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Secondary aneurysmal bone cyst of the spine: Clinicopathological features, surgical modalities and outcomes

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ABSTRACT

Objectives: Spinal secondary aneurysmal bone cyst (SABC) is extremely rare with few published reports available at present. Our aim is to explore the clinicopathologic features, surgical modalities and outcomes of spinal SABC.
Patients and methods: A retrospective study of 33 patients with spinal SABC who were surgically treated in our center between 2010 and 2018 was performed. Clinical data, treatment options, complications and outcomes were analyzed.
Results: Of the 33 patients, 12 were male and 21 were female, with a mean age of 32 years. Eleven lesions were located at the lumbar spine. The underlying lesions included giant cell tumor (GCT) (n = 20), osteoblastoma (n = 7), hemangiaoma (n = 3), fibrous dysplasia (n = 2) and osteosarcoma (n = 1). Preoperative selective arterial embolization was applied in 24 patients. All the patients were treated surgically through either subtotal resection (n = 1), piecemeal total resection (n = 21), or total en bloc resection (n = 11). Four patients experienced recurrence and one patient died during the follow-up period.
Conclusion: Spinal SABC is popular in the third and fourth decade of life with female predominance. GCT is the most common underlying lesion. Preoperative arterial embolization is recommended, while surgery is the mainstay of treatment for spinal SABC. En bloc resection is recommended for spinal SABCs especially when underlying tumor is aggressive or malignant.

1. Introduction

Aneurysmal bone cysts (ABCs) are defined as aggressive, expansile and osteolytic lesions, accounting for about 2.5% of all primary bone tumors and roughly 15% of all primary spine tumors [1–3]. ABCs fall into two categories: primary lesions (PABCs) and secondary lesions (SABCs). Nearly 70% ABCs are primary, and the remaining 30% are secondary to other tumors, such as osteoblastoma, giant cell tumor (GCT), hemangioma, osteosarcoma, chondroblastoma, and fibrous dysplasia [4].

Previously, we reported 11 ABCs secondary to spinal GCT, which represent the largest case series about spinal SABCs [5]. However, spinal SABCs are not only secondary to GCT but also secondary to other underlying tumors, such as osteoblastoma, chondromyxoid fibroma and fibrous dysplasia [6–8]. Because of the rarity of the literature related to spinal SABCs, the clinical features and appropriate treatments remain poorly understood. Tang et al. reported that 53.3% SABCs secondary to GCT in extremities recurred, and inappropriate treatments (such as curettage and subtotal resection) may lead to recurrence [5,9]. Therefore, a better understanding of the clinicopathologic features, treatments and outcomes for spinal SABCs have great clinical significance.

In this study, we report our experience with 33 spinal SABC patients who received surgical treatment in our center, in an attempt to illustrate the clinicopathologic features, surgical modalities and outcomes of this rare disease.

2. Materials and methods

Initially investigated in this study were 74 patients with spinal ABCs who received surgery in our center between August 2010 and June 2018. Inclusion criteria were: 1) patients with pathologically diagnosed spinal secondary ABCs; and 2) the follow-up period was more than

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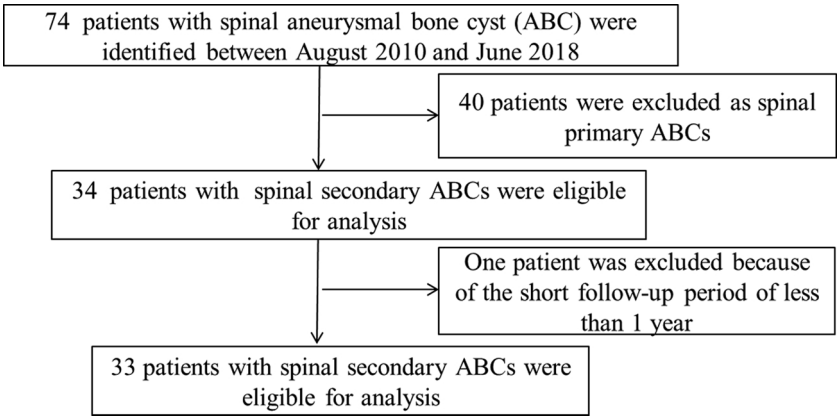

Fig. 1. Patient flow diagram for spinal secondary ABCs.

1 year. While the exclusion criteria were: 1) patients with pathologically diagnosed spinal primary ABCs; and 2) the follow-up period was less than 1 year. Finally, 33 patients met the criteria and were enrolled in this study (Fig.1). Relevant clinical data were retrieved, including age, gender, location, Weinstein–Boriani–Biagini (WBB) staging [10], diagnosis of the underlying tumor, pre- and post-operative Frankel scores, resection mode, embolization details, complications, adjuvant therapy and outcomes. Needle biopsy or open biopsy was carried out in order to obtain a definite diagnosis before surgery. Angiography was carried out in all patients. Selective arterial embolization was usually performed when the tumor was located below T6.

The surgical strategy for spinal SABC was decided for each patient according to Tomita classification and WBB surgical staging system [10,11]. Surgery for spinal SABC consisted of three steps. The first step is pedicle screw placement and the principle for instrumentation was based on the stability of the spine according to the SINS score [12]. Then tumor resection is performed through subtotal resection, total piecemeal resection or total en bloc resection. The third step is vertebrae reconstruction. For the cervical spine, vertebral reconstruction is usually accomplished via the anterior approach [13]. While for thoracic and lumbar lesions, vertebrae reconstruction is usually carried out via the posterior-lateral approach, with the titanium mesh or expandable cage carefully inserted into the vertebrectomy defect and then rotated to match the long axis of the spine [14].

Postoperative radiotherapy (RT) was usually recommended in our center for ABCs secondary to GCT, especially for patients receiving piecemeal resection upon informed consent from the patients [5]. Additionally, bisphosphonates such as zoledronic acid were suggested to these patients once a month for two years.

Follow-up clinical and radiological examinations were performed every 3 months in the first year, every 6 months for additional 2 years, and annually thereafter. The length of the follow-up was defined as the period from the date of surgery to Jun 2019. This study was approved by the hospital ethics committee, and informed consent was obtained from each patient or family members of those who had passed away.

3. Results

3.1. Patient features

The general data of the patients are listed in Table 1. There were 12 male and 21 female patients with M/F ratio of 1:1.75 and a mean age of 32 years (median: 31.5, range: 15–64 years). Among these patients, 25 (75%.8) patients were between 20 and 40 years, only 5 patients (15.2%) were younger than 20 years. Six lesions (18.2%) were located in the cervical spine, 8 (24.2%) in the thoracic spine, 11 (33.3%) in the lumbar spine (33.3%), and the other 8 (24.2%) in the sacrum. For underlying tumors, GCT (20, 60.6%) was the most common lesion, followed by osteoblastoma (7, 21.2%, including 3 aggressive osteoblastomas), hemangioma (3, 9.1%), fibrous dysplasia (2, 6.1%) and osteosarcoma (1, 3.0%). Thirty-one patients (93.9%) presented with progressive, nonspecific, localized pain or radicular pain. Cord compression of varying degrees was observed in 17 cases (51.5%) at the time of diagnosis.

3.2. Radiological study

All patients showed lytic bone destruction on radiological imaging. Sixteen lesions (48.5%) contained a cystic mass with a fluid-fluid interface with hypointense signals on T1-weighted imaging and hyperintense signals on T2-weighted imaging. Nine patients (27.3%) showed soap-bubble or balloon-like expansible appearance on plain radiographs and CT. Pathological fractures were uncommon in our cases (3, 9.1%). Soft tissue involvement was seen in 9 cases (27.3%).

3.3. Treatments

Twelve patients (36.4%) received biopsy (5 needle and 7 open) before surgery. Intraoperative frozen biopsy was carried out in 13 patients (39.4%), and the remaining 8 patients underwent surgery or biopsy in other hospitals and therefore definite diagnosis was obtained. Selective arterial embolization was performed on 24 patients pre-operatively. Total resection was performed in 32 patients, including en bloc resection in 11 and piecemeal resection in 21, while subtotal resection was carried out in the remaining patient because of the huge cervical lesion and terrible general condition. Twenty-four patients received a posterior approach, and 8 patients received a combined anterior and posterior approach, including 5 cervical lesions, 2 lumbar lesions, 1 thoracic lesion. Only one patient received the single anterior approach, whose lesion was located at C6 (case 2). Corpectomy was performed in 23 patients, expandable cage was used in 3 patients, and titanium mesh was used in 20 patients.

Of the 24 patients who were affected by malignant or aggressive underlying tumors, including 20 GCT, 3 aggressive osteoblastoma and 1 osteosarcoma, 9 patients received total en bloc resection, 14 patients underwent piecemeal total resection, and 1 patient received subtotal resection (Fig.2). Of the 9 patients who were affected by benign underlying lesions, including 4 osteoblastoma, 3 hemangioma, and 2 fibrous dysplasia, en bloc and piecemeal total resection was conducted in 2 and 7 patients respectively (Fig. 3). Postoperative radiotherapy was recommended and applied in 12 patients who received piecemeal resection, while bisphosphonate therapy was administered in 23 patients.

3.4. Follow-up outcomes

All patients were followed up regularly for clinical and radiographic

Table 1
Patients' demographic details of spinal secondary ABCs.

No.	Age /gender	Location	WBB staging	F-S Pre/ Post	Biopsy	SAE	Surgery/Adjuvant	Reconstruction	Complications	Underlying tumor	LR(m)	FU time (m)/Last status
1	33/F	L5	8-11, A-B	D/E	Intra-operation	Yes	Piecemeal(A + P)/RT + BP	Pedicle screw fixation	Wound infection	GCT	Y(58)	100/NED
2	30/F	C6	6-10, B-D	E/E	Intra-operation	No	Piecemeal(A)/RT + BP	Corpectomy + titanium mesh + allograft	None	GCT	Y(10)	97/NED
3	33/F	T9-10	3-9, B-D	C/E	Intra-operation	Yes	En bloc(P)/none	Corpectomy + titanium mesh + allograft	None	OBL	N	91/NED
4	33/F	T1	3-7, A-D	D/E	Intra-operation	No	Piecemeal(A + P)/RT + BP	Corpectomy + titanium mesh + allograft	None	GCT	N	88/NED
5	20/F	C2	4-7, B-C	D/E	Intra-operation	No	Piecemeal(A + P)/BP	Corpectomy + titanium mesh + allograft	None	GCT	N	88/NED
6	50/F	T2-4	3-6, A-B	E/E	Intra-operation	No	Piecemeal(P)/RT + BP	Pedicle screw fixation	Pleural defect	GCT	N	81/NED
7	18/F	C5	5-11, A-D	E/E	None	No	Piecemeal(A + P)/none	Corpectomy + titanium mesh + allograft	No	OBL	N	81/NED
8	32/F	S	5-12, A-D	D/E	Open biopsy	Yes	Piecemeal(P)/RT + BP	Pedicle screw fixation	Rod breakage	GCT	Y(27)	80/NED
9	49/F	S	7-11, A-D	D/E	Open biopsy	Yes	Piecemeal(P)/none	Pedicle screw fixation	None	FD	N	79/NED
10	20/M	T4-5	1-12, A-D	B/D	Intra-operation	No	Piecemeal(P)/RT + BP	Corpectomy + titanium mesh + bone cement	None	GCT	N	73/NED
11	35/M	T10	3-11, A-D	C/E	Intra-operation	Yes	En bloc(P)/BP	Corpectomy + titanium mesh + allograft	None	GCT	N	72/NED
12	47/F	L4	4-11, B-D	E/E	None	Yes	Piecemeal(P)/RT + BP	Corpectomy + titanium mesh + bone cement	None	GCT	N	68/NED
13	21/M	L3-4	1-2, 8-12, A-D	D/E	None	Yes	Piecemeal(P)/none	Corpectomy + titanium mesh + bone cement	None	OBL	N	60/NED
14	31/M	S	1-12, A-D	E/E	Open biopsy	Yes	En bloc(P)/RT + BP	Pedicle screw fixation	None	GCT	N	54/NED
15	25/M	T12	1-5, 11-12, A-D	D/E	Intra-operation	Yes	En bloc(P)/BP	Corpectomy + titanium mesh + allograft	None	Aggressive OBL	N	53/NED
16	22/F	C2	4-9, B-C	D/E	Intra-operation	No	Piecemeal(A + P)/BP	Corpectomy + titanium mesh + allograft	None	GCT	N	50/NED
17	29/F	L3	2-8, B-D	E/E	Needle biopsy	Yes	En bloc(P)/none	Corpectomy + titanium mesh + bone cement	None	HE	N	48/NED
18	40/F	S	7-9, B-C	D/E	Open biopsy	Yes	Piecemeal(P)/none	Pedicle screw fixation + cement augumentation	None	FD	N	48/NED
19	26/F	L4	2-10, A-D	C/E	None	Yes	Piecemeal(P)/RT + BP	Corpectomy + titanium mesh + allograft	Wound infection	GCT	N	43/NED
20	46/M	S	1-12, A-D	E/E	Open biopsy	Yes	Piecemeal(P)/RT + BP	Pedicle screw fixation	None	GCT	N	43/NED
21	34/M	L2	6-11, A-D	E/E	Needle biopsy	Yes	En bloc(P)/BP	Corpectomy + titanium mesh + allograft	Rod breakage	Aggressive OBL	N	42/NED
22	19/F	C2	4-9, B-C	E/E	Intra-operation	No	Piecemeal(A + P)/none	Corpectomy + titanium mesh + allograft	None	HE	N	42/NED
23	23/F	L4	2-7, A-D	D/E	None	Yes	En bloc(A + P)/RT + BP	Corpectomy + titanium mesh + allograft	Pedicle screw loosen	GCT	N	40/NED
24	37/F	L3	2-7, A-D	D/E	Needle biopsy	Yes	En bloc(P)/BP	Corpectomy + titanium mesh + allograft	None	GCT	N	36/NED
25	15/M	S	6-10, B-D	E/E	None	Yes	Piecemeal(P)/none	Pedicle screw fixation	None	OBL	N	34/NED
26	39/M	L1	2-11, A-D	E/E	Intra-operation	Yes	Piecemeal(P)/BP	Corpectomy + titanium mesh + allograft	None	GCT	N	22/NED
27	31/M	T9	6-10, B-D	E/E	None	Yes	En bloc (P)/RT + BP	Corpectomy + expandable cage + allograft	None	GCT	N	18/NED
28	26/M	L1	1-12, A-D	C/E	Needle biopsy	Yes	En bloc(P)/CT + BP	Corpectomy + titanium mesh + bone cement	None	OS	N	43/NED
29	64/F	S	6-10, B-C	E/E	Open biopsy	Yes	Piecemeal (P)/none	Pedicle screw fixation + bone cement augumentation	None	HE	N	12/NED
30	32/M	C2-4	1-9, A-D	B/C	Intra-operation	No	Subtotal (A + P),two stage	Corpectomy + titanium mesh + allograft	None	Aggressive OBL	Y(10)	13/DOD
31	24/F	L4	3-8, A-D	D/E	None	Yes	En bloc (P)/BP	Corpectomy + expandable cage + allograft	None	GCT	N	12/NED
32	38/F	S	2-10, A-D	E/E	Open biopsy	Yes	Piecemeal (P)/BP	Pedicle screw fixation	None	GCT	N	12/NED
33	28/F	L5	2-7, A-D	E/E	Needle biopsy	Yes	Piecemeal(P)/BP	Corpectomy + expandable cage + allograft	None	GCT	N	12/NED

A: anterior; P: posterior; RT: radiotherapy; CT: chemotherapy; BP: Bisphosphonate; F-S: Frankel score; FU: follow up; LR: local recurrence.
SAE: selective arterial embolization.
NED: None evidence of disease; DOD: Died of disease; GCT: giant cell tumor; OBL: osteoblastoma; HE: hemangioma; FD: fibrous dysplasia.
OS: osteosarcoma.

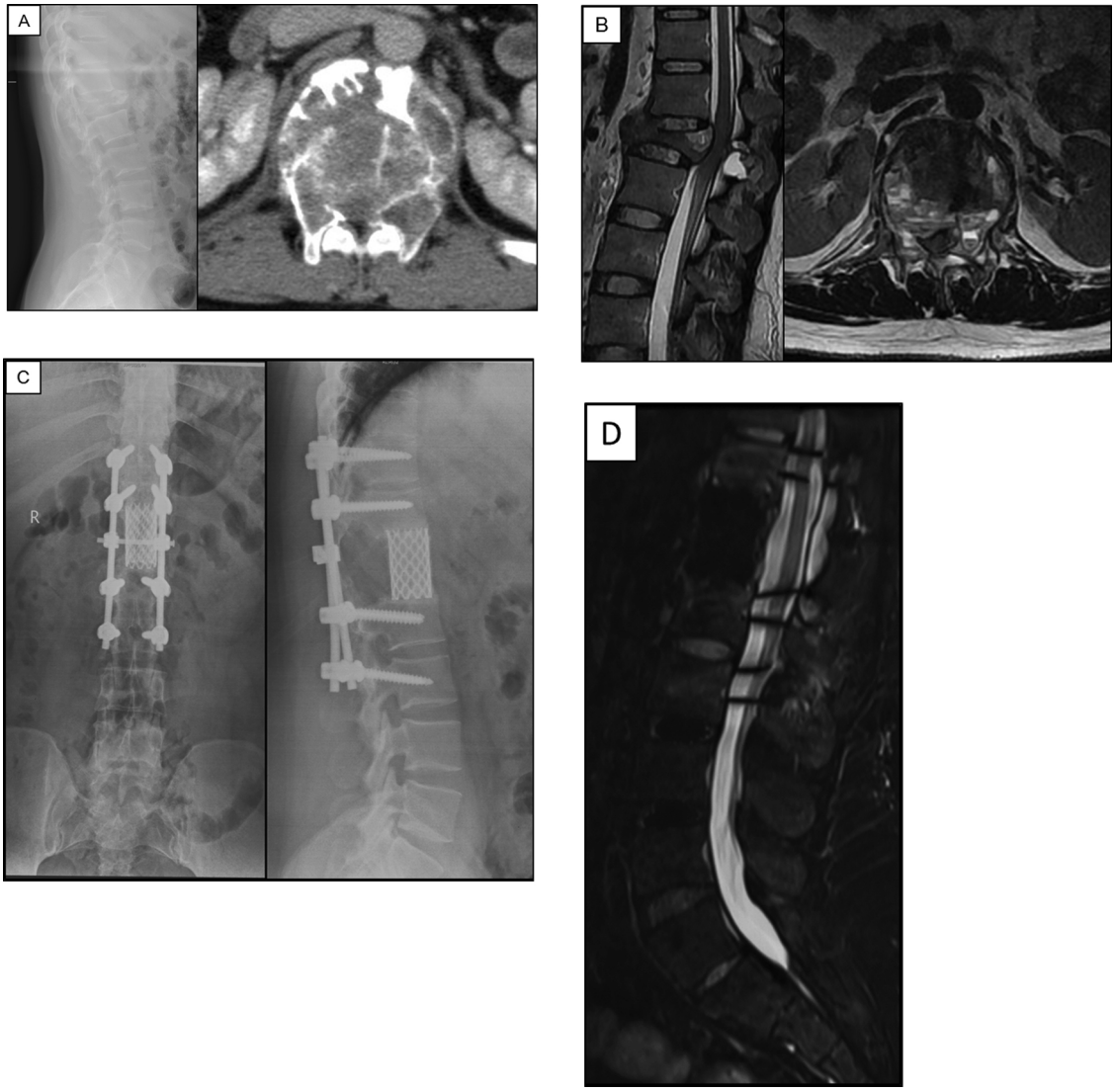

Fig. 2. Spine ABC secondary to GCT (case 26). (A) Lateral X ray and axis CT showed lytic lesion and pathological fracture of L1. (B) Sagittal and axis MRI showed fluid-fluid level of the vertebral and posterior elements. (C) X ray showed reconstruction with titanium mesh combined with posterior screw-rod system. (D) MRI showed no relapse 6 years after surgery.

evaluation for a mean of 52.6 months (median 48, range: 12–100 months). Four patients experienced recurrence with a mean follow-up period of 26.3 months (median: 18.5, range: 10–58 months), among whom one patient died 13 months after surgery. For the recurrent cases, the underlying tumors were all aggressive lesions treated by piecemeal resection, including 3 GCTs and 1 aggressive osteoblastoma. While no recurrence occurred in patients with benign underlying lesions or treated by en bloc resection (Table 2).

3.5. Complications

Complications occurred in 6 patients (18.2%). Implant failure was observed in 3 patients, including rod breakage in 2 cases and pedicle screw loosening in 1 case, all of which were amended by revision surgery. Wound complications occurred in 2 cases. Both cases were cured after debridement and sensitive antibiotics in one case, and debridement, anti-infection therapy and flap transplantation in the other. Hydropneumothorax due to intraoperative pleural injury occurred in one case, for which pleural reconstruction and drainage were applied. All complications were relieved after treatment.

4. Discussion

Spinal PABC predominantly affects children and young adults, with about 60% cases occurring in individuals younger than 20 years. In addition, it shows a slight female predilection (ratio 1.16) [15]. It seems that the diagnosis of spinal SABCs is later in age than primary ones, and they are more likely to occur in women. In our series, the mean age of the SABCs patients was 32 years at the time of diagnosis, and 25 (75.8%) patients were between 20–40 years. Compared with primary ones, SABCs frequently occur among females with a ratio of 1.75. The lumbar spine is the most commonly affected site, followed in sequence by the thoracic, sacral and cervical spine. The lesion distribution of spinal SABCs is consistent with that of PABCs [16].

In our series, the most common pre-existing tumor of SABCs is GCT (60.6%), which is consistent with the study by Manaster et al., who reported that 30% ABCs arose within some primary bone lesions, and GCT in particular [17]. Osteoblastoma is the second common accompanying tumor (21.7%). Della Rocca and Huvos [18] pointed out that there was an association between osteoblastoma and ABC occurring in 14.5% cases of their series, while our previous study also indicated that SABC occurred in 15.1% of spinal osteoblstoma [19]. Our study indicates that ABC can also be associated with spinal hemangioma,

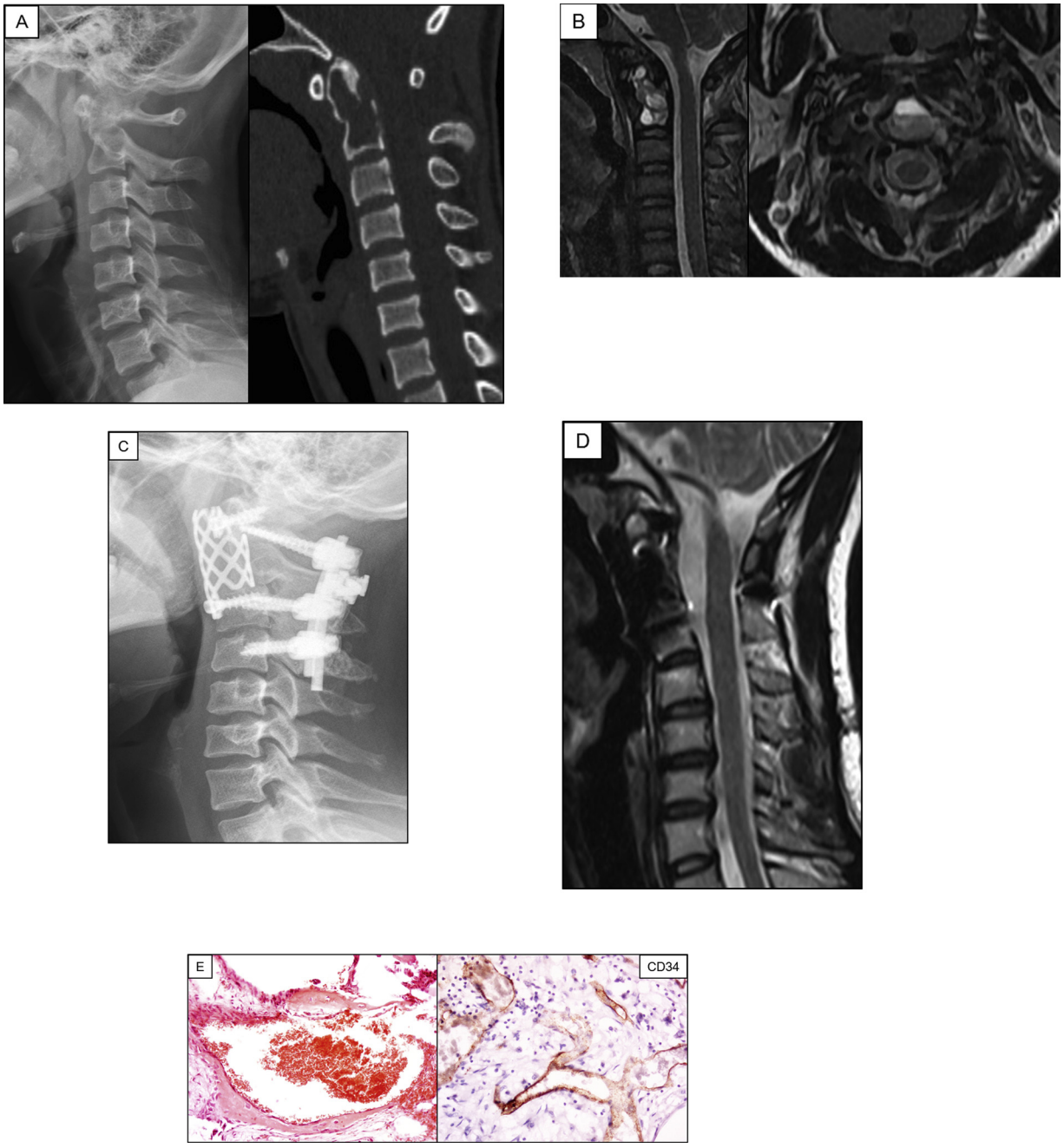

Fig. 3. ABC secondary to hemangioma (case 22). (A) Preoperative X ray and sagittal reconstruction CT showed lytic lesion of the axis with pathological fracture of the odontoid. (B) Sagittal and axial MRI showed fluid-fluid level of the axis. (C) 3-month follow-up showed sound reconstruction by anterior titanium mesh filled with allograft bone combined with posterior screw-rod system. (D) MRI at 3-year follow up showed no relapse. (E) HE and immunohistochemical staining of the lesion (x 400).

fibrous dysplasisa and osteosarcoma, which are seldom reported in the literature.

The etiology of ABC is controversial. PABCs have recently been identified as an independent neoplasm, in which oncogene ubiquitin-specific protease USP6 was reported to be responsible for the formation of PABCs [20]. Previous reports suggested that SABC may arise from abnormal hemodynamic conditions causing an increase in venous pressure, resulting in hemorrhage, or cystic change degenerated from underlying tumors [4]. The different etiologies of PABC and SABC signify the different appearance on radiological images.

In our series, the most common radiological manifestation for spinal SABCs is lytic destruction, while typical cystic change with a fluid-fluid interface is seen in about half of patients. The common features for PABC and SABC on MRI are a lytic mass with cystic change and a low signal rim on both T1-and T2-weighted sequence [21,22]. There is not much evidence for differential diagnosis of PABC and SABC on MRI. First, the major component of PABC is a cyst while most part of SABC is a solid pre-existing tumor. Second, the cystic change in PABC often shows separation of the hyperintense cyst by a hypointense internal septum of various sizes, while cystic change in SABC often manifests as multiple and sporadic hyperintense cystic spaces without septum. Discrimination between PABC and SABC only based on radiological findings is not enough, and biopsy is often required to confirm the final diagnosis. In our center, needle biopsy or open biopsy is usually carried out for patients presenting with only a lytic or expansible lytic appearance on CT. For those who have a characteristic fluid-fluid

Table 2
Different relapse rates for several variants in the treatment of spinal SABCS.

variants	Number of patients	Relapsed cases
Sex		
female	21(63.6%)	3
male	12(36.4%)	1
Age		
≤20	5(15.2%)	0
> 20	28(84.8%)	4
Location		
Cervical	6(18.2%)	2
Thoracic	8(24.2%)	0
Lumbar	11(33.3%)	1
Sacrum	8(24.2%)	1
Pre-existing tumor		
Giant cell tumor	20(60.6%)	3
Osteoblastom	7 (21.2%)	1
Hemangioma	3 (9.1%)	0
Fibrous dysplasia	2 (6.1%)	0
Osteosarcoma	1 (3.0%)	0
Resection mode		
En bloc	11 (33.3%)	0
Piecemeal	21 (63.6%)	4

interface on MRI and highly suggestive of the diagnosis of ABC before surgery, intraoperative frozen biopsy is an alternative. Histologically, SABC can be diagnosed when the primary lesion coexists with a secondary cyst. The secondary cyst is usually composed of a cyst, red blood cells and multinucleated giant cells [4], while the diagnosis of the primary lesion usually depends on the combination of histopathological appearance and immunohistochemical markers.

Besides surgery, there are some other treatment choices for spinal PABC, including arterial embolization, radiotherapy, and some novel treatments such as bisphosphonates or denosumab, and concentrated bone marrow injection [23–27]. Unlike PABC, SABC arising from the spine appears to require a more aggressive treatment to achieve local tumor control [5]. The role of surgery seems to be paramount. There are several concerns that need to be illuminated in resection for spinal SABC. First, the principle of SABC treatment is based on the appropriate treatment for the underlying tumor. Aggressive total resection of ABC and the underlying tumor is recommended. Second, preoperative embolization of the feeding artery is usually used as an adjuvant to decrease blood loss during surgery. Third, direct piecemeal resection may cause massive hemorrhage because the cystic cavity is usually filled with blood. Therefore, we usually use gauze to blunt dissect the tumor's boundaries and cut off the peripheral feeding vessel before en bloc or piecemeal resection is performed. Fourth, to reduce the recurrence rate, total resection is superior to subtotal resection, including resection of the cyst wall. Finally, en bloc resection is recommended for aggressive or malignant underlying tumors, knowing that all recurrences occurred in the piecemeal resection group in our series.

In our series, postoperative RT was recommended for aggressive or malignant pre-existing tumors, especially for piecemeal resection cases. Although there are some disputes regarding RT for spinal ABC or GCT for the possible radiation myelopathy and radiation-induced sarcoma transformation, both our experience and previous reports show that RT can be used as a supplement after removal of the gross tumor [5,28,29]. Bisphosphonates have been advocated as the definitive treatment of spinal primary ABC patients with no instability or progressive neurology which need surgery intervention [24]. Moreover, our former study showed that long term use of bisphosphonates after nerve-sparing surgery for the treatment of sacral GCT could reduce local recurrences [30]. Therefore, the patients with aggressive or malignant preceding lesions were advised to receive bisphosphonate therapy after surgery in our series.

In summary, spinal SABC is popular in the third and fourth decade of life with female predominance. GCT is the most common underlying lesion. Preoperative arterial embolization is recommended, and surgery is the mainstay of treatment for spinal SABC. En bloc resection is recommended for spinal SABCs especially when the underlying tumor is aggressive or malignant.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

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