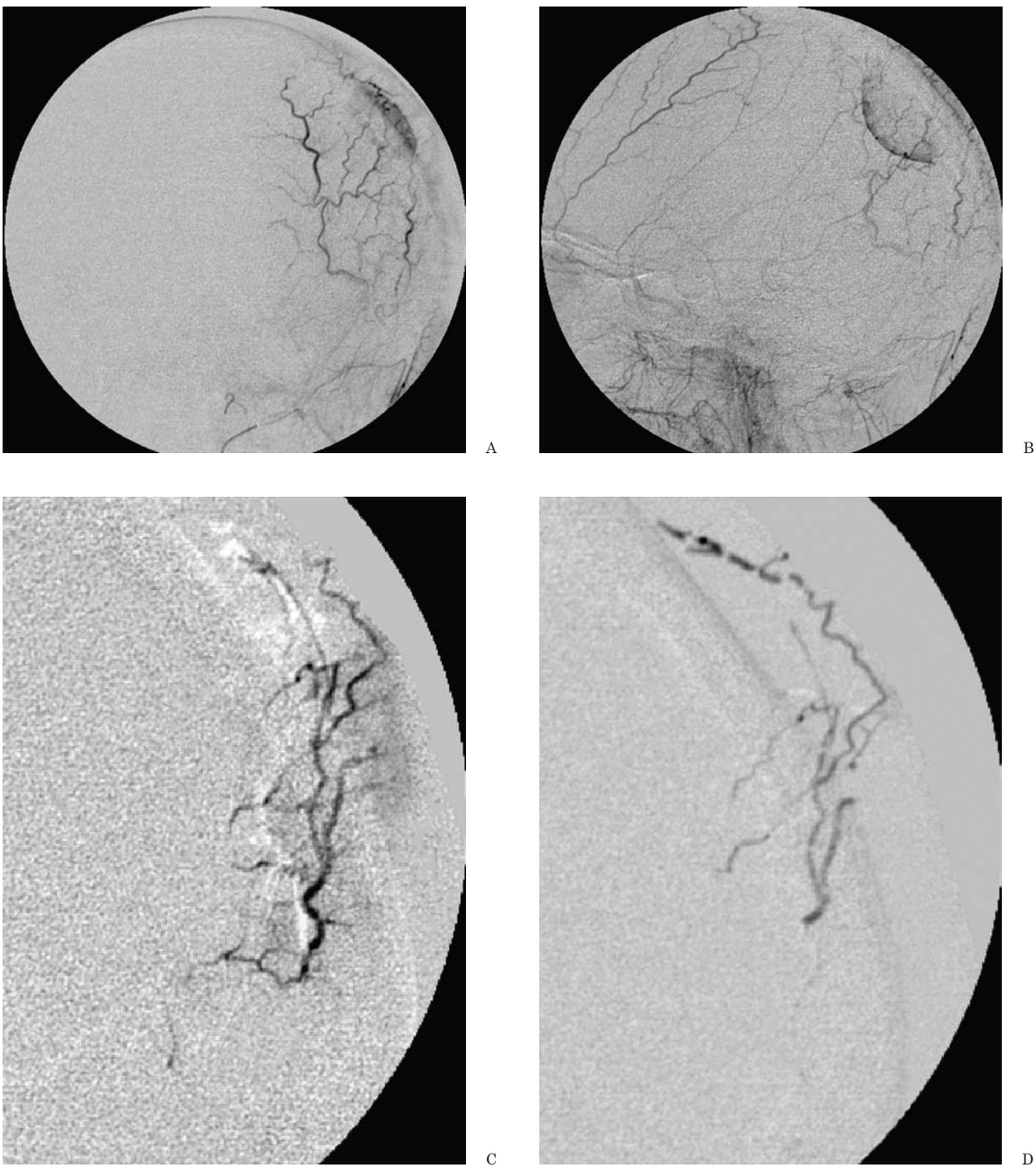
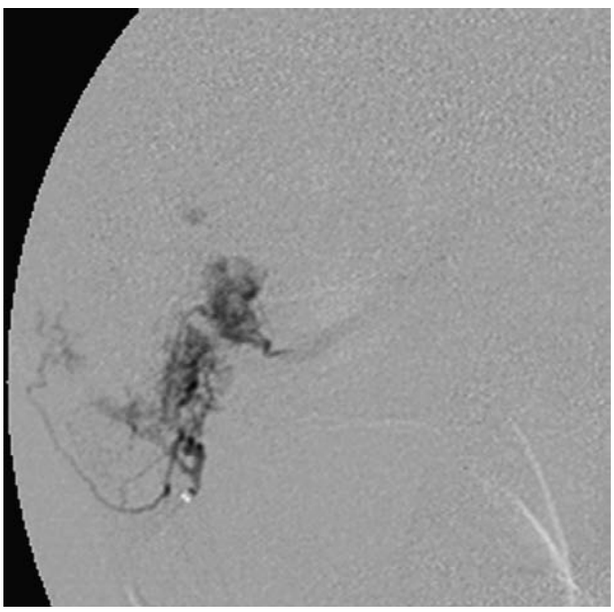


Figure 3 Extradural metastasis. A) Right external carotid angiography, arterial phase, anteroposterior view. B) Right external carotid angiography, arterial phase, lateral view. Note the pathological circulation feeding the tumour from the middle meningeal artery. C) Superselective angiography of the tumour's pathological circulation. D) Injection of Glubran 2® and its diffusion within the pathological circulation.

seven patients displayed the exact intralesional penetration of the glue and its distribution (figures 1 E-G, figures 6 C-D). Glubran 2® was seen to diffuse distally into the tumour – a key requirement for permanent devascularization.

The subjective impression of the neurosurgical team was positive with a significant reduc-



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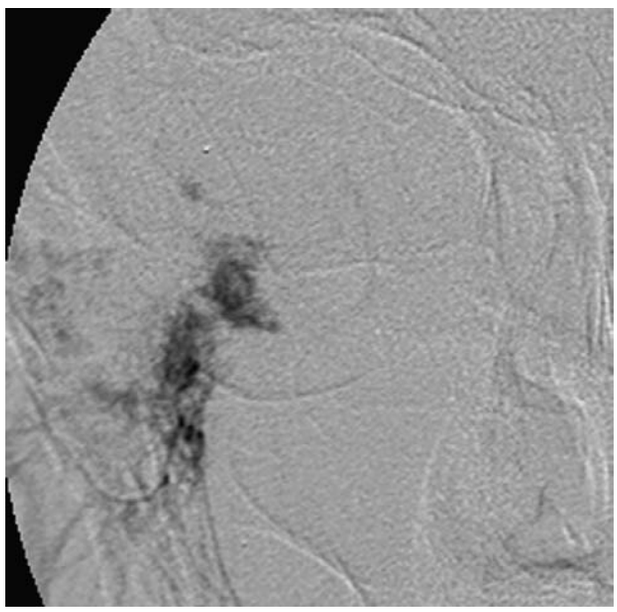

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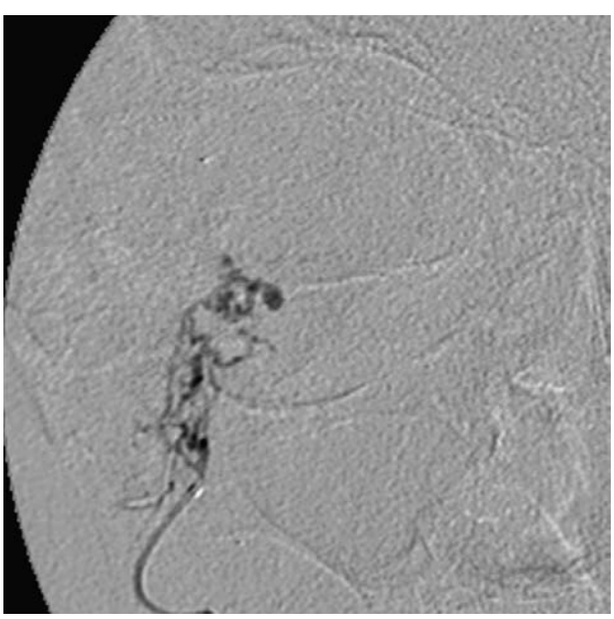

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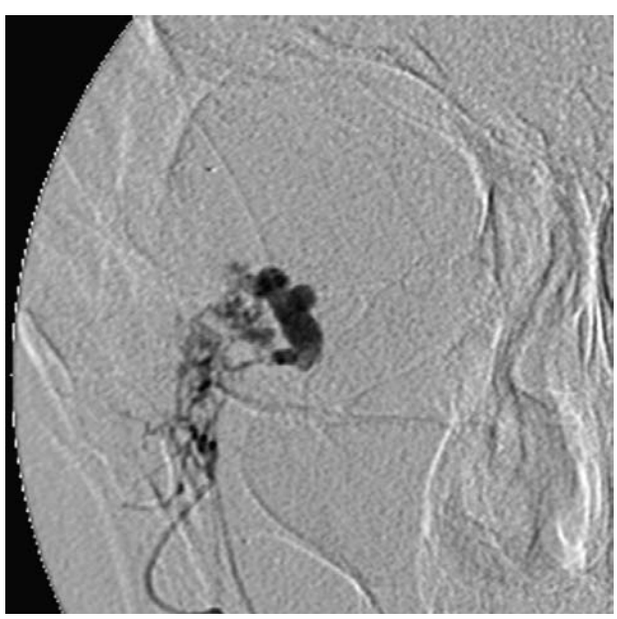

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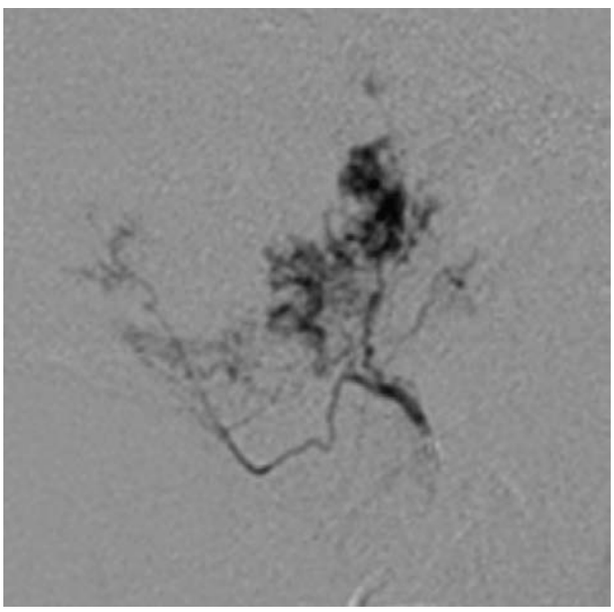
tion of peri-operative bleeding compared with both untreated cases and patients treated in the past with particles.

Discussion

The discussion focuses on the different stages of the embolization procedure.

Angiographic work-up. The embolization of meningiomas is generally considered a low risk procedure as the pathological circulation of these tumours mainly arises from the external carotid artery. However, care must be taken as in all endovascular procedures to avoid opening external-internal and external-vertebral artery shunts or leakage of embolizing material. An excellent knowledge of the vascular anatomy in this region is essential and a full angiographic study prior to embolization is a prerequisite [8,23].



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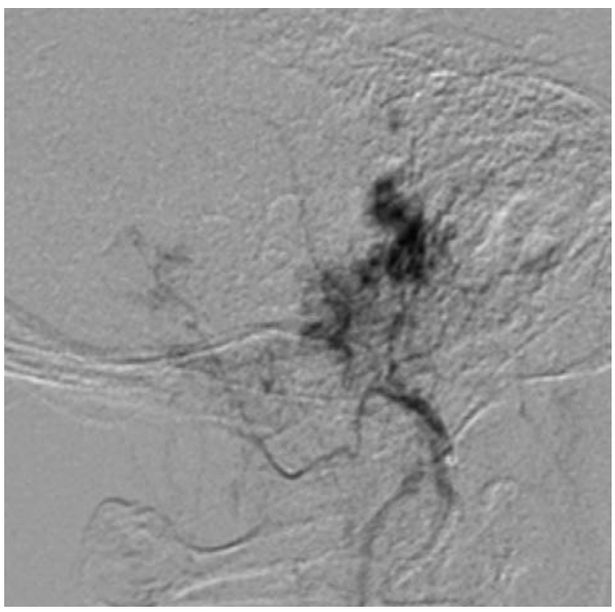

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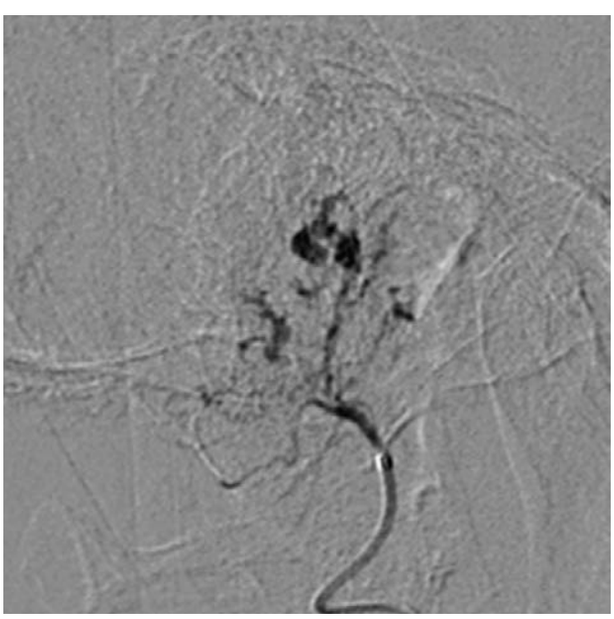

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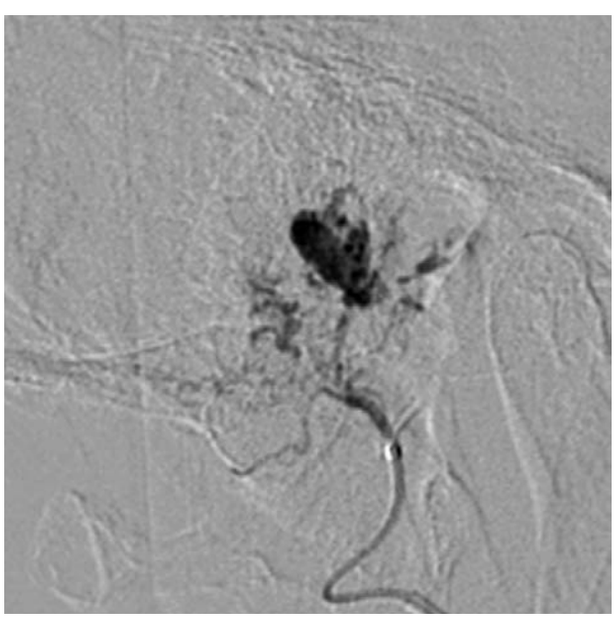

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Figure 4 Intra- and extracranial right jugular paraganglioma. A-B) Right external carotid: superselective angiography of the tumour's pathological circulation; early and late arterial phase, anteroposterior views. C-D) Injection of Glubran 2® and its diffusion within the pathological circulation. E-F) Right external carotid: superselective angiography of the tumour's pathological circulation; early and late arterial phase, lateral views. G-H) Injection of Glubran 2® and its diffusion within the pathological circulation.

Technically speaking, angiography should always include selective injection of the external and internal carotid arteries and the vertebral artery ipsilateral to the tumour to disclose:

1. Arterial supply

a) Type, number, and geometry of feeding arteries (extracranial, dural, pial, abnormal origins)

b) Collateral circulation

c) Dangerous arterio-arterial anastomoses (see below)

d) Cranial nerve supply

e) Skin supply

2. Vascular composition and angioarchitecture of the tumour

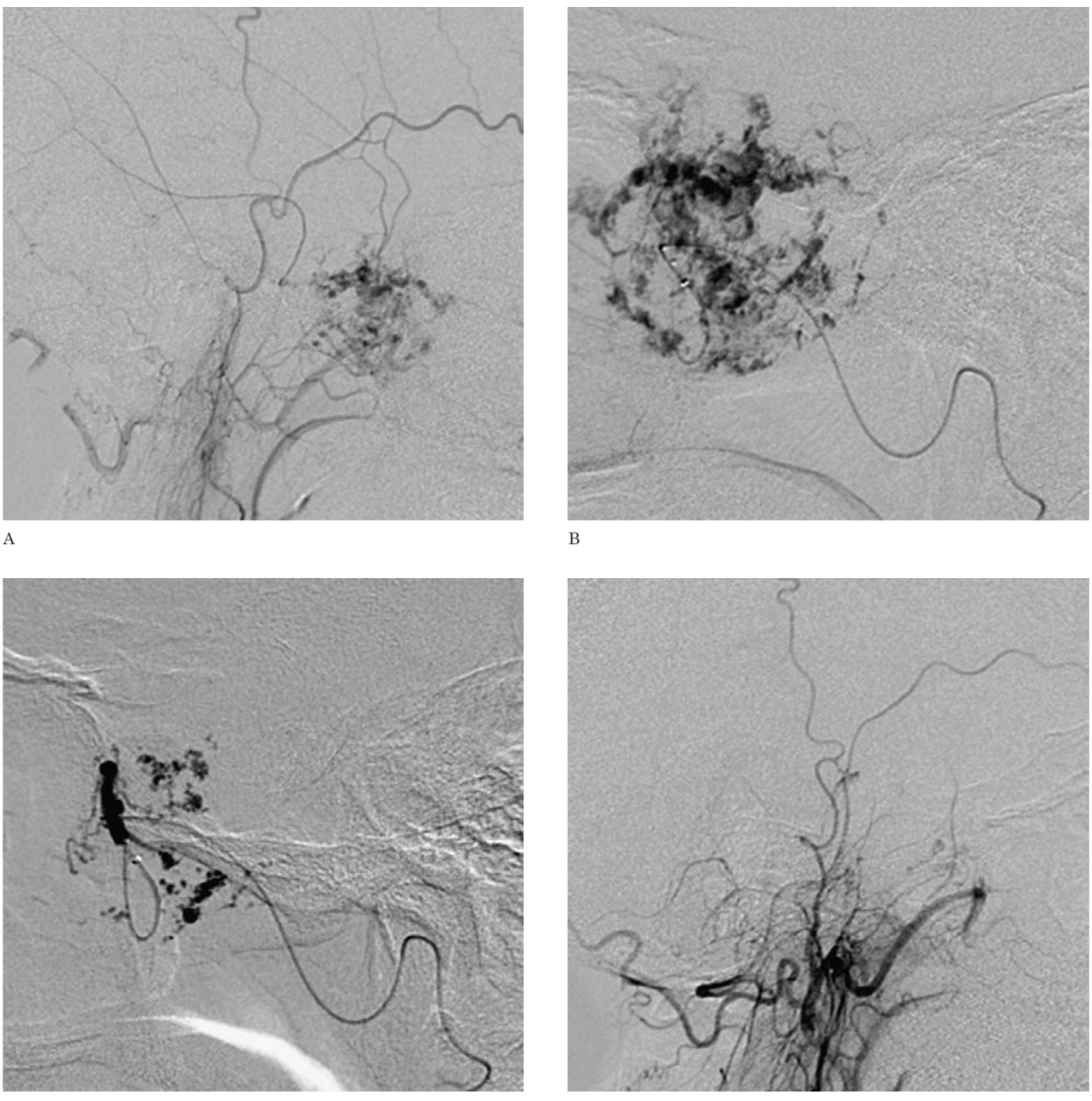

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Figure 5 Chordoma. A) Right external carotid angiography, arterial phase, lateral view. Note the pathological circulation feeding the tumour. B) Superselective angiography of the tumour's pathological circulation. C) Injection of Glubran 2® and its diffusion within the pathological circulation. D) Right external carotid angiography, arterial phase, lateral view. Post-embolisation findings.

a) Mono- or multicompartments
b) Flow characteristics
c) Arteriovenous shunts
3. Venous drainage
a) Cortical/dural
b) Dural sinuses
c) Venous plexuses
d) Obstruction of sinuses by intraluminal extension or external compression.

From the anatomic point of view, below is a list of commonly encountered anastomoses between branches of the External Carotid Artery (ECA) and Internal Carotid Artery (ICA), the ophthalmic artery, and the vertebral artery [8,21]:

– Anastomoses between the internal maxillary artery and the cavernous segment of the ICA:
  - Cavernous branch of middle meningeal artery
  - Cavernous branch of the accessory meningeal artery
  - Artery of the foramen rotundum

– Anastomoses between the ascending pharyngeal artery and the cavernous segment of the ICA :
  - Carotid branch of the superior pharyngeal artery
  - Lateral clivaI branch of the jugular division of the ascending pharyngeaI artery
  - Medial clival branch of the hypoglossal division of the ascending pharyngeal artery

– Anastomoses between the internal maxillary artery and the petrous segment of the ICA:
  - Anterior tympanic artery
  - Vidian artery

– Anastomoses between the ascending pharyngeal artery and the petrous segment of the ICA:
  - Mandibular anastomosis of the superior pharyngeal artery
  - Inferior tympanic artery

– Anastomoses between the posterior auricular artery or the occipital artery and the petrous segment of the ICA :
  - Stylomastoid branch

– Anastomoses between the occipital artery and the vertebral artery:
  - Cl anastomotic branch
  - C2 anastomotic branch

– Anastomoses between the ascending pharyngeal artery and the vertebral artery:
  - Hypoglossal branch of the odontoid arch system
  - Musculospinal artery

– Anastomoses between the ascending cervical artery and the vertebral artery:
  - C3 anastomosis
  - C4 anastomosis

– Anastomoses between the posterior cervical artery and the vertebral artery:
  - C2 anastomosis
  - C3 anastomosis
  - C4 anastomosis

– Anastomoses between the ECA trunk and the vertebral artery:
  - C4 collateral

– Anastomoses between the internai maxillary artery and the ophthalmic artery:
  - Orbital branch of the infraorbital artery
  - Anterior ethmoidal branch of the sphenopalatine artery
  - Meningo-ophthalmic branch of the middle meningeal artery
  - Recurrent meningeal branch of the middle meningeal artery
  - Orbital branch of the anterior deep temporal artery.

The presence of any such anastomoses does not represent an absolute contraindication to embolization with fluid materials like glue, if it is possible to position the microcatheter tip distal to the origin of the anastomotic artery and good flow control is achieved.

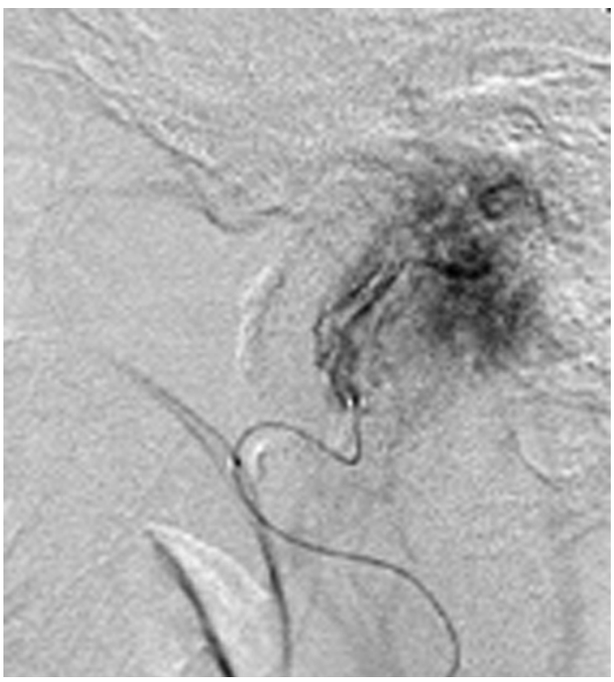
Microcatheterization. Microcatheterization was performed by the usual co-axial technique using the Terumo 4 F diagnostic catheter as a guide with the curvature best suited to diagnostic catheterization, thereby avoiding:
– larger calibre more rigid catheters such as the commercially available guiding catheters, with a lower incidence of spasm in a highly sensitive territory like the external carotid artery, spasm of the arteries feeding the lesion being one of the major causes of unsuccessful embolization [21];
– the need to exchange the guiding catheter in anatomically complex cases, thereby avoiding the rare but potential incidence of embolic complications during this manoeuvre.

The only disadvantage of this technique is that it precludes good quality road-mapping due to the lack of a valid lumen between the microcatheter and diagnostic catheter. This drawback was overcome by undertaking panoramic road mapping before inserting the microcatheter and then proceeding with superselective road-mapping from the microcatheter.

Different microcatheters were used with calibres from 0.018 to 0.014, advanced by the over-the-wire technique using microwires compatible with the microcatheters because of the poor flow in the district and the type of tumours being treated.

Microcatheter insertion was generally straightforward despite the notorious sharp bends in the middle meningeal artery which are often difficult to penetrate given the artery's lack of flexibility constrained between the bone surface and the dural sheath.

A sufficiently superselective distal position was reached in all cases without creating an unacceptable degree of risk for patients: the goal of embolization should be to render surgery safer and easier, but not at the expense of adding an-



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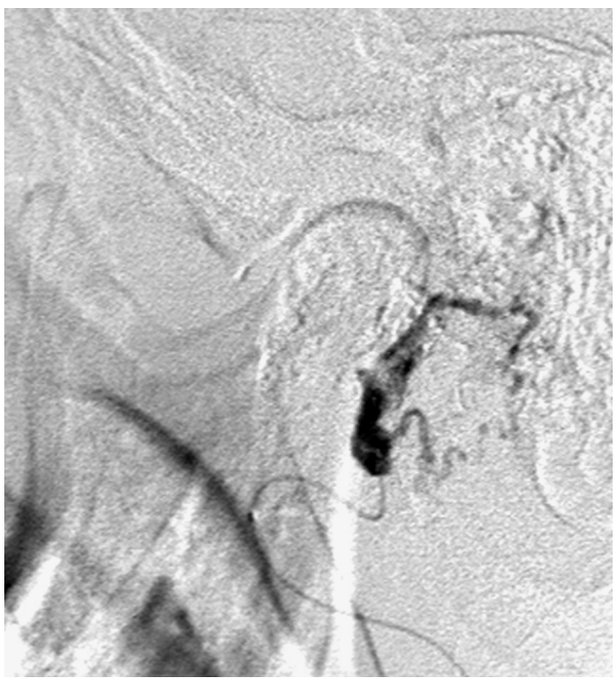

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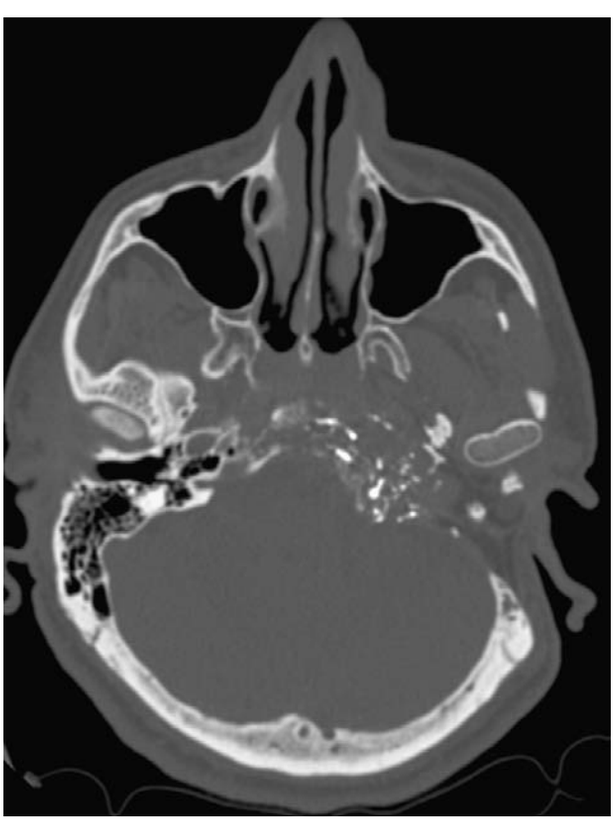

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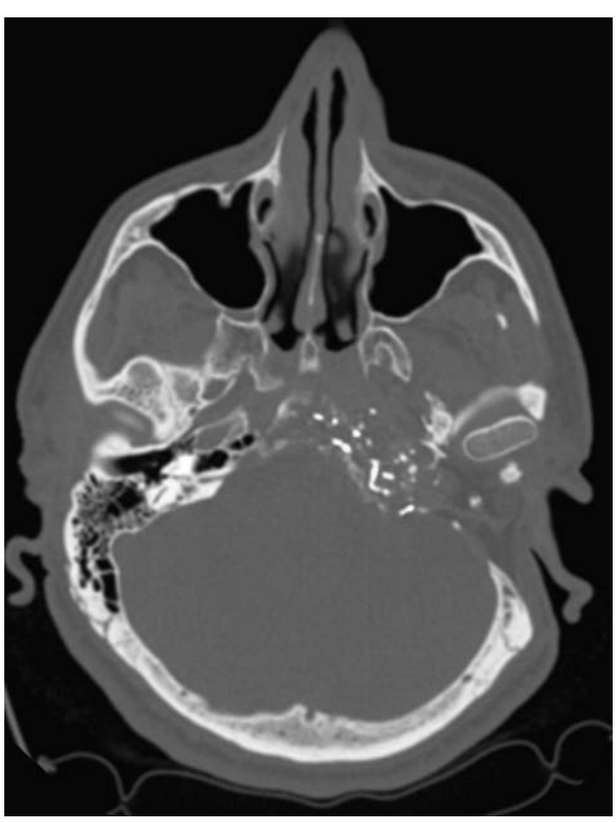

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Figure 6 Intra- and extracranial left jugular paraganglioma. A) Superselective angiography of the tumour's pathological circulation. B) Injection of Glubran 2® and its diffusion within the pathological circulation. C-D) CT scan without contrast administration after embolization. The scans show intralesional penetration of the glue.

other potentially dangerous procedure to the danger already associated with surgery.

Once the position was reached, superselective angiography was performed (figures 1C, 2 E, G-I, 3C, 4 A-B, E-F, 5 B and 6 A) to establish the stability of the microcatheter and the probable diffusion of the embolizing agent.

Angiography also served to further document the absence of dangerous shunts which may have been missed during the panoramic investigation.

Superselective catheterization targets the injection into the tumour in question, avoiding embolization of non pathological branches.

Injection of Glubran 2®

Glue adhesion or blockage of the microcatheter did not occur (figures 2 F,L), even in the case of moderate leakage of the embolizing agent. One of the main arguments against the use of cyanoacrylate glues for presurgical embolization [7-20] was the risk of gluing the microcatheter given the ready leakage occurring in these arterial branches (relatively low flow, narrow calibre) [4-20]. The progressive gradual polymerization of Glubran 2® noted in experimental tests and early clinical applications is an important safety factor.

Post-procedural stage. In the hours immediately following embolization, three patients presented headaches with features different from those usually encountered in intracranial extra-axial tumours. Analgesic treatment was given by intravenous administration of 100 mg ketoprofen, repeated as needed.

Conclusions

Particles are generally preferred to glue in the embolization of intracranial extra-axial tumours because they are easier to use. However, we note the following:

– very small particles (50 m) show good intralesional penetration, but are hazardous as they may pass through invisible tiny intra-extracranial shunts and hence larger particles are deemed safer (150-250 e 250-350 m);

– in addition to diffusing in an unexpected (and hence potentially dangerous) fashion, larger particles often tend to agglutinate, sometimes giving rise to highly proximal embolizations;

– simply occluding the main large feeding arteries may look good on a post-embolization angiogram, but may result in a persistent near-normal transtumoral blood flow due to the recruitment of collateral arterial supply. Even if no significant arterial collaterals develop by the time of surgery, the lack of intratumoral vascular occlusion can result in a bloody tumour during surgery because of preservation of these vessels and extensive retrograde filling from the venous side;

– conversely, simply filling the capillary bed with embolic material may be counterproductive. While it may also make the final angiogram appear satisfactory, it can make the tumour difficult to manipulate by the surgeon (more friable or rupturable) and still preserve the vascular supply to the operative region thereby retaining the potential for excessive bleeding during surgery.

Glubran 2® allowed permanent embolization of tumour afferents with good intralesional penetration and without the excessive drying properties typical of adhesive materials, but sufficient to prevent massive recruitment of collaterals or the filling of venous vessels.

Our results are encouraging and given the stability of vessel occlusion embolization could be extended to partial or palliative treatment of patients with inoperable tumours.

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