

Presurgical Embolization of Spinal Tumours Using Glubran 2 Acrylic Glue

L. RAFFI, L. SIMONETTI, P. CENNI, S. BANDIERA*, A. GASBARRINI*, S. BORIANI*, M. LEONARDI

Servizio di Neuroradiologia, Ospedale Bellaria, Bologna

**Divisione di Ortopedia, Ospedale Maggiore, Bologna; Italy*

Key words: acrylic glue, tumours, embolization

Summary

This study aimed to define the indications, technique and results of presurgical embolization of spinal tumours using Glubran 2 acrylic glue. Embolization was performed prior to surgery in eight patients with benign tumours and 11 patients with malignant lesions. The main embolization agent used was Glubran 2, a new acrylic glue with the EC mark, suitable for permanent embolization of the pathological circulation of primary and secondary spinal tumours.

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 correlated with the degree of vascular occlusion achieved.

Introduction

The prognosis of aggressive benign tumours and malignant tumours of the spine has recently been improved¹ by application of en bloc resection techniques^{2,3,4} used for many years to treat musculoskeletal tumours of the limbs⁵. These techniques are not always applicable due to anatomical restrictions characteris-

tic of the spine (continuity of non resectable structures). In these cases, local and systemic disease control depends on complete intralesional resection including removal of the tumour's pseudocapsule ("extracapsular excision"), combined with adjuvant therapies. However, extracapsular intralesional surgery of the spine is often hampered or prevented by severe tumoral haemorrhage. In these cases, embolization is an essential prerequisite to surgery, making resection possible and minimizing the risks. Embolization may also serve for palliative purposes to give pain relief. Technically speaking, it is a relatively straightforward neuroradiological procedure, but care must be taken to determine the vascular afferents of the level(s) involved and those of the over and underlying segments.

Angiographic identification of the anterior spinal axis deserves special attention as an anterior spinal artery arising at the same level as pathological branches is an obvious contraindication to embolization.

Particles are widely used embolizing agents as they are easy to handle and offer the advantage of good intralesional penetration, but they only achieve temporary occlusion so that embolization and surgery times need to be strictly coordinated^{6,8}.

Glubran 2 is a new acrylic glue bearing the CE mark and sold in Europe to replace His-

toacryl which has been shown to spread in the pathological vascular network causing endothelial injury and necrosis⁷. Glubran diffuses in a very similar way to Histoacryl but appears to have a more homogeneous fluidity and an excellent correspondence to the angiographic picture of superselective catheterization.

Macro and microscopic anatomical specimens of experimental studies on Glubran 2 have shown vessel occlusion and a strong chronic inflammatory reaction of the vessel wall⁶. 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.

We describe a series of 19 tumours deemed suitable for presurgical embolization and selected on the basis of histological type, hypervascularization, size, and type of surgery envisaged. The paper dwells on the main aim of embolization which was to resect the tumour afferents to make the operating field as blood-free as possible. The criteria adopted to assess the success of endovascular treatment were: degree of bleeding during surgery and the extent of radical extracapsular resection.

Material and Methods

Nineteen patients (10 males and 9 females aged between 10 and 70 years) were treated at the Neuroradiology Service at Bellaria Hospi-

Table 1 Patients Treated from January 2002 to March 2003

PT.	SEX	AGE	HISTOPATHOLOGICAL FINDING	LOCATION	TYPE OF TREATMENT	N° EMBOLIZATION SESSIONS
1	F	10	ANEURYSMAL CYST	CERVICAL	EMB. + SURG.	3
2	F	25	NEUROFIBROMA	LUMBAR	EMB. + SURG.	1
3	F	32	SCHWANNOMA	CERVICAL	EMB. + SURG.	1
4	M	49	SCHWANNOMA	DORSAL	EMB. + SURG.	1
5	M	46	HAEMANGIOMA	DORSAL	EMB. + SURG.	1
6	M	43	HAEMANGIOMA	DORSAL	EMB. + SURG.	1
7	M	30	OSTEOBLASTOMA	LUMBAR	EMB. + SURG.	1
8	M	51	OSTEOBLASTOMA	CERVICAL	EMB. + SURG.	1
9	F	43	CHORDOMA	DORSAL	EMB. + SURG.	1
10	F	70	METASTASIS	DORSAL	EMB. + SURG.	1
11	F	37	METASTASIS	LUMBAR	EMB. + SURG.	1
12	F	35	METASTASIS	DORSAL	EMB. + SURG.	1
13	M	58	METASTASIS	LUMBAR	EMB. + SURG.	1
14	M	49	METASTASIS	LUMBAR	EMB. + SURG.	1
15	M	67	METASTASIS	LUMBAR	EMB. + SURG.	1
16	M	70	METASTASIS	LUMBAR	EMB. + CHIR.	1
17	M	61	METASTASIS	DORSAL/LUMBAR	EMB.+ CHIR.	2
18	F	65	METASTASIS	LUMBAR	EMB.+ CHIR.	1
19	F	69	METASTASIS	SACRAL	EMB.+ CHIR.	1

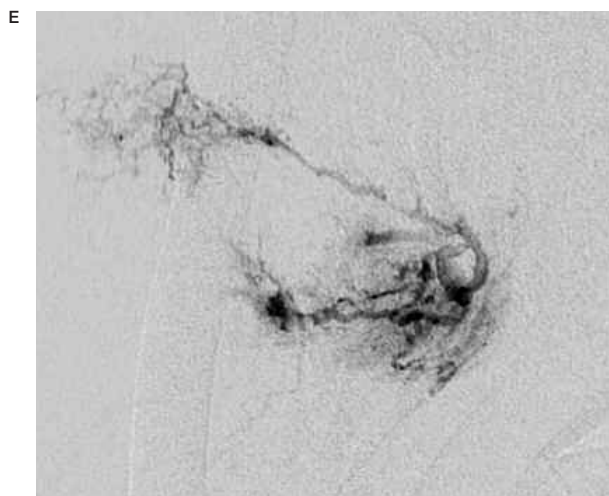
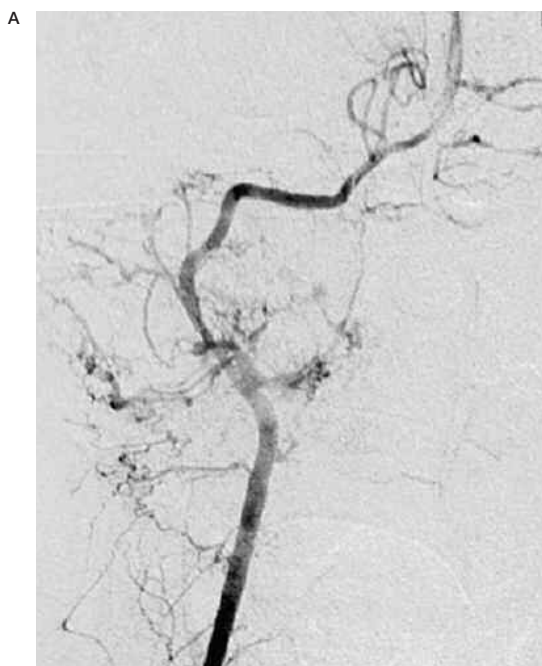
Table 2 **Outcome of Embolization**

CASE	GLUE	PARTICLES *	EMBOLIZATION **
1	GLUBRAN 2	CONTOUR (2b)	COMPLETE
2	GLUBRAN 2		COMPLETE
3	GLUBRAN 2		PARTIAL Confined to the thyrocervical artery
4	GLUBRAN 2		COMPLETE
5	GLUBRAN 2	CONTOUR (1)	COMPLETE
6	GLUBRAN 2	CONTOUR (2a)	COMPLETE
7	GLUBRAN 2	EMBOSPHERES (2b)	COMPLETE
8	GLUBRAN 2		PARTIAL Confined to the thyrocervical arteries
9	GLUBRAN 2	CONTOUR (2b)	COMPLETE
10	GLUBRAN 2	CONTOUR (2b)	COMPLETE
11	GLUBRAN 2		COMPLETE
12	GLUBRAN 2		PARTIAL Confined to one metamere
13	GLUBRAN 2		PARTIAL Confined to the visible afferents
14	GLUBRAN 2	CONTOUR (2a e 2b)	COMPLETE
15	GLUBRAN 2	CONTOUR (2b)	COMPLETE
16	GLUBRAN 2	CONTOUR (1)	COMPLETE
17 (D1)		CONTOUR (1)	SUBTOTAL
17 (D8 e L5)	GLUBRAN 2		COMPLETE
18	GLUBRAN 2	EMBOSPHERES (2b)	COMPLETE
19	GLUBRAN 2		COMPLETE(*)See text

(*)See text (**)Degree of embolization refers to the whole vascularization of the lesion

tal, Bologna between January 2002 and March 2003. All patients had spinal tumours characterized by highly vascularized lesions giving rise to spinal cord-nerve root compression. Eight patients had benign primary tumours (one aneurysmal cyst, two schwannomas, two haemangiomas, two osteoblastomas and one neurofibroma) and 11 had malignant lesions (one chordoma and ten bone metastases). Tumour locations were: three cervical, seven dorsal, eight lumbar and one sacral. All patients had

CT and/or MR evidence of the lesion whose circulation was studied by angiography and embolization often undertaken at the same sitting. Presurgical embolization was carried out in only one session in 17 patients. Case 1 (aneurysmal cyst) required three embolization sessions on the same lesion and case 17 presenting two dorsal (D1 and D8) and one lumbar (L5) metastases was treated in two sessions with embolization of the D1 lesion in the first session and the D8 and L5 metastases in the second.



Angiography was undertaken in the cervical lesions (cases 1,3 and 8) to study the vertebral, ascending cervical and deep cervical arteries, thyrocostocervical and external carotid arteries. The intercostal and/or lumbar arteries of the level involved and at least those of the two levels above and below the lesion were studied in cases of dorsolumbar tumours. In low lumbar and sacral lesions, the hypogastric arteries were catheterized in addition to the lower lumbar metameres. The anterior spinal axis was scrutinized to disclose any significant medullary afferents.

Before each injection of Glubran 2, the microcatheter was washed with a glucosate solution to remove the saline solution and blood.

In all patients, embolization was achieved with Glubran 2 glue (GEM Srl, Viareggio, Italy). The glue was combined with Contour particles (Boston Scientific, Target Therapeutics, Fremont, USA) of various sizes in nine cases and Embosphere particles (Biosphere Medicals, Roissy CH de Gaulle Cedex, France) in two patients. Glubran 2 and the particles were injected after superselective microcatheterization of the pathological circulation. Glubran 2 was



Figure 1 Case 1, 10-year-old, female. On the right, a large highly vascularized aneurysmal cyst with irregular ectasic vessels and dilated drainage veins with most blood to the lesion supplied by the ipsilateral ascending cervical artery (A) but also with afferents from the vertebral artery (B) and external carotid artery. The ipsilateral vertebral artery is enveloped within the tumour causing stenosis (B). Before surgery, three successive embolization sessions were required: the first reduced the size of the tumour by injection of particles into the ascending cervical artery. In the second session, a more posterior portion of the mass fed by a occipital artery branch of the external carotid artery (C) was embolized and in the third session the vertebral artery (D) was occluded by two balloons released above and below the comb-like afferent branches feeding the lesion and the ascending cervical artery was embolized with Glubran 2. E) The injection of contrast medium before injection of the glue (F). Note the similar diffusion of the embolizing agent and the contrast medium. The last follow-up angiogram failed to disclose pathological afferents.

mixed with Lipiodol (Guerbet, Roissy CdG Cedex, France) at different concentrations: Glubran 2 : Lipiodol 1:1, 1:2, 1:3, depending on the characteristics of the pathological circulation. The injection was made using a continuous column of glue and the flow and placement of Glubran 2 was monitored by digital angiography, stopping the injection when retrograde flow was visible in the afferent vessel.

In case one (aneurysmal cyst), the tumour enveloped the vertebral artery causing severe stenosis. As this artery had to be sacrificed to achieve complete surgical resection and the contralateral compensation was deemed good, the artery was closed with two Gold Valve balloons (8x21) (Nycomed Amersham, Medical System, Paris, France).

Particles were confined to certain situations (table 2):

1. Failure to achieve stable catheterization with Glubran 2 alone.

2. In the work-up to embolization with glue to (a) achieve a preferential flow route for Glubran 2 and (b) reduce the circulation in large tumours with an extensive pathological circulation.

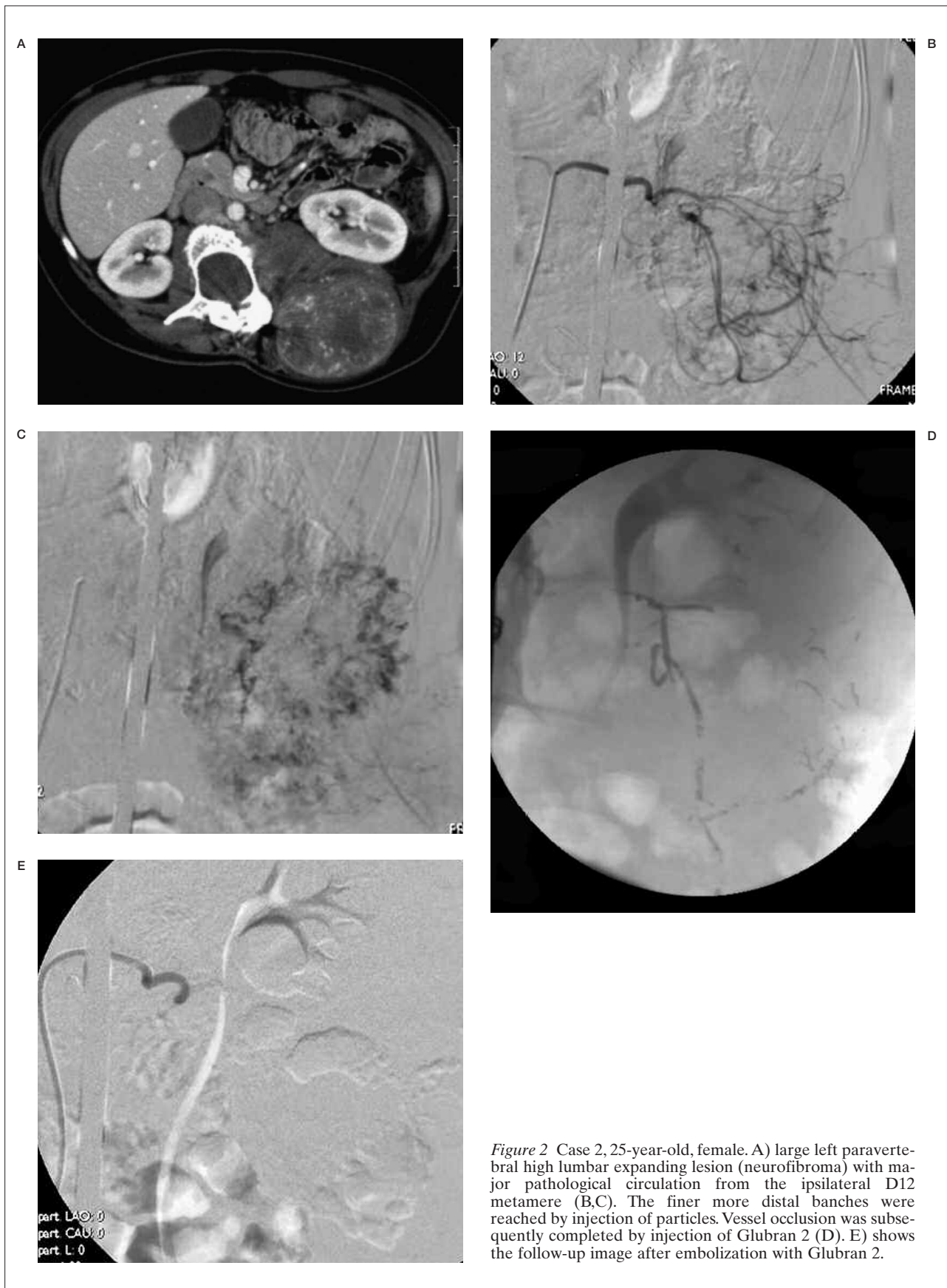
Results

The results were analysed on the basis of the tumour treated, its location and the features of the pathological circulation.

Benign Lesions

Case 1 - C2-C3 Aneurysmal cyst

The pathological circulation of this large right laterocervical aneurysmal cyst was characterized by irregular ectasic vessels with dilated drainage veins and most blood supply to the lesion through the ipsilateral ascending cervical artery and afferents from the vertebral artery, external carotid and cervical thyrocostal arter-



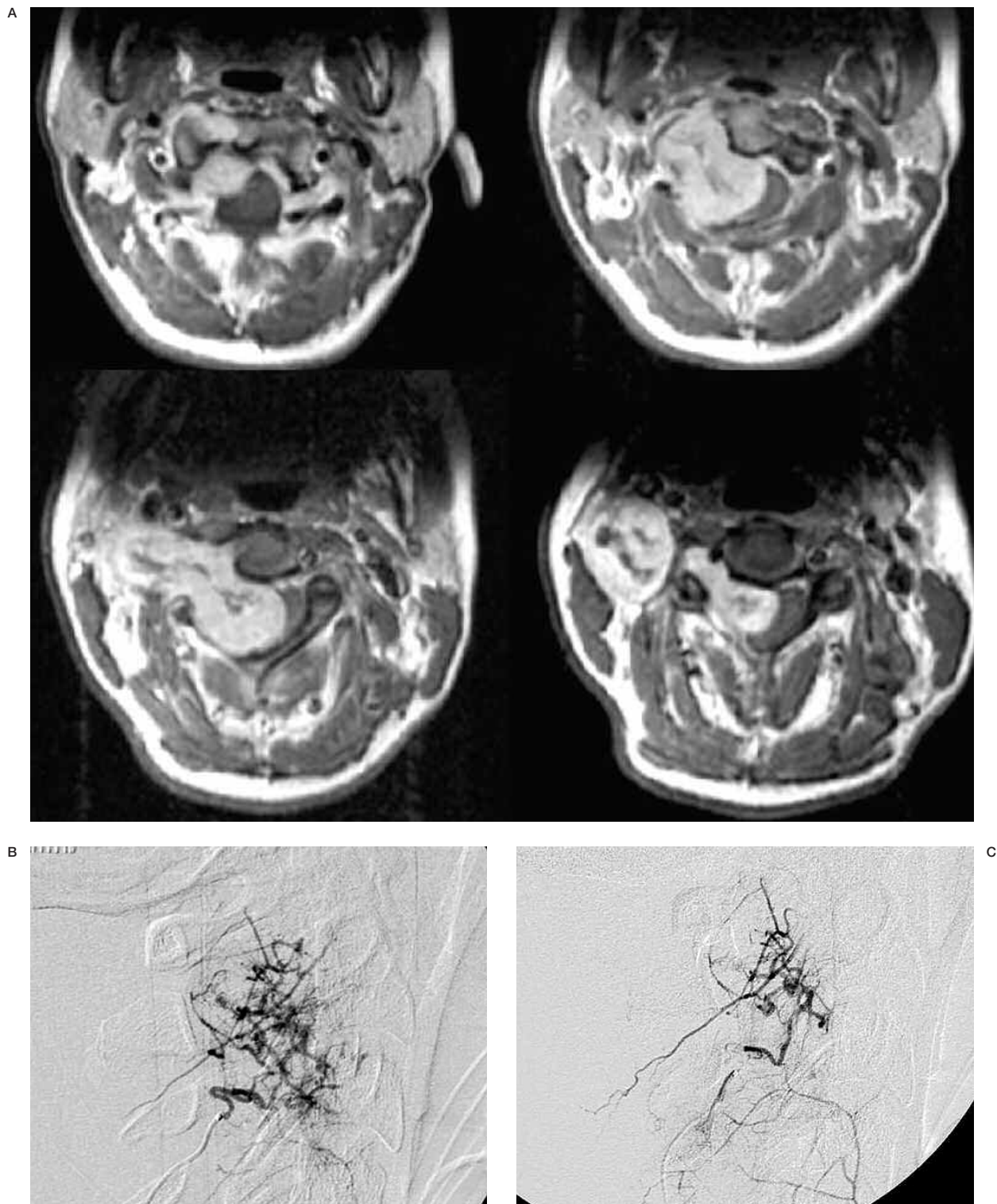


Figure 3 Case 3, 32-year-old, female. Intradural neurinoma extending from C1 to C5 with extra-canal growth through the C2-C3 and C3-C4 root canals (A, MR tomography) with a rich pathological vascularization from branches of the vertebral artery and thyrocervical artery and stenosis of the vertebral artery enveloped by the tumour. A stable position was reached in the thyrocervical artery-right ascending cervical artery pathological circulation (B) and the Glubran 2 injected to achieve complete embolization of the afferent (C). Note the similar diffusion of the embolizing agent (C) and the contrast medium (B).

ies (figure 1). The ipsilateral vertebral artery appeared stenotic as it was enveloped within the tumour (figure 1A). Three sessions were required before surgery.

The first reduced the size of the lesion by injection of particles into the ascending cervical artery. A more posterior portion of the mass fed by the occipital artery branch of the external carotid artery was embolized during the second session (figure 1C). During the third session, the vertebral artery was occluded with two balloons (figure 1D) released above and below the comb-like branches feeding the lesion and the ascending cervical artery was embolized with Glubran 2 (figure 1E,F). The last follow-up angiogram failed to disclose pathological afferents.

Case 2 - *Neurofibroma*

This large left paravertebral upper lumbar expanding lesion presented a pathological circulation from an ipsilateral metamere. The finer more distal branches were reached by slow injection of particles followed by Glubran 2 (figure 2).

Cases 3 and 4 - *Schwannoma*

Case 3 was an intradural neurinoma extending from C1 to C5 with extracanal development through the C2-C3 and C3-C4 root canals with a rich vascularization supplied by branches of the vertebral artery and the thyrocervical artery and vertebral artery stenosis caused by tumour envelopment. A stable position was reached within the thyrocervical pathological circulation and Glubran 2 was injected to achieve complete embolization (figure 3). The para and intravertebral D10 neurinoma in case 4 was highly vascularized by the ipsilateral intercostal artery which was embolized using Glubran 2 alone (figure 4).

Cases 5 and 6 - *Haemangioma*

A partially disrupted capillary circulation of the D6 vertebral body in case 5 was embolized from the right side by injection of Glubran 2. As a stable position for glue injection could not be reached on the left side, Contour particles were injected.

The capillary circulation in the D8 vertebral body in case 6 fed by both metameres was embolized distally using particles and proximally using Glubran 2.

Cases 7 and 8 - *Osteoblastoma*

The L3 osteoblastoma fed by the L2 and L3 metameres in case 7 was embolized by Glubran 2 on L2 and Embosphere particles directly from the Cobra catheter on L3. The C5 osteoblastoma in case 8 was supplied by four afferents: the vertebral artery, ascending cervical artery and branches of the thyrocervical artery. Glubran 2 was chosen for embolization of all afferents because the anterior spinal artery arose from the ascending cervical artery.

Embolization was a presurgical procedure in the eight patients with benign primary tumours. Embolization was complete in six and partial in two (cases 3 and 8) as the lesion was fed by several afferents and the afferent allowing the most stable position for injection was chosen (case 3, figure 3). In addition, one of the multiple tumour afferents gave rise to the anterior spinal artery (case 8).

Malignant Lesions

Case 9 - *Chordoma*

The chordoma located in D6 presented a hypervascularization from the left metameric artery and very thin branches of the contralateral metamere. Complete embolization of the lesion was achieved by injection of Glubran 2 on the right and Contour particles on the left.

Case 10 -19 - *Metastases*

In the ten patients with malignant lesions, complete embolization of the tumour was achieved in seven cases with good penetration of the embolizing agent into the pathological circulation. Embolization was not complete in three patients. In case 12, the pathological circulation presented afferents from D7 and D8 on the left and the anterior spinal artery injected from D8 and left D10, allowing complete occlusion from the D7 metamere alone. Case 13 had no afferents suited to catheterization of one of the two tumours present. Only partial embolization using particles was possible in the D1 lesion in case 17 as the tortuosity of the branches arising from the thyrocostocervical artery precluded stable superselective microcatheterization.

Embolization was technically successful in all patients without periprocedural complications. The outcome was deemed highly satisfac-



Figure 4 Case 4, 68-year-old, male. A D10 neurinoma with mainly paravertebral development, highly vascularized by the ipsilateral intercostal artery (A) embolized using Glubran 2 alone. B) Catheterization of the D10 intercostal artery using a coaxial microcatheter. When the washing flow of the guiding catheter had stopped, the catheter wedged in the opening of the intercostal artery allowed complete control of flow below when injecting from the microcatheter. C) Glue injection under full flow control. D) Cast of Glubran 2 confined to the arch of the intercostal artery surrounding the tumour mass with occlusion of the afferents sparing the distal stretch of the intercostal artery.

tory in terms of subsequent surgery since reduced or absent bleeding from tumoral tissue allowed radical resection of the microscopically visible tumour and its pseudocapsule.

Discussion and Conclusions

The embolization of tumours is an ongoing field of research. Spine and spinal cord tu-

mours have been widely treated by this approach using different materials, mainly particles and acrylic glue. The two prerequisites for safe and effective injection of particles or glue are superselective catheterization and flow control. Superselective catheterization targets the injection into the tumour in question, avoiding embolization of non pathological branches. Control of injected flow is ensured by

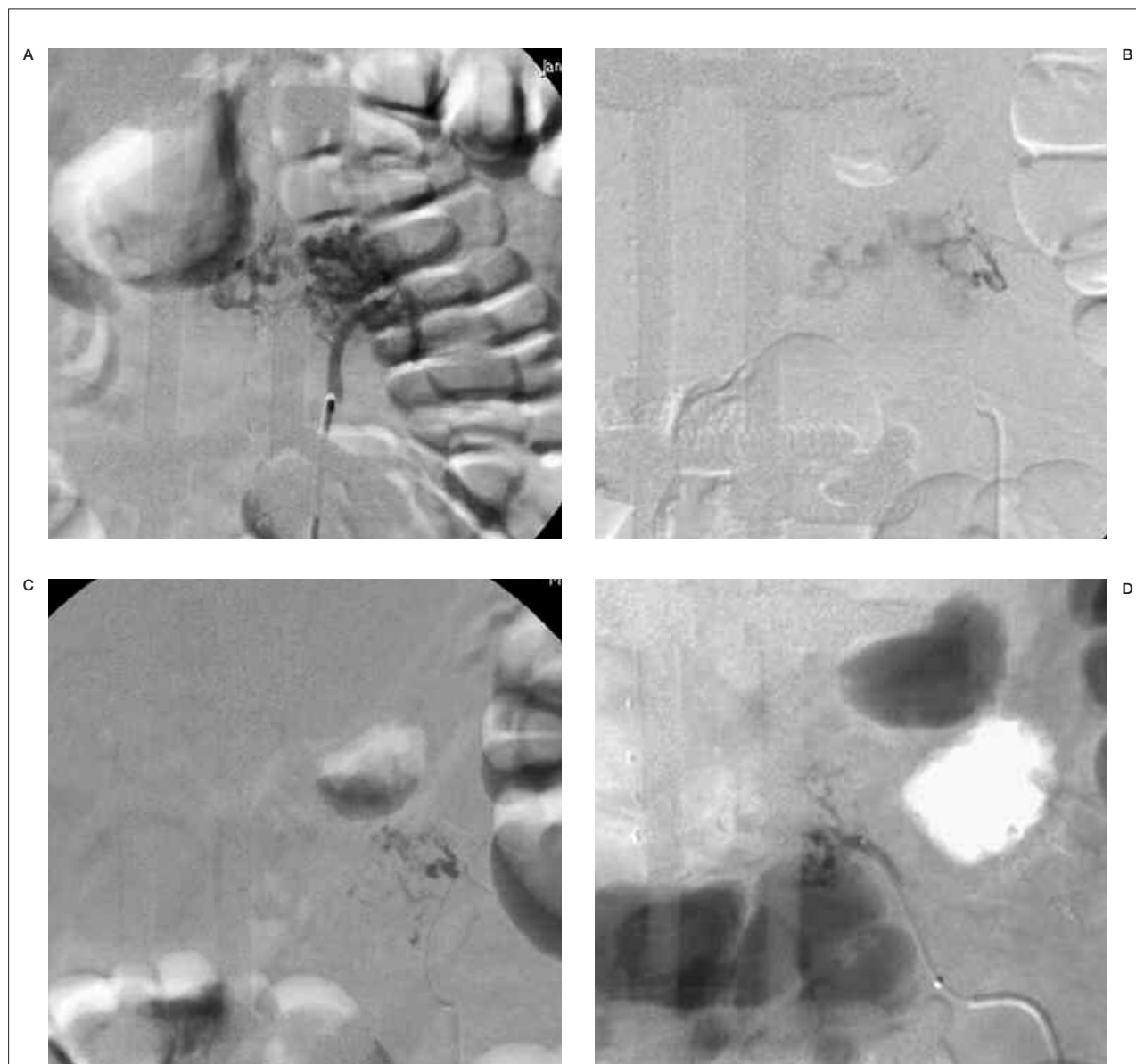


Figure 5 Case 15, 68-year-old, male. Metastasis from a hypernephroma with a large pathological circulation from the bilateral L1 metameres. A) Catheterization of the corresponding left metamere with a view of the pathological circulation and subsequent superselective catheterization sufficiently distal (B) to allow glue injection (C). On the right, microcatheterization (D) allowed a stable position to be reached for glue injection with good distal penetration. Final follow-up after embolization shows the intralesional penetration of the glue into the proximal and distal segments (E).

careful assessment of the haemodynamic features of the main pathological branches. Embolization of arterial afferents using particles is a temporary measure based on the thrombogenic power of the particles. Recanalization of the thrombosed vessel is readily triggered by a proteolytic enzyme cascade at different times after embolization depending on the type of particles injected. Care must be taken to inject the particles slowly using a diluted solution⁸.

Unlike particles, Glubran 2 must be injected from a more stable and distal position of the microcatheter and navigation may be hampered by tortuous vessels or narrow angles.

Glubran 2 penetrates well into the tumoral microvasculature and dilution of the glue was adjusted to facilitate penetration in individual cases. Intravasal penetration closely depends on glue dilution and the characteristics of tumour vascularization and flow. A high dilution



of the glue in a Glubran 2 : Lipiodol mixture of 1:3 proved especially useful for easier more effective penetration to reach more distal branches and was the mixture most often administered.

References

- 1 Boriani S, Weinstein JN: Differential diagnosis and surgical treatment of primary benign and malignant neoplasms. In: Frymoyer JW, ed The adult spine: Principles and practice. 2nd edition Philadelphia. Lippincott-Raven Publishers, 1997: 951-987.
- 2 Roy-Camille R, Monpierre H et Al: Technique de vertebrectomie totale lombaire. in: Roy-Camille R (ed) Rachis Dorsal et Lominaire. Septieme Journees d'Orthopedie de la Pitié. Masson, Paris 1990: 49-52.
- 3 Tomita K, Kawahara N, Baba et Al: Total en bloc spondylectomy for solitary spinal metastases. Int Orthop (SICOT) 18: 291-298, 1994.
- 4 Boriani S: Subtotal and total vertebrectomy for tumors. Editions Scientifique at Medicales Elsevier SAS (Paris). Surgical Techniques in Orthopedics and Traumatology. 55-070-A-10, 2000.
- 5 Enneking WF, Spanier SS, Goodman M: A system for surgical staging of musculoskeletal sarcoma. Clin Orthop 153: 106-120, 1980.
- 6 Gellad FE, Sadato N et Al: Vascular metastatic lesions of the spine:preoperative embolization. Radiology 176: 683-686, 1990.
- 7 Leonardi M, Barbara C et Al: Glubran 2: a new acrylic glue for neuroradiological endovascular use- Experimental study on animals. Interventional Neuroradiology 8: 245-250, 2002.
- 8 Maciunas RB: Endovascular Neurological Intervention, Park Ridge, Illinois, USA 139-284, 1995.
- 9 Matias S, Vilela P et Al: Vertebral and perivertebral tumors and tumor-like conditions. Rivista di Neuroradiologia 14: 201-206, 2001.
- 10 Perini S, Maschio M et Al: Angiografia ed embolizzazione dei tumori vascolarizzati del rachide. Rivista di Neuroradiologia 1: 37-52, 1988.
- 11 Schumacher M, Klisch J et Al: The role of embolization in the interdisciplinary treatment of extradural space-occupying lesions in the vertebral canal, Klin Neuroradiol 12: 160-167, 2002.
- 12 Shi HB, Suh DC et Al: Preoperative Transarterial embolization of spinal tumor: embolization techniques and results, Am J Neuroradiol 20: 2009-2015,1999.

In most cases treated by superselective microcatheterization, glue injection tended to follow the route of preferential flow in tumour vessels, especially in the presence of hypervascularized pathological circulation (haemangiomas, hypernephroma, metastases). On occasion, superselective catheterization proved difficult or impossible due to the size and direction of the pathological branches.

When one main afferent was present giving rise to numerous comb-like branches, it was useful to occlude the segmental artery with the guiding catheter to control the flow of the glue and ensure good intralesional penetration. Glubran 2 could then be injected from the microcatheter into the main afferent vessel after closure of washing from the guiding catheter. This technique ensured an absence of flow preventing polymerization of the glue which could be injected under full control into the most distal branches.

Glubran 2 proved an excellent embolizing agent in all cases allowing safe and technically straightforward embolization. Presurgical embolization was permanent allowing surgery to be delayed for excellent deafferentation of the tumour and better surgical management.

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.

Dr L. Raffi
Servizio di Neuroradiologia,
Ospedale Bellaria
40139 Bologna, Italy