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Aneurysmal Bone Cysts: Treatment with Direct Percutaneous Ethibloc Injection: Long-Term Results

Piergiorgio Falappa,[1] Fausto M. Fassari,[2] Arturo Fanelli,[1] Elisabetta Genovese,[3] Elio Ascani,[4] Marco Crostelli,[4] Vittorio Salsano,† Antonello Montanaro,[5] Antonio Di Lazzaro,[6] Fabrizio Serra[7]

[1]Department of Radiology, Hospital IDI IRCCS, Via Monti di Creta, 104, I-00167 Rome, Italy
[2]Department of Radiology, Pediatric Hospital Bambino Gesù IRCCS, Via della Torre di Palidoro, I-00050 Passoscuro (Rome), Italy
[3]Department of Physics, Tor Vergata University, Via della Ricerca Scientifica, 1, I-00133 Rome, Italy
[4]Department of Orthopedics 1st Division, Pediatric Hospital Bambino Gesù IRCCS, Via della Torre di Palidoro, I-00050 Passoscuro (Rome), Italy
[5]Department of Orthopedics 2nd Division, Pediatric Hospital Bambino Gesù IRCCS, Via della Torre di Palidoro, I-00050 Passoscuro (Rome), Italy
[6]Department of Orthopedics, Pediatric Hospital Bambino Gesù IRCCS, Via S. Onofrio, 4, I-00165 Rome, Italy
[7]Department of Orthopedics, Policlinico Gemelli Catholic University, Largo Gemelli, 1, I-00168 Rome, Italy

Abstract

Purpose: To assess the efficacy and long-term results of Ethibloc treatment in aneurysmal bone cysts (ABC).
Methods: Thirteen patients with ABC were treated with direct percutaneous Ethibloc injection. Four patients had only one injection and the other nine patients from two to four injections. No severe complications were observed; in two patients a local leakage of Ethibloc from the cyst into the soft tissues occurred but it was temporary and the consequent inflammation self-healed without residua and sequelae. Imaging follow-up lasted from 6 to 67 months and included conventional radiology (CR) and magnetic resonance imaging (MRI), both used in the presurgical phase.
Results and Conclusions: All images demonstrated a remarkable shrinkage of the cystic lesion and bone cortex thickening. In all patients, circumscribed areas of lucency persisted at radiography, corresponding to residual cystic areas without fluid–fluid levels at MRI. Pain, which was present in all the patients before treatment, was relieved within a month. According to our experience, direct percutaneous Ethibloc injection is effective in the treatment of ABC and can be recommended as the first-choice treatment. Due to its higher sensitivity MRI must be included either in the pretreatment phase to study the multilocular structure or in the imaging follow-up to evaluate the efficacy of Ethibloc in persistently non-responsive areas.

Key words: Aneurysmal bone cysts—Ethibloc—Percutaneous injection—Conventional radiology—Magnetic resonance imaging

Aneurysmal bone cyst (ABC) is a tumor-like lesion of the bone, first described as a distinct clinicopathologic entity by Jaffe and Litchtenstein in 1942 [1], and represents from 3% to 6% of all primary bone tumors; about 80% patients are under 20 years of age. The must common locations are the long tubular bones, axial skeleton, feet, hands, pelvis and craniofacial bone [2]. ABC may present as a primary osteolytic lesion (65%), including the solid variant [3], or as secondary changes in another lesion (35%) [4, 5]. Secondary forms are described in association with benign or malignant bone pathologies already histologically proved (fibrous dysplasia, giant-cell tumor, unicameral bone cyst, chondromyxoid fibroma, non-ossifying fibroma, chondroblastoma, hemangioma, hemangioendothelioma, osteogenic sarcoma, chondrosarcoma, metastasis [2, 6, 7]. No case of malignant transformation of a primary ABC has ever been reported [5]. Only primary forms, excluding the solid variant, were considered in this study.

†*Vittorio Salsano is deceased.*

Correspondence to: Prof. P. Falappa; *email:* piergiorgio@falappa.net

The purpose of this study was to assess the possibility for Ethibloc treatment as an alternative to the usual treatment, i.e., surgery, including curettage combined with bone grafting [7, 8] with phenol [9], with cryotherapy [10] or with cementation [11] and total resection [12]. As reported in the literature, radiation therapy was considered as a treatment for ABC [13], but its use is limited and it is now obsolete. Minimally invasive treatments such as selective embolization [14, 15] and, more recently, based on the experience of direct puncture of a simple bone cyst with injection of methylprednisolone [16], direct percutaneous injection of sclerosing and embolizing substances [17–20], have been performed.

This study analyses the long-term results of treatment with direct percutaneous injection of Ethibloc, monitored with both conventional radiology (CR) and magnetic resonance imaging (MRI), assuming that a viscose sclerosing and embolizing substance is able to occlude at the venous side the multiple parietal arteriolar afferents of ABC.

Materials and Methods

Thirteen patients (9 females, 4 males; age 5–23 years) underwent direct percutaneous Ethibloc injection. Eight had a histologic diagnosis of ABC; in five the diagnosis was based on the typical imaging and clinical features such as the aspiration of blood at the puncture and negative cytologic analysis for malignancy. Table 1 shows the details of our cases and includes previous unsuccessful treatments performed. All patients were treated after completing a detailed informed consent that specified the use of a substance not licensed for injection into bone. All potential complications were explained. In the literature [17–19] other studies refer to the use Ethibloc for the treatment of simple cysts and ABC. Before treatment all patients underwent CR and MRI; eight had computed tomography (CT) also. Four patients needed one treatment each; from two to four treatments were needed by the other nine patients.

Ethibloc is a hydroalcoholic radiopaque solution. One milliliter contains 210 mg of zein, 162 mg of sodium amidotrizoate tetrahydrate, 145 mg of oleum papaveris, 316 mg of 95% ethanol and 249 mg of aqua ad injectabilia. It is available in sterilized 7.5 ml syringes. Ethibloc preparation consists of mixing all the substance contained in the syringe (7.5 ml) with 1–2 ml of 95% ethanol to obtain a homogeneous suspension (by alternately pushing the substance between two extremities, i.e., two syringes connected via a three-way tap).

The injection was performed with a 18 G Seldinger needle under general anesthesia because any injection into a bone cystic cavity causes unbearable pain. In large lesions or in noncommunicating multilocular cysts we inserted two or more needles. The injection was fluoroscopy-guided in 11 patients, and CT-guided in two. A small quantity of hydrosoluble contrast medium was first injected to verify the contrast distribution and any possible venous drainage. After this preliminary test, the Ethibloc mixture was injected slowly under fluoroscopic control to fill identified cavities. In large communicating lesions the possible maximum filling relative to the dose was verified by the introduction of two needles into opposite sides of the cyst, one used to inject Ethibloc, the other to permit the drainage of blood from the cyst. According to the suggested dosage the maximum introduced amount was 7.5 ml of Ethibloc (one syringe) plus 1–2 ml of ethanol for each single treatment. After the injection, manual compression on the entrance hole of the needle was performed for at least 10 min. The distribution of Ethibloc was immediately documented by radiographs in two projections and confirmed after 1 or 2 days. After the procedure prophylactic therapy was prescribed including antibiotic (cephalosporin, 20 mg/kg per day), analgesics (ketorolac trometamol 30–60 mg/day) and steroids (methylprednisolone 40 mg/day) for 5–7 days. Follow-up consisted of radiologic examinations and MRI: radiographic controls at 1, 3, 6 and 12 months and then annually; MRI controls at 6 and 12 months and then annually. Additional MRI controls may be useful to monitor fractionated multiple treatments performed, especially in the largest and non-communicating multilocular cysts.

Results

At imaging the results of the treatment consisted of endosteal bone reconstruction, reduction of the aneurysmal cavity and a return to normal morphology of the involved skeletal segment. The results were classified as: “no response”, “just detectable response”, “well detectable response”, “almost total response” and “total response” at CR as well as at MRI controls (Table 1; Figs. 1, 2).

In all cases at MRI the restructuring areas appeared isointense to the bone marrow or showed low signal intensity on T1-weighted images and low signal intensity on T2-weighted images. At radiography, generally, small circumscribed radiolucent areas persisted; at MRI, these areas showed low signal intensity on T1-weighted images and increased signal intensity on T2-weighted images with no fluid–fluid levels.

Clinically the pain, present in all patients before treatment, was relieved totally within a month. During follow-up three patients reported pain again at the site of the lesion: at imaging, two did not show any modification of the lesion while one showed the growth of a circumscribed residual area and needed a second injection 5 years after the first one (Fig. 3).

All patients returned to a normal life in a short time. As a sign of therapeutic response to the sclero-embolization treatments, a progressive reduction of skin hyperthermia in the area close to the cyst was noticed; this sign, caused by hypervascularization and hypermetabolism of the cystic wall, is evidenced by touch in superficial cysts.

Complications

Major complications due to sclero-embolizing treatment are described in literature [18, 19], such as aseptic bone necrosis, venous leakage in soft tissues, deep venous thrombosis, pulmonary embolism, abscess in soft tissues and, possible in theory [17, 20], osteomyelitis, fractures, epiphyseal necrosis, limb length discrepancy and inflammatory reactions of neurologic structures in spinal locations. In this study only minor complications (fever and temporary local pain in 8 cases, a self-healed inflammatory reaction to Ethibloc leakage in soft tissues in 2) occurred. We believe that careful

Table 1. Aneurysmal bone cysts treated by percutaneous Ethibloc injection

Patient no.:	1	2	3	4	5	6	7	8	9	10	11	12	13
Sex/age (years):	F/23	F/11	F/14	M/8	M/9	M/5	F/18	F/10	F/17	F/13	M/7	F/9	
Site:	Femoral neck	Proximal tibia metaphysis	Femoral neck and metaphysis	Femoral neck and metaphysis	Proximal humerus metaphysis and diaphysis	Ischium and acetabulum	Proximal femur metaphysis	Peroneum malleolus	Distal femur metaphysis	Proximal tibia metaphysis	Femoral neck	Calcaneus	
Size (cm):	5 × 2.5	4.5 × 4	14 × 7	10 × 7	13 × 4	7 × 4.5	6 × 4	7.5 × 5.5	6 × 5	5 × 3	8 × 6	2 × 1	2 × 1.5
Morphology and contrast filling:[a]	**	*	***	****	***	***	***	***	***	***	**	***	**
Epiphyseal involvement:	No	No	No	No	Yes	No	–	No	No	No	Yes	No	No
Pathologic fracture:	No	No	No	Yes	Yes	Yes	No	No	No	No	No	No	No
Previous surgery:	Yes	No	No	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No
No. of sclerosing treatments:	2	1	4	2	4	3	3	2	3	1	4	1	1
Complications:[b]	+	++	+	0	0	0	++	+	+	+	+	0	0
Results (MRI):[c]	WDR	WDR	WDR	WDR	ATR	WDR	TR	ATR	ATR	WDR	WDR	ATR	ATR
Results (CR):[c]	ATR	WDR	ATR	TR	TR	ATR	TR	ATR	TR	ATR	ATR	TR	TR
Follow-up (months):	67	60	50	44	38	32	26	13	12	10	8	7	6

[a]Morphology and contrast filling: *unilocular polycyclic margin; **multilocular communicating; ***multilocular non-communicating; ****multilocular non-communicating with periosteal involvement.
[b]Complications: 0, no fever; +, fever and pain; ++, fever, pain and leakage
[c]Results at CR and at MRI: Response to treatment expressed as: no response (NR), just detectable response (JDR), well detectable response (WDR), almost total response (ATR), total response (TR)

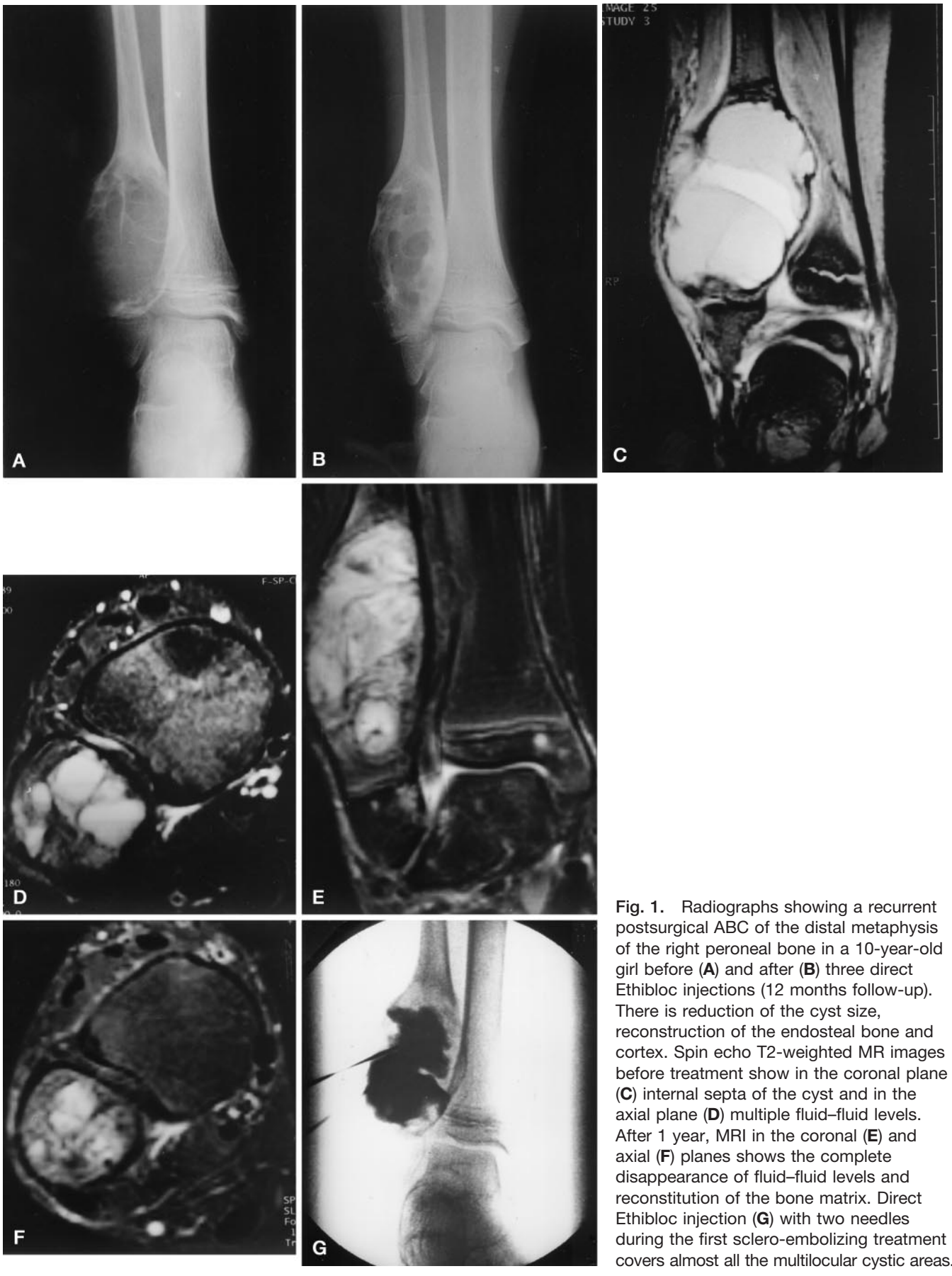


Fig. 1. Radiographs showing a recurrent postsurgical ABC of the distal metaphysis of the right peroneal bone in a 10-year-old girl before (**A**) and after (**B**) three direct Ethibloc injections (12 months follow-up). There is reduction of the cyst size, reconstruction of the endosteal bone and cortex. Spin echo T2-weighted MR images before treatment show in the coronal plane (**C**) internal septa of the cyst and in the axial plane (**D**) multiple fluid–fluid levels. After 1 year, MRI in the coronal (**E**) and axial (**F**) planes shows the complete disappearance of fluid–fluid levels and reconstitution of the bone matrix. Direct Ethibloc injection (**G**) with two needles during the first sclero-embolizing treatment covers almost all the multilocular cystic areas.

Fig. 2. Radiographs of multilocular recurrent post-surgical ABC of the proximal metaphysis and diaphysis of the left humerus in an 8-year-old boy before (**A**) and after (**B**) four sclero-embolizing treatments (38 months follow-up). There is healing of the cyst. Direct Ethibloc injection (**C**) was carried out with two needles at the extremities of the cyst. Spin echo T2-weighted MR images in the coronal (**D**) and axial planes (**E**) after treatment show very few residual cavities without fluid–fluid levels to be controlled in the follow-up.

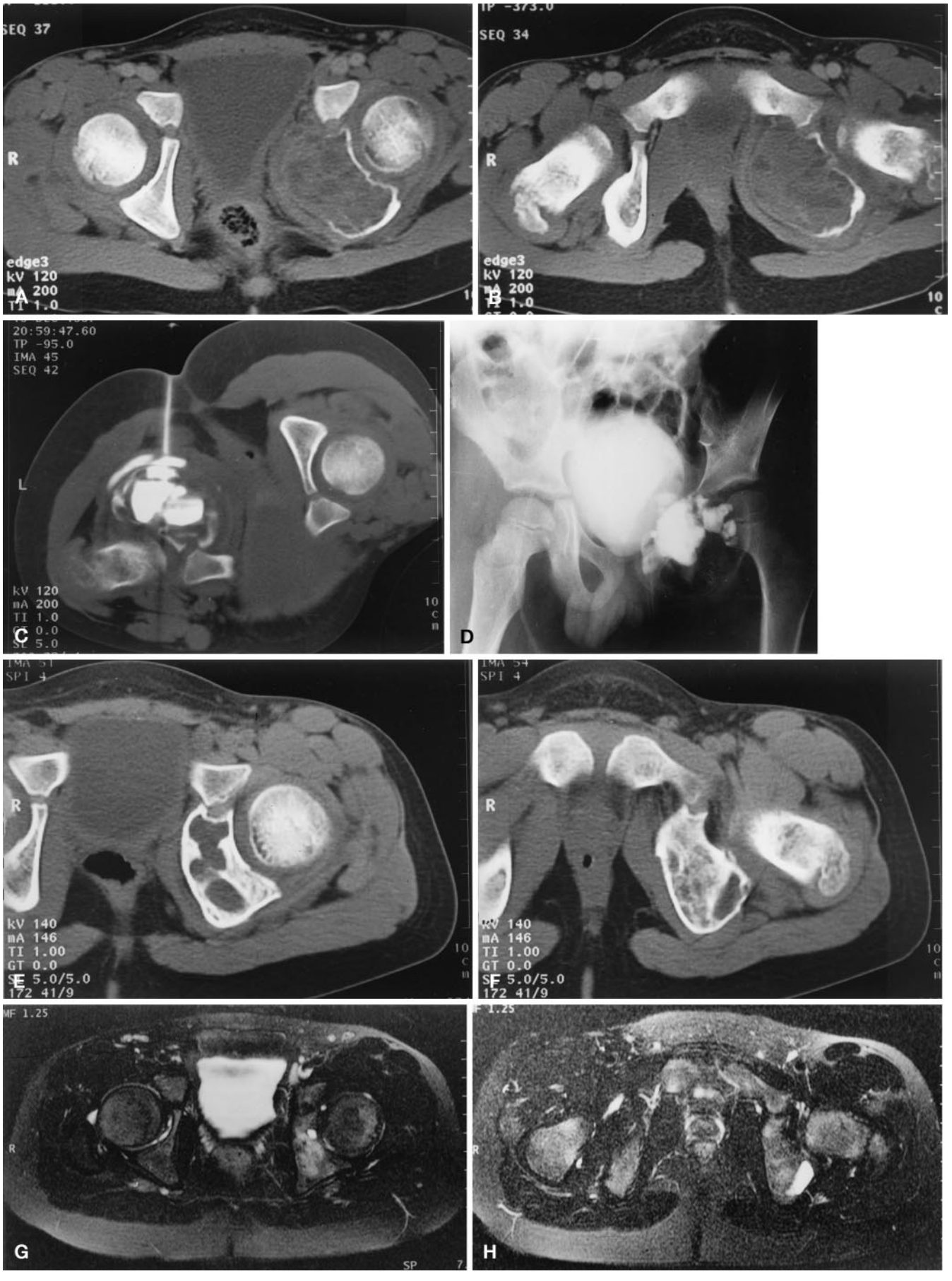
asepsis, preliminary injection of hydrosoluble contrast medium, simultaneous monitoring during Ethibloc injection, 10 min of manual pressure on the injection site and postprocedural antibiotic therapy could prevent major complications. If, at fluoroscopy-guided monitoring, contrast medium shows significant venous drainage the procedure must be interrupted or improved by changing the position of the needle.

Discussion

Percutaneous Ethibloc injection for the treatment of ABC was very effective in seven patients who had never been treated and six previously treated unsuccessfully with surgery and bone grafting or with arterial embolization. It was effective also in patients with unhealed pathologic fractures (3 of 13). The relief of pain observed in all the patients within a month of the injection could be considered as a clinical sign of the success of Ethibloc treatment.

MRI was more accurate in the evaluation of bone reconstruction and in visualizing residual cavities. MRI was more sensitive more precise than CR and this emerges from different evaluations in our series (10 of 13). The persistence of small cystic areas at MRI suggests a longer follow-up. A recurrence of pain during follow-up, although not a definite indication of a new expansion of the cyst, suggests the need

Fig. 3. **A** Radiograph of the left femoral neck showing polycyclic recurrent post-surgical and post-arterial embolization ABC in a 23-year-old woman. Two endomedullary nails have been placed to avoid fracture. **B** Radiograph 1 day after the first sclero-embolization treatment showing partial filling of the cystic cavity. **C** Radiograph after 1 year with reconstitution of the medial cortex of the femoral neck. **D** Radiograph after removing two endomedullary nails. **E** Radiograph after 64 months follow-up showing enlargement of a residual cystic cavity better demonstrated on the spin echo T2-weighted MR coronal image (**F**). **G** Radiograph during the second sclero-embolizing treatment. **H** Spin echo T2-weighted MR coronal image after 3 months shows low signal intensity of the residual cavity with disappearance of the fluid content.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R
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mA 200
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IMA 45
SEQ 42
L
kV 120
mA 200
TI 1.0
C
D
SPI 4
R
kV 140
mA 146
TI 1.00
GT 0.0
5.0/5.0
172 41/9
E
SPI 4
R
kV 140
mA 146
TI 1.00
GT 0.0
5.0/5.0
172 41/9
F
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for further monitoring examinations in addition to those of the protocol. In the serial controls the appearance of fluid–fluid levels, the increase in cavities and the disappearance of osseous trabeculae were evaluated as a recurrence (activity of lesion) and another treatment was performed (one case only).

Direct percutaneous Ethibloc injection is in line with the tendency to reduce invasiveness, producing similar results to surgical treatments. The aim is to bring a sclerosing substance in contact with the cystic wall to obstruct at the venous side the multiple parietal arteriolar afferents of the ABC. Ethibloc is a very viscose substance that progressively hardens in a wet milieu until it becomes solid, satisfying the criteria of a sclerosing substance. Ethibloc is then absorbed by macrophages until its total disappearance. It is very important to completely fill the cavity because the therapeutic effect of Ethibloc is due to its contact with the wall of the cyst. In the largest and communicating cysts the therapy requires multiple repeated treatments at intervals of 1–2 months, caution dictating the one-dosage administration available on the market. In each treatment the maximum possible filling is verifiable by inserting two needles, as already described, to check the complete replacement of the haematic content. In multilocular non-communicating cysts every single cavity has to be reached. This explains the higher number of injections performed in our studies compared with those of other authors [18, 19].

For a better result of the treatment, preliminary shaking of the components of the Ethibloc is advisable before injection into the cyst. Fluoroscopic guidance during injection of the sclerosing agent detects any possible venous drainage; CT guidance and, when possible, MR guidance have the advantage of controlling more precisely specific points of the cysts (residual cavities). Moreover CT guidance can also reach difficult sites in the cyst (Fig. 4). Our 13 cases include five in which the diagnosis was limited to imaging highly suggestive for aneurysmal cyst, strengthened by a negative cytologic examination for malignancy and by a follow-up long enough to exclude other pathologies. However, given that sclero-embolizing treatment is an alternative to surgery, the histologic diagnosis is mandatory before sclero-embolizing therapy. For this reason we have in some recent cases taken a sample from the cyst wall by inserting through a 10 G needle a flexible pincer that is able to ablate multiple fragments for histologic examination. In such situations the first sclero-embolizing treatment could use the same 10 G needle. The risk of treating a secondary ABC must be excluded histologically. Systematic multiple biopsies before any treatment are not advisable since malignant transformation of primary ABC has never been reported [5].

In conclusion, since direct Ethibloc sclero-embolization of aneurysmal cysts is minimally invasive, does not produce skin scars, and is highly effective even in long-term follow-up, with no severe complications, we believe that it could be the first-choice treatment even in operable cysts. Direct sclero-embolization does not preclude subsequent surgical treatment. For histologic purposes, performing a biopsy, using a 10 G needle with a flexible pincer, is mandatory before sclero-embolizing treatment. Control imaging in the follow-up should include MRI in addition to plain radiographs.

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Fig. 4. **A**, **B** CT images at two levels of the left ischium bone in a 5-year-old boy showing an ABC with disappearance of the medial cortex of the bone. There had been no previous surgical treatment. **C** CT control during direct sclero-embolizing injection shows multilocular filled cavities with fluid–fluid levels. **D** Radiograph 1 day after Ethibloc injection shows the distribution of the sclero-embolizing agent. **E**, **F** CT images at the same two levels after 26 months follow-up show a partial disappearance of the cyst but spin echo T2-weighted MR images at the same levels (**G**, **H**) demonstrate a good result, detecting only one small residual fluid cavity with no levels.

References

1. Jaffe HL, Litchtenstein L (1942) Solitary unicameral bone cyst, with emphasis on the roentgen picture, pathologic appearance and pathogenesis. Arch Surg 44:1004–1007
2. Kricun ME (1996) Imaging dei tumori delle ossa. Italian translation Verduci Editore, pp 52–54 (Imaging of bone tumors. WB Saunders, Philadelphia)
3. Bertoni F, Bacchini P, Capanna R, Ruggieri P, Biagini R, Ferruzzi A, Bettelli G, Picci P, Campanacci M (1993) Solid variant of aneurysmal bone cyst. Cancer 71:729–734
4. Bonakdarpour A, Levy WM, Aegerter E (1978) Primary and secondary aneurysmal bone cyst: A radiologic study of 75 cases. Radiology 126:75–83
5. Hecht AC, Gebhardt MC (1998) Diagnosis and treatment of unicameral and aneurysmal bone cysts in children. Curr Opin Pediatr 10:87–94
6. Haddad GF, Hambali F, Mufarrij A, Nassar A, Haddad FS (1998) Concomitant fibrous dysplasia and aneurysmal bone cyst of the skull base: Case report and review of the literature. Pediatr Neurosurg 28: 147–153
7. Campanacci M, Capanna R, Picci P (1986) Unicameral and aneurysmal bone cysts. Clin Orthop 204:25–36
8. Koskinen EV, Visuri TI, Holmstrom T, Roukkula MA (1976) Aneurysmal bone cyst: Evaluation of resection and of curettage in 20 cases. Clin Orthop 118:136–146
9. Capanna R, Sudanese A, Baldini N, Campanacci M (1985) Phenol as an adjuvant in the control of local recurrence of benign neoplasms of bone treated by curettage. Ital J Orthop Traumatol 11:381–388
10. Schreuder HW, Veth RPH, Pruszczynski M, Lemmens JAM, Koops HS, Molenaar WM (1997) Aneurysmal bone cysts treated by curettage, cryotherapy and bone grafting. J Bone Joint Surg Br 79:20–25
11. Ozaki T, Hillmann A, Lindner N, Winkelmann W (1997) Cementation of primary aneurysmal bone cysts. Clin Orthop 337:240–248
12. Capanna R, Campanacci DA, Manfrini M (1996) Unicameral and aneurysmal bone cysts. Orthop Clin North Am 27:605–614
13. Nobler MP, Higinbotham NL, Phillips RF (1968) The cure of aneurysmal bone cyst: Irradiation superior to surgery in an analysis of 33 cases. Radiology 90:1185–1192
14. Misasi N, Sadile F (1991) Selective arterial embolization in orthopaedic pathology: Analysis of long-term results. Chir Organi Mov 76:311–316
15. De Cristofaro R, Biagini R, Boriani S, Ricci S, Ruggieri P, Rossi G, Fabbri N, Roversi R (1992) Selective arterial embolization in the treatment of aneurysmal bone cyst and angioma of bone. Skeletal Radiol 21:523–527
16. Scaglietti O, Marchetti PG, Bartolozzi P (1979) The effects of meth-

ylprednisolone acetate in the treatment of bone cysts: Results of three years follow-up. J Bone Joint Surg Br 61:200–204
17. Adamsbaum C, Kalifa G, Seringe R, Dubousset J (1993) Direct Ethibloc injection in benign bone cysts: Preliminary report on four patients. Skeletal Radiol 22:317–320
18. Guibaud L, Herbreteau D, Dubois J, Stempfle N, Berard J, Pracros JP, Merland JJ (1998) Aneurysmal bone cysts: percutaneous embolization with an alcoholic solution of zein—series of 18 cases. Radiology 208:369–373
19. Garg NK, Carty H, Walsh HPJ, Dorgan JC, Bruce CE (2000) Percutaneous Ethibloc injection in aneurysmal bone cysts. Skeletal Radiol 29:211–216
20. Leclet H, Adamsbaum C (1998) Intraosseous cyst injection. Orthop Clin North Am 36:581–587