Skeletal Radiol
DOI 10.1007/s00256-009-0757-z

SCIENTIFIC ARTICLE

Selective arterial embolization of 36 aneurysmal bone cysts of the skeleton with N-2-butyl cyanoacrylate

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Received: 4 March 2009 / Revised: 30 June 2009 / Accepted: 7 July 2009

Abstract
Background Aneurysmal bone cyst (ABC) is a lytic benign bone lesion representing about 1% of all primary bone tumors. The lesion causes pain and swelling, which are generally present for less than 3 months.
Methods From April 2003 to April 2008 36 patients affected by aneurysmal bone cysts were treated by selective arterial embolization with N-2-butyl cyanoacrylate. The study population comprised 20 male and 16 female patients with an age range of 3.3–60.8 years. Nine lesions were localized in the appendicular skeleton (1 in the upper and 8 in the lower limb), 4 in the thoracic cage (1 rib lesion and 3 scapular lesions), 17 in the pelvis and 6 in the spine (1 thoracic and 5 sacral localizations).
Results A total of 55 embolizations were performed: in 22 cases (61%) only one embolization was needed, whilst two embolizations were necessary in 9 cases (25%) and 3 in the remaining 5 patients (14%). The treatment was effective in 32 patients (94%): follow-up was 0.9–5 years. In one patient, previously surgically treated, only the cyanoacrylate embolization turned out to be useful for healing the lesion. Another 7 patients underwent surgery during the study period. In the 55 procedures we performed we had 3 complications (5%): 2 cases of skin necrosis and 1 of transient paresis.
Conclusions Arterial embolization with cyanoacrylate may be the treatment of choice for aneurysmal bone cysts. Embolization is a less invasive, lower cost, simpler procedure than surgery and is easily repeatable.

Keywords Aneurysmal bone cyst (ABC) · Tumor-like lesion · Digital subtraction angiography (DSA) · Selective arterial embolization (SAE) · N-2-butyl cyanoacrylate

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Introduction

Aneurysmal bone cyst (ABC) is a lytic benign bone lesion representing about 1% of all primary bone tumors [1–3]. The lesion causes pain and swelling, which are generally present for less than 3 months. Previous trauma in the same skeletal site has been reported. Sometimes the onset or progression is observed during pregnancy.

Jaffe and Lichtenstein introduced the term aneurysmal bone cyst in 1942. Its definitive etiology still remains to be

Published online: 08 August 2009

defined. Jaffe's original hypothesis was that of a hemorrhagic "blow-up" with elevated internal pressure enclosed in a pre-existing bone lesion [4–6]. On this basis other authors suggested that ABCs were arteriovenous malformations associated with other primary bone lesions including giant cell tumor, hemangioma, chondroblastoma, osteoblastoma, non-ossifying fibroma, fibrous dysplasia, chondromyxoid fibroma, and eosinophilic granuloma [2, 7, 8]. Even though abnormalities in the karyotype of the tumor cells have recently been described, ABC is commonly regarded as a benign tumor with reactive and hyperplastic histological features and is characterized by cystic cavities lined by mesenchymal tissue and filled with blood.

These lesions may lead to very rapid bone expansion and may show aggressive behavior.

Bone expansion may limit the range of motion of a neighboring joint and mild to severe neurological impairment may result from spine lesions. Pathological fractures are uncommon. Spontaneous healing, though reported in the literature, is very rare [9]. Because of its radiological and pathological aggressiveness it is sometimes mistaken for a malignant tumor [10, 11]. The radiological findings of ABC are well described in the literature and the morphological features of the lesion are well identified by conventional radiography, CT, MRI and bone scanning; the classic radiographic appearance is that of an expansile eccentric osteolytic lesion with a geographic pattern or less frequently with a lytic permeative pattern [1–3, 12].

Any osseous segment may be affected, but the most common sites are represented by the metadiaphyseal regions of the long bones (femur, tibia, humerus) and spine (in decreasing order of frequency: thoracic, lumbar, cervical, and sacral). The posterior vertebral elements are often involved, sometimes in combination with the vertebral body. The adjacent vertebra may be involved and neighboring ribs may be affected as well [13]. About 9% of ABC's arise in the pelvis. The small bones of the hand and feet account for approximately 10 to 14% [1].

The lesion is slightly more frequent in females (ratio F/M 1.5/1–2/1) and mostly found in the second decade of life: 85% of cases occur before 20 years of age. It is rare in patients older than 50 years [1].

The standard treatment for ABC is curettage, but there is a high risk of local recurrence [2, 7]. Embolization with resorbable materials and/or coils, was initially introduced as a preoperative procedure to reduce intraoperative hemorrhage and for the treatment of sites with difficult surgical access. Percutaneous intralesional injection with fibrosing agents was also used as an alternative to surgery [14–16]. Because of the success of these less invasive procedures the indication for

Table 1 Demographic data for the 36 patients at the onset of the ABCs: 20 male, 16 female: age 3.2–60.8 (median 16 SD±11); April 2003 to April 2008

Site	Number	Size (cm)		Sex		Age (years)			Radiographic features	Vascularization
		0-5	>5	M	F	<10	10–20	>20		
Thorax	4									
Rib	1[a]	1[a]	–	1[a]	–	–	–	1[a]	1 geographic[a]	1H[a]
Scapula	3[b]	3[b]	–	3[b]	–	1	2[b]	–	2 geographic[b], 1 permeated	1H, 2P[b]
Upper limb	1									
Humerus	1	1	–	1	–	–	1	–	1 geographic	1H
Pelvis	17									
Ilium	9	4	5	3	6	1	7	1	8 geographic, 1 permeated	3S, 3P, 3H
Ischium and pubis	8	6	2	5	3	2	4	2	4 geographic, 4 permeated	4S, 1P, 3H
Lower limb	8									
Femur	7	3	4	4	3	3	–	4	7 geographic	5P, 2H
Tibia	0	–	–	–	–	–	–	–	–	
Fibula	1	–	1	–	1	–	1	–	1 geographic	1P
Spine	6									
Cervical	0	–	–	–	–	–	–	–	–	
Thoracic	1	–	1	–	1	–	1	–	1 geographic	1H
Lumbar	0	–	–	–	–	–	–	–	–	
Sacral	5	2	3	3	2	–	3	2	5 geographic	2S, 2P, 1H

S = slight; P = pronounced; H = huge, regardless of the number of embolizations

[a] 1 Male patient underwent surgery 3 months after the first embolization

[b] 1 Male patient underwent surgery for skin necrosis

Table 2 Recurrence % rate according sex (male/female), age, site, size, radiographic features at the onset, and vascularization. There were 14 patients (39%): 8 male (22%), 6 female (17%). The follow-up ranged from 0.9 to 5 years

Patients, 36 (100%)	I Embolization		II Embolization		III Embolization		Follow-up	
	22 patients (61%)		9 patients (25%)		5 patients (14%)		<2years	>2years
	No R (nr)		I R (1r)		II R (2r)		Asymptomatic	Healed
Sex	12 male						5 male (nr)[a]	7 male (nr)
	10 female						3 female (nr)	7 female (nr)
			6 male				1 male (1r)	5 male (1r)[b]
			3 female				1 female (1r)	2 female (1r)
					2 male		–	2 male (2r)
					3 female		2 female (2r)	1 female (2r)
Age (years)								
< 10	3		2		1		–	
10–20	13		7[b]		4			
> 20	6[a]		–		–			
Site	Scapula	2	Scapula	1[b]	Ilium	3	–	
	Rib	1[a]	Femur	3	Ischium and pubis	2		
	Humerus	1	Ilium	2				
	Ilium	4	Ischium and pubis	1				
	Ischiumand pubis	5	T-spine	1				
			S-spine	1				
	Femur	4						
	Fibula	1						
	S-spine	4						
Size (cm)							–	
0-5	15[a]		4[b]		–			
> 5	7		5		5			
Radiographic features	16 geographic[a] 6 permeated		8 geographic[b] 1 permeated		4 geographic 1 permeated		–	
Vascularization	5S, 7P, 10H[a]		3S[b], 2P, 4H		3S, 1P, 1H		–	

S = slight; P = pronounced; H = huge, regardless of the number of embolizations

[a] 1 Male patient underwent surgery after 3 months from first embolization

[b] 1 Male patient underwent surgery for skin necrosis

embolization of ABC has been extended [17–22]. Nowadays, in our Institute, selective arterial embolization (SAE) with acrylic glue is considered the treatment of choice for almost all ABCs of the musculoskeletal system, and surgery is limited to ABCs of the extremities and the cervical spine.

Materials and methods

From April 2003 to April 2008, 36 out of 43 consecutive patients affected with solitary ABCs were treated with SAE with N-2-butyl-cyanoacrylate. Six patients underwent surgery because of the increased risk of ischemic complications; in 4 the ABC was distal to the knee, whilst in 1 patient the ABC was localized in the second lumbar vertebra and the spinal artery of Adamkiewicz originated from the stalk of the lesion, and in 1 patient, common arterial vessels fed both the lesion and the normal femoral epiphysis. In another patient, affected by ABC of the proximal femur, SAE was not performed because no pathological vessels were identified at digital subtraction angiography (DSA).

All embolized ABCs were primary forms; there were no secondary ABCs in our series.

Diagnosis was achieved by CT-guided percutaneous needle biopsy except in three cases (2 pelvis and 1 fibula) in which an incisional biopsy was performed.

Of the 36 patients treated with embolization, 20 were male and 16 female, with an age range of 3–60 years. Demographic data and number of procedures for the 36 patients are shown in Table 1.

All the DSA and SAE were performed by inserting a catheter through the common femoral artery (Seldinger

Table 3 Radiographic results (R) and clinical results (C) in relation to sex (male/female), age, site, and size. Follow-up 0.9–5 years

Patients (36, 100%)	Sex and age (years)	Site		Size (cm)		Radiographic results (R)			Clinical results (C)	
				0–5	>5	L	P	O	FD	H
1st embolization (22 patients, 61%)	12 male, 10 females			15	7					
	3 (<10)	Scapula	2	2	–	m	m	–	m	m
	13 (10–20)	Rib	1	1[a]	–	m[a]	–	–	m[a]	–
	6[a] (>20)	Humerus	1	1	–	–	–	m	–	m
		Ilium	4	1	3	f	m	mf	mf	mf
		Ischium and pubis	5	4	1	2m	f	2f	2mf	2f
		Femur	4	3	1	–	f	2mf	f	2mf
		Fibula	1	–	1	–	–	f	–	f
		S-spine	4	3	1	–	–	2m2f	–	2m2f
2nd embolization (9 patients, 25%)	6 male, 3 female			4	5					
	2 (<10)	Scapula	1[b]	1[b]	–	m[b]	–	–	–	m[b]
	7[b] (10–20)	T-spine	1	–	1	–	f	–	f	–
	– (>20)	S-spine	1	1	–	–	–	m	–	m
		Femur	3	1	2	–	m	mf	–	2mf
		Ilium	2	–	2	–	m	f	–	mf
		Ischium and pubis	1	1	–	–	–	m	m	–
3rd embolization (5 patients, 14%)	2 male, 3 female			–	5					
	1 (<10)	Ilium	3	–	3	–	3f	–	2f	f
	4 (10–20)	Ischium and pubis	2	–	2	–	–	2m	–	2m
	– (>20)									

m = male; f = female; 2mf = two males and 1 female; FD = free of disease (follow-up <2 years); H = healed (follow-up ±2 years); L = little ossification <25%; PO = partial ossification 25–50%; O = ossification >75%

Ossification evaluated on X-ray film and CT

[a] 1 Male patient underwent surgery 3 months after first embolization

[b] 1 Male patient underwent surgery for skin necrosis

technique) under local anesthesia. General anesthesia was used only in pediatric patients. Glubran 2 surgical glue (N-2-butyl-cyanoacrylate) was mixed with Lipiodol ultrafluid (dilution 33%) and the compound was injected "sandwiched" with glucosate solution 5% to prevent polymerization with blood. The materials used for carrying out DSA and SAE were Introducer 4 F (Cordis Corporation, Miami, FL, USA) and Introducer 5 F (Terumo Corporation, Tokyo, Japan), and the catheters used were Pigtail 4 F (Cordis Corporation), Cobra 4 F-Simmons 4 F (Terumo Corporation) and Coaxial Catheters System (2.7-2.9 F preshaped MC-PP27131, 130 cm; Terumo Corporation).

The procedure was divided into three steps. The first step was a DSA of the anatomical site of the ABC to obtain a vascular map of the pathological vessels (Introducer, Pigtail, Cobra, Simmons). The second step was selective and superselective catheterizations (Coaxial Catheters System) and subsequent embolization of the lesion feeding vessels; after every single embolization a control DSA was performed to verify the quality of the occlusion and the residual pathological bloodstream. At the end of the

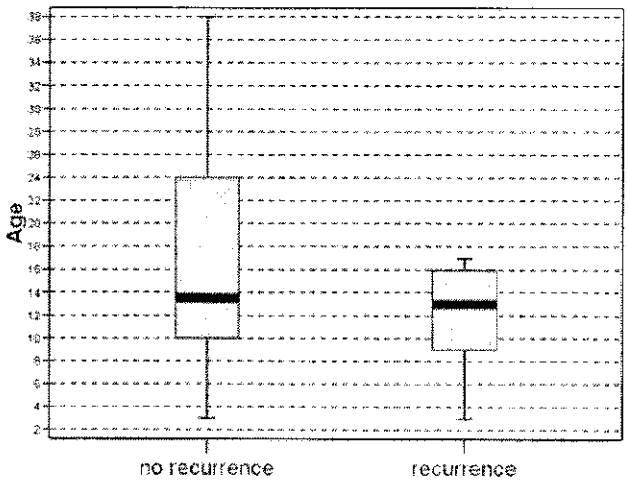

Fig. 1 Mann–Whitney test $p=0.05$. Distribution of the patients' age in relationship to recurrence

procedure (third step) another DSA of the ABC was performed in order to evaluate the efficacy of the occlusion.

All the procedures were carried out with a Philips Integris V3000 Cesar-SCP-Visub angiographic system (Philips Medical Systems, Eindhoven, the Netherlands).

Usually 100–200 cc of Omnipaque (iohexol; 350 mg/ml; GE Healthcare, Princeton, NJ, USA) contrast medium was used for a diagnostic angiographic, selective and final angiographic check. The time needed for a single procedure ranged from 1 to 2 h. All the procedures were carried out after informed consent had been obtained. The ABCs were considered completely healed if recurrences did not occur within 2 years of embolization.

Results

The rates of recurrence and/or persistence of disease are shown in Table 2. Clinical and radiographic results are shown in Table 3. In 21 patients, the lesions did not recur after the first embolization. One patient with a thoracic cage ABC, despite lesion stability, requested a surgical operation 3 months after the first embolization. Only in 24 patients (67%), 14 male and 10 female, was the follow-up longer than 2 years and therefore only these patients can be considered healed; in the remaining 12 patients (33%), 6 male and 6 female, the follow-up was shorter than 2 years (range 0.9–2 years), so we consider these patients asymptomatic, but still not healed.

Recurrences and/or persistence of disease occurred in 14 patients (39%), 8 male and 6 female. In 9 patients (25%) we had one recurrence and/or persistence, in 5 patients (14%) we had two recurrences. All these developed about 0.1–0.11 years (median 0.6 SD±0.5) after the first embolization. The patients with recurrent disease underwent another SAE. Three complications occurred (6 %): 2 cases of skin necrosis, 1 in the scapula (this patient had undergone a flap procedure), the other in the groin, and 1 case of transient paresis. These complications had no influence on the patient's outcome.

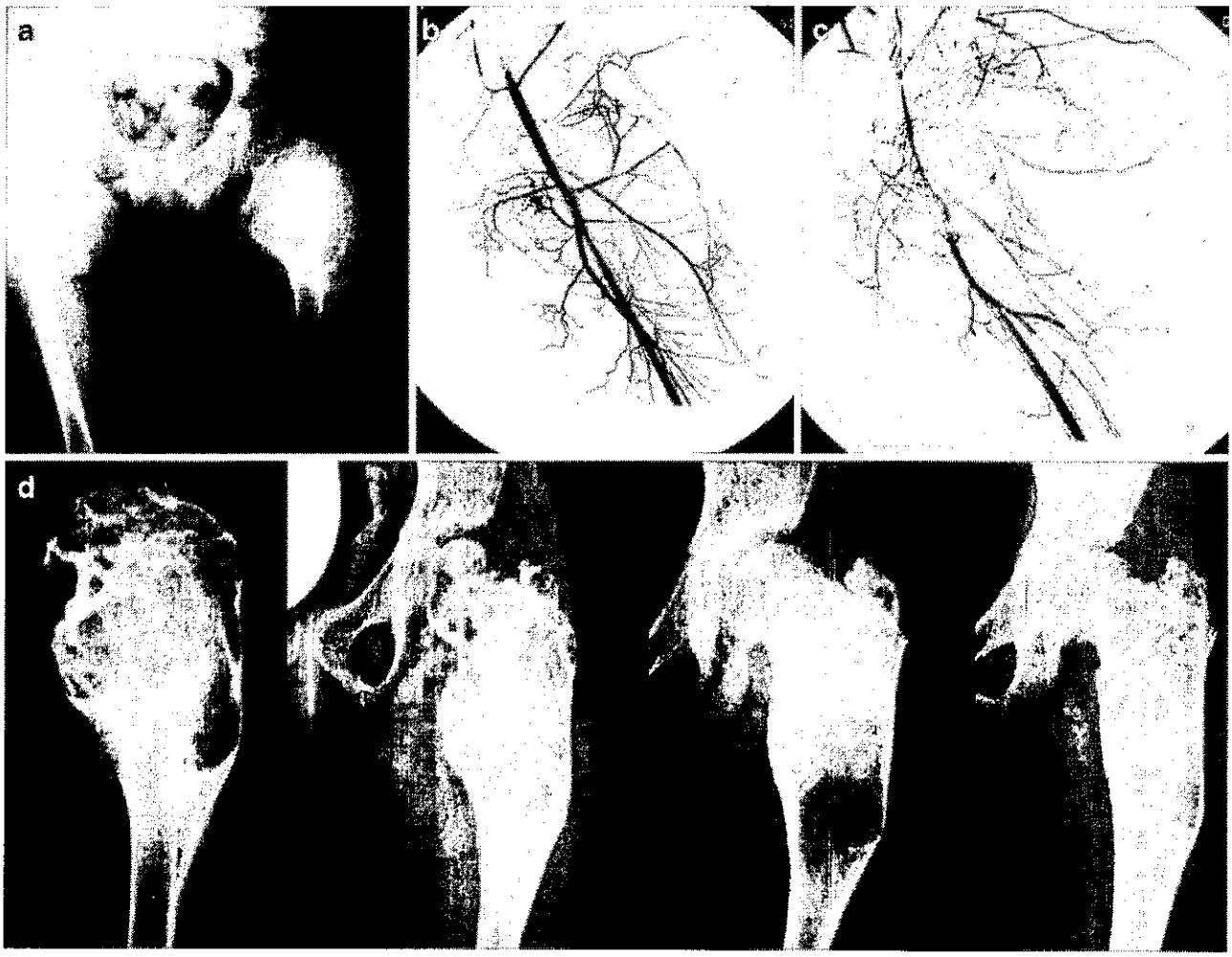

Fig. 2 Four-year-old girl. **a** Radiograph before embolization: geographic and partially permeated lytic lesion of the proximal left femur. **b**–**c** DSA: lesion vascularization before and after second embolization. **d** Follow-up radiographs demonstrating progressive recalcification in 3 years

Our data (Tables 2, 3) were analyzed by Pearson's Chi-squared test and Chi-squared test using Fisher's method. We used the Mann–Whitney nonparametric test to determine the relationship between recurrences and patient age. Local recurrence was higher in patients younger than 16 years: Mann–Whitney nonparametric test p=0.05. Patients with recurrence had a median age of 12.2±4.5 (range 3–17) years. Patients without recurrence had a median age of 18.9±13.8 (range 3–60) years (Fig. 1).

There were no statistically significant differences with regard to sex, site, radiographic appearance (lytic geographic, lytic permeated), and tumor stain (vascularization) between recurrences and healed lesions.

There was a tendency (although not statistically significant in Pearson's Chi-squared test) for lesions with reduced initial vascularization to show little ossification (less than 25%) in the post-embolization healing period. Instead, a partial or total post-embolization ossification was more frequently encountered in lesions with pronounced or extensive vascularization from the onset.

There was a statistically significant difference according to the Chi-squared test using Fisher's method (p 0.02) between the lesion initial size and the recurrence rate.

In the patients with a lesion size smaller than 5 cm, there were 4 out of 19 recurrences (21.2%) whilst there were 10 out of 17 recurrences (58.8%) in patients with lesion size greater than 5 cm.

Among the 7 patients with ABCs who were treated with curettage during the study period, none developed a local recurrence after a follow-up ranging between 0.7 and 3 years.

Discussion

Lesion size and patients' age represented important prognostic factors for the outcome of the lesion. Patients younger than 16 years and lesions larger than 5 cm in diameter were more often associated with local recurrence or persistent disease.

Regardless of the number of embolizations, 24 patients, 14 male and 10 female (67% of the total) were considered healed after a follow-up period longer than 2 years. All recurrences occurred within 1 year of the first embolization.

Recurrence or persistent disease are the main problems in other kind of treatments too: after surgical treatment (curettage alone or curettage with bone grafting) or percutaneous injection with fibrosing agents, recurrences are frequently encountered, usually as an early complica-

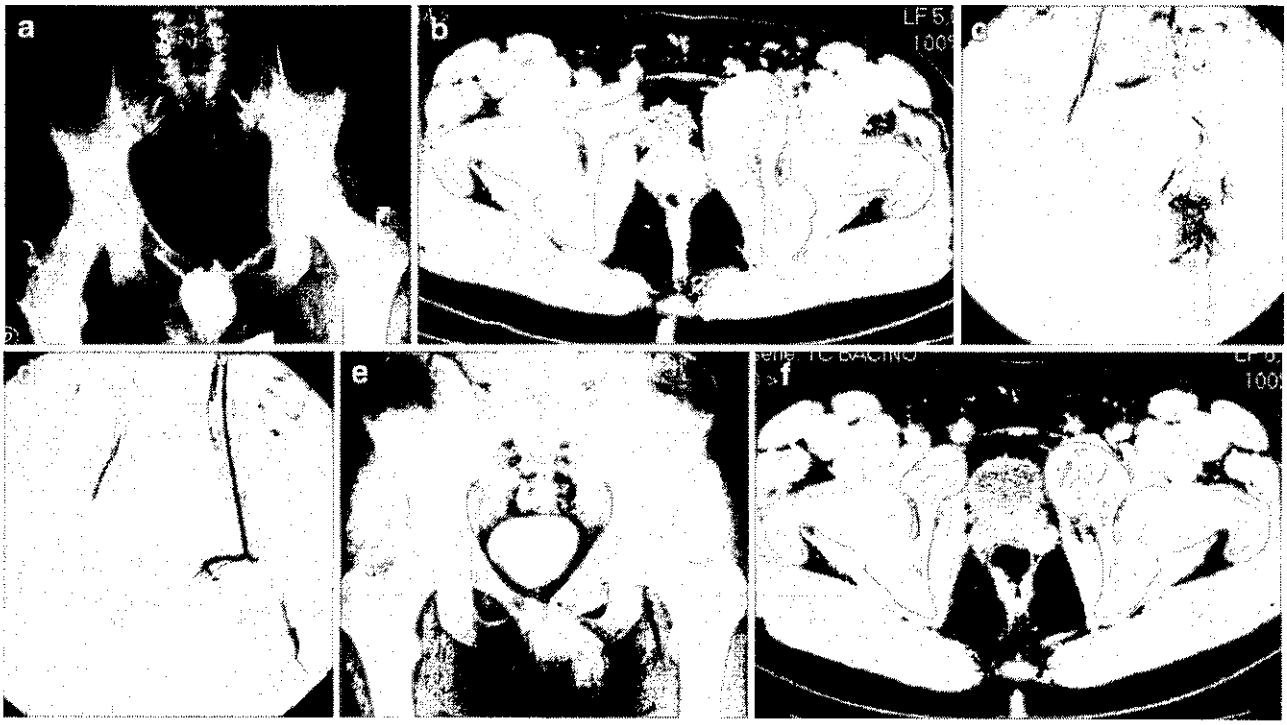

Fig. 3 A 16-year-old male patient. **a** Radiograph: geographic lytic lesion of the left ileo-pubic branch. **b** CT after contrast medium. **c** DSA: huge vascularization from the obturator artery. **d** SAE with cyanoacrylate. **e** Follow-up at 2 years: radiograph. **f** CT with contrast: complete healing of the ileo-pubic branch

tion. Recurrence rates after curettage vary widely in the literature. Cottalorda and Bourelle performed a review of the literature including series of 20 cases or more and the recurrence rate of 669 ABCs treated with curettage with or without bone graft was 31% [23].

The 7 patients who were treated in our Institute with curettage (with or without bone grafting) during the study period did not develop local recurrence until today. However, the follow-up period was relatively short.

Two authors have recently reported their experience of intralesional injections with fibrosing agents (Ethibloc). Adamsbaum et al. [15] reported 17 patients with a mean follow-up of 5 years. Three patients (18%) required surgical treatment of a local recurrence/persistent disease. Topouchian et al. [16] reported 15 patients with a mean follow-up of 6 years. Four patients (27%) required surgical treatment of a local recurrence/persistent disease. The 12 patients, 6 male and 6 female (33% of the total), with follow-up of less than 2 years, cannot be considered healed, even in the absence of any symptoms.

On the basis of our experience with selective arterial embolization with N-2-butyl cyanoacrylate for ABCs, we can say that in the presence of subtotal or total recalcification with reduction of the mass, asymptomatic lesions can be considered healed, even if the follow-up is less than 2 years. In the case of partial recalcification, regardless of the reduction in diameter of the mass, asymptomatic lesions can be considered healed if the follow-up is equal to or more than 2 years. (Figs. 2, 3).

Conclusions

Selective arterial embolization is indicated in the treatment of ABC, especially in those sites with difficult surgical access or in patients at high risk of extensive intraoperative bleeding [17–22]. In our experience selective arterial embolization with N-2-butyl cyanoacrylate was associated with good curative results and a low complication rate. Today, together with the injection of fibrosing agents [14–16], this procedure may be considered a less invasive, more feasible, more effective, more easily repeatable alternative to standard surgical treatments, allowing lesion healing at lower cost and lower risk.

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