Research Paper

Surgical management and outcome of Extra-adrenal myelolipomas at unusual locations: A report of 11 cases in a single center

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1. Introduction

Myelolipoma is a rare benign and nonfunctioning tumor composed of both mature adipose and hematopoietic tissues with unclear etiology. There have been only sporadic case reports about the clinical characteristics and management of EAMs. Here we present our experience and practice in the clinical diagnosis and treatment of 11 consecutive patients with EAMs.

Method: We retrospectively reviewed 11 consecutive patients, who received surgeries in our department and were confirmed as having EAMs by postoperative histopathology from April 2016 to December 2021. Clinical information and follow-up data of all patients were collected and analyzed afterwards.

Result: Of the 11 EAM patients (7 male and 4 female) with a mean age of 47.6 years, 3 were asymptomatic and 8 were symptomatic with a mean symptom duration of 6.07 months. EAMs were found in the thoracic spine in 4 cases, paravertebral mediastinal regions in 3 cases, ilium in 2 cases, humerus in 1 case, and rib in 1 case. All patients were initially misdiagnosed as other tumors by radiologists. All 11 patients received gross total excision or curettage with a mean intraoperative blood loss of 781.82 ± 114.33 ml and a mean operation duration of 180.91 ± 98.41 min. Patients’ Frankel scores and Karnofsky Performance Status score were improved or at least preserved postoperatively. No significant complications occurred postoperatively. All the 11 patients survived, and no local recurrence or distant metastasis occurred during the mean follow-up period of 42.0 months.

Conclusion: The surgical outcome and prognosis of EAMs are excellent and surgery can serve as the method of radical treatment.

Abbreviations: EAMs, Extra-adrenal myelolipoma.

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the management of 11 consecutive patients with EAMs, hoping that it could provide more useful data regarding the clinical features and management strategies of this rare benign tumor in the spinal and intraosseous regions.

2. Materials and methods

2.1. Patients

This study retrospectively reviewed all patients who underwent surgeries and were pathologically confirmed as having EAMs of the spinal and intraosseous regions in our institution from April 2016 to December 2021. All patients’ general information, clinical and imaging manifestations, operation details, pathological findings, and follow-up outcomes were collected. All patients were followed up regularly after surgeries. Follow-up observation ended at the date of patient death or in February 2022. Informed consent was obtained from all participating patients before initiation of the study. The study procedures were conducted according to the principles of the Declaration of Helsinki and approved by the ethics committee of our hospital.

2.2. Imaging assessment

Imaging examinations mainly included plain radiographs, CT and MRI with gadolinium-contrast enhancement. Reconstructed 3D CT or CTA would be performed in patients with fractures. Imaging diagnosis was performed by two senior musculoskeletal radiologists.

2.3. Surgery

For patients with spinal or paravertebral involvement, posterior middle incisions were made in a prone position. In remaining cases, the posture and incision area depended on the location of the lesion. Tumors were all removed as completely as possible. Tumor resection and protection of the surrounding structures were assisted by using the binocular magnifier. Spinal reconstruction was implemented by using the screw and rod system or in-situ lamina replantation with tiny titanium plate fixation according to the specific location of the lesion. Bone defect-filling materials mainly included the titanium mesh, artificial vertebral body, bone cement and bone allograft.

3. Results

3.1. General information

The general information of the 11 patients included in this study are demonstrated in Table 1. They aged from 13 to 69 years with a mean of 47.55 ± 20.76 and a median of 55 years with a male-female ratio of 7:4. They all received surgery and were diagnosed with myelolipoma by postoperative histopathology. Of them, 8 patients (72.73%) presented the clinical symptoms with a mean symptom duration of 6.07 ± 8.24 months, including pain or discomfort, limb numbness or weakness (Case 3, Fig. 1), and pathological fracture accompanied with spinal kyphosis (Case 4, Fig. 2), and the remaining 3 patients were asymptomatic. The mean duration of symptoms was 6.07 ± 8.24 months (range: 1 week to 24 months). The EAMs in these patients were mainly distributed in the thoracic spine (n = 7) and intraosseous regions (n = 4). The former included two cases involving the vertebral body (Case 1 and 4), one involving the thoracic spinal epidural area (Case 3, Fig. 1), and four involving the paravertebral mediastinal regions (Case 2, 5, 6 and 7). Intraosseous EAMs were found in the left (Case 8) and right (Case 9) ilium, right humerus (Case 10) and the right 8th posterior rib (Case 11).

3.2. Imaging assessment

Of the 11 patients, 8 underwent MRI scan and 9 received CT exams...
for review. The imaging characteristics of the 11 patients are presented in Table 2. MRI and CT showed that most of the lesions appeared as localized well-defined soft tissue masses in an oval or round shape, except for Case 4 and 8 with blur margins. The mean diameter of the masses was 4.35 ± 3.24 cm. Bone destruction or pathological changes of bone were observed in 8 cases, but not in the 3 patients with para-vertebral mediastinal EAMs. In most cases, high signal intensities were presented on both T1- and T2-weighted sequences. Varying degrees of enhancement were displayed in 7 of the 8 MRI exams and 4 of the 9 CT exams. It is noteworthy that the initial preoperative impression given to the radiologists was not EAM in all cases. Four cases were misdiagnosed as malignant tumors including liposarcoma in Case 1 and 9, solitary plasmacytoma in Case 4 (Fig. 2), malignant bone tumor of unknown tissue origin in Case 10. One lesion in Case 11 confined to the 8th posterior rib demonstrated expansive growth, which was considered as giant cell tumor of bone. Although the rest were classified as benign, they originated in various tissues, including neurogenic (Case 2 and 5), cartilaginous (Case 8), and adipose (Case 3 and 7).

### 3.3. Treatment details

All surgical procedures were all performed by senior surgeons. All...

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**Fig. 1.** A 13-year-old boy with a thoracic spinal epidural EAM. Preoperative MRI scan consisted of (A) T1 sagittal, (B) T2 sagittal, (C) T1+C sagittal, (D) T1+C axial, and (E) T1+C coronal images, showing a strip-like lesion growing dorsally within the spinal canal at T4-T7 with the characteristics of T1 hyperintense, T2 hyperintense, and enhancement changes on T1+C. (F) Laminoplasty was performed after resection of the lesion; (G) Completely resected lesion; (H) Postoperative X-ray showed decompression and instrumentation.

**Fig. 2.** A 13-year-old boy (A) X-ray showing the compression fracture of T8 before surgery; (B-E) Preoperative sagittal 3D CT&MRI scan (T1, T2, T1+C) showing a compression fracture in the vertebral body of T8; (F) Intraoperative picture showing total spondylectomy and instrumentation; (G) Postoperative X-ray showing decompression and instrumentation.
patients received gross total excision or curettage, including spinal reconstruction with the titanium screw-rod systems in 6 cases, laminoplasty with titanium microplates in one case, and no internal fixation in the remaining cases. The bone defects were repaired by the artificial vertebral body filled with bone allograft in Case 4 (Fig. 2), bone allograft alone in Cases 8 to 11, and bone cement alone in Case 1. The mean intraoperative blood loss was 781.82 ± 1143.3 (50–4000) ml. The mean duration of surgery was 180.91 ± 98.41 (50–390) min. Case 5 and 9 received intraoperative blood transfusion due to respective 1500 ml and 4000 ml blood loss during operation. Although preoperative imaging demonstrated vertebral body involvement in Case 2 and 6, it was not detected during surgery. No significant postoperative complication occurred. Light microscopy of the hematoxylin and eosin (H&E)-stained sections revealed adipose tissues and hematopoietic components in the tumors (Fig. 3A–C). Frankel scores of patients with spinal EAMs were at least raised one level or preserved postoperatively. Symptomatic patients were all relieved with the promotion of life quality, as presented by the increased postoperative Karnofsky Performance Status scores. All patients received neither radiotherapy nor chemotherapy after surgeries.

### 3.4. Follow-up

All patients were followed up for 1 and 3 months routinely after surgery; with an interval of 3 months in the first year, every 6 months in the second year and yearly afterwards. The average follow-up period was 41.9 months (range from 3 to 70 months). All the patients survived. Neither local recurrence nor distant metastasis was observed in any patient during follow-up (Table 1).

### Table 2

| No. | MRI Margin | Bone destruction | T1WI Signal | T2WI Signal | Enhance change | Morphology | CT Margin | Bone destruction | Enhance change | Morphology | Imaging diagnosis |
|-----|------------|------------------|-------------|-------------|----------------|------------|------------|------------------|----------------|------------|----------------|
| 1   | Clear      | N                | High-low mixed | High-low mixed | Moderate        | Massive    | Clear      | N                | N              | Fatty density | Liposarcoma    |
| 2   | Clear      | Y                | Slightly high | Slightly high | Moderate        | Round-like | \         | \                | \              | \          | Neurogenic tumor |
| 3   | Clear      | N                | High         | High         | Moderate        | Strip      | Blur \    | Blur             | Y              | Significant | Angiolipoma    |
| 4   | Blur       | Y                | High         | High         | Significant     | small patchy opacity | Blur     | Y                | Significant     | small patchy opacity | SP          |
| 5   | Clear      | N                | Slightly high | Slightly high | Significant     | Round-like | Clear     | N                | Slight-moderate | Round-like | Neurogenic tumor |
| 6   | Clear      | N                | Equal        | High         | Moderate        | Oval mass  | Clear     | Y                | Slight-moderate | Fatty density | Lipoma cartilaginous tumor |
| 7   | Clear      | Y                | Equal-low mixed | High          | Slight         | None       | Clear     | N                | None           | Round-like | Liposarcoma malignant tumor |
| 8   | Blur       | N                | Equal-low mixed | Equal-low mixed | None       | Oval mass | Clear     | Y                | Moderate       | Fatty density | Flaky          |
| 9   | \          | \                | \            | \            | \              | \          | Clear     | N                | N              | Fatty density | Liposarcoma malignant tumor |
| 10  | \          | \                | \            | \            | \              | \          | Clear     | N                | Moderate       | Flaky       | Malignant tumor |
| 11  | \          | \                | \            | \            | \              | \          | Clear     | Y                | N              | Mass with localized expansive growth | GCT         |

MRI: Magnetic resonance imaging; CT: computed tomography; T1WI: signal intensity of T1WI; T2WI: signal intensity of T2WI; N: none; Y: yes; SP: solitary plasmacytoma; GCT: giant cell tumor of bone.

Fig. 3. Histopathologic examination of EAM (A-C) and normal bone marrow (D-E). (A) At low magnification (40 ×), the tumor showed clear boundaries; (B) At high magnification (400 ×), the tumor consisted of scattered mature adipocytes and three lines of hematopoietic cells; (C) Myeloid cells with MPO positive expression in hematopoietic tissues (Vision method); (D) Trabecular bone (D, red arrow) and thin-walled sinuses (E, blue arrow) are seen in the normal bone marrow. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
4. Discussion

Myelolipoma is a rare benign tumor composed of nature adipose cells and a mixed proportion of myeloid and erythroid elements, usually occurring in the adrenal gland without endocrine function [2,3]. As reported in many studies [2,3,8], EAMs have a woman predominance with the female to male ratio of 2:1, and are susceptible to the ages from 50 to 70 years. However, Cheng Shen et al. reported that EAMs mainly occurred in males between 50 and 70 years of age with the male to female ratio ranging from 2:1 to 1:1 [5]. Consistently, our study demonstrated that the male to female ratio was 1.75:1 (M: F = 7: 4). Most EAMs were found in the presacral region or peritoneal cavities and rarely in other locations [2,7]. As presented in Table 3, our research on Pubmed (http://www.ncbi.nlm.nih.gov/pubmed) only retrieved 8 EAMs in the spine (n = 2) or intraosseous region (n = 6) [2,3,9-13]. Of the 2 EAMs in the spine, one was in the thoracic spinal canal [13] and the other in the lumbar vertebral body [3]. The 6 EAMs in the intraosseous regions involved the mandible [9], rib [10], acetabulum [11] and femur (n = 3) [2,11,12]. To the best of our knowledge, this study reports the largest case series of the spinal and intraosseous EAMs so far even though 4 cases of parathoracic EAMs were not included, which can also be classified as mediastinal EAMs. It is remarkable that EAMs were observed in the thoracic vertebral body (n = 2) and the humerus (n = 1) in our series, which are all the first report in the English literature. Furthermore, we provide the second report of EAMs located in the thoracic spinal canal, rib and ilium (n = 2).

The exact etiology of EAMs remains unclear, although several hypotheses have been put forward to explain the pathogenesis. The more accepted explanation is metaplasia in reticuloendothelial cells, caused by various stimuli including infection, stress, obesity, hypertension, diabetes and Cushing’s disease[14]. Several studies believe that embolization of the bone marrow tissue or the metaphasic alterations of embryonic primitive mesenchymal cells is also the possible cause of EAMs [3,5,15,16]. In addition, chromosomal translocations have been identified in myelolipoma cells, which are also observed in lipomatous neoplasms [5,17]. Most thoracic EAMs tend to attach to the spinal vertebral bodies, considering that microfractures may cause hematopoietic tissue to project from the spinal vertebral bodies to the paravertebral spaces. The ectopic hematopoietic tissue may contain stem cells, which would be the origin of EAMs [18].

EAMs are usually asymptomatic and found by chance, unless the mass effect generated by the tumor’s growing size causes compression on the surrounding tissues or organs [3]. But the symptoms lack specificity and vary with different tumor locations. As previously mentioned in this study, 8 (72.73%) of the 11 cases were symptomatic, including local pain in 5 cases (45.45%) and discomfort in 3 cases (27.27%). Of them, Case 4 was also accompanied with pathologic fracture and thoracic vertebral kyphosis (Fig. 2). Neurological defects were observed in a 13-year-old male patient with a thoracic spinal epidural EAM (Case 3, Fig. 1), who presented numbness and limb weakness of the right lower extremity (Frankel score = 4) (Table 1). Through review of the literature, Cheng Shen et al. summed up the clinical characteristics of thoracic EAMs in 36 patients, of whom 20 (55.56%) were asymptomatic at their first visit, 9 (25%) had cough and 6 (16.67%) had fever [5]. Other symptoms such as urinary retention or sciatic pain in presacral lesions, gait disturbance in intraspinal lesions have also been also reported [5]. Acute hemorrhage, as the most significant complication, could occur in large myelolipomas [19].

Imaging examination plays a critical role in establishing the diagnosis of EAMs or excluding malignancy of the tumors. EAMs typically occur in solitary forms depicted as an oval or round shape with clear boundaries. However, the tumor boundary was obscure in 2 cases of our series, which misled the initial imaging diagnosis of the tumor. Generally, a low-attenuation area can be observed in EAM on the CT scan, and the diversity of CT densities could be explained by various proportions of the adipose and bone marrow tissues in EAM. It is of great importance to discern the predominant myeloid element with high-attenuation area in the fatty element with the low-attenuation area[20,21]. Littrell et al. [22] reported 11 patients with presacral EAMs and observed mild-to-moderate enhancement on CT imaging in all their patients. However, enhancement change was observed in only 4 (44.44%) of the 9 patients who underwent CT scan in our study, and the enhancement was significant in Case 4. On MRI, EAMs are relatively homogeneous with the characteristics of high-signal intensity in both T1- and T2-weighted sequence for mature adipose tissues. Given the low signal of the myeloid element on T1-weighted imaging and moderate signal on T2-weighted imaging, the adipose tissue can be detected easily on MRI through a fat saturation technique [21]. Most cases in our series

Table 3

| No. | Author [ref.] | Age, sex | Symptoms | DOC (months) | Accompanied disease | Location | Tumor Size (cm) | Imaging diagnosis | Operation | Comp | Follow-up (months) | LR/meta | Last status |
|-----|---------------|----------|----------|-------------|---------------------|----------|-----------------|------------------|-----------|------|-------------------|---------|-------------|
| 1   | Chiariini L et al. [9] | NA, M | Mass formation | 12 | NA | Right mandible | NA | NA | Excision | NA | 18 | None | Alive |
| 2   | Wen J et al. [10] | 18, M | None | NA | None | Rib | 2 | NA | Radical resection | None | 24 | None | Alive |
| 3   | Sundaram M et al. [11] | 35, F | Pain | NA | None | the right acetabulum | 4 | FD | Curettage | NA | NA | NA | NA |
| 4   | Sundaram M et al. [11] | 51, M | Pain | NA | DM, DA, SF | proximal femur | NA | FD | Resection + PR | NA | NA | NA | NA |
| 5   | Papapetropoulos N et al. [12] | 80, M | Pain | NA | PC | proximal femur | 5 | NA | Curettage + BA | None | 18 | None | Alive |
| 6   | Sakai T et al. [2] | 25, F | NA | 120 | CCH | Distal femur | 20 | OS | Observation | NA | 24 | NA | AWD |
| 7   | Omidal D et al. [13] | 49, M | Numbness,GD, pain, IBI | 6 | None | TS | NA | NA | Piecemeal + LAM | NA | 10 | None | Alive |
| 8   | Rezaee H et al. [3] | 62, M | Pain, limp weakness | 156 | NA | LS | 7.6 | NA | Piecemeal + TSS + BA | NA | 3 | NA | Alive |

Ref.: references; Comp: Complication; LR/meta: local recurrence/metastasis; NA: not available; F: female; M: male; GD: gait disturbance; IBI: intermittent bladder incontinence; DM: diabetes mellitus; DA: degenerative arthritis; SF: stress fracture; PC: prostate cancer; CCH: congenital cytomegalovirus hydrocephalus; TS: thoracic spine; LS: lumbar spine; FD: fibrous dysplasia; OS: Osteosarcoma; PR: prosthetic replacement; BA: bone allograft; LAM: laminectomy; TSS: titanium screw-rod systems; AWD: alive with disease.
exhibited high signal intensities on T1- and T2-weighted sequences, while two patients (Case 1 and 9) presented mixed signal intensities on both T1- and T2-weighted sequences. Enhancement was typically moderate but 2 of the 8 cases with MRI exams showed mild enhancement and one had no enhancement. It has been also reported that calcification could be observed in very rare cases of EAMs [3,23].

Despite advances made in imaging techniques, it is still difficult for radiologists to make a differential diagnosis only based on radiology, including lipomas, liposarcomas, angiomylipomas, teratomas and extramedullary hematopoiesis [2,3,24]. All 11 patients in our report were initially misdiagnosed as other tumors by radiologists. The high rate of misdiagnosis might be explained by the absence of specific imaging manifestations in EAMs, extensiveness of fat-containing lesions requiring differential diagnosis, and the rarity of EAMs, all of which may limit the correct diagnosis of EAMs, especially in radiologists with less experience. It is extremely difficult to establish a definitive diagnosis by imaging presentations alone [2,21]. Pathology remains the gold standard for the diagnosis of EAMs. Pathologically, typical EAMs are characterized by different forms of hematopoietic cells (erythroid cells, erythroid cells and megakaryocytes) mixed with mature adipocytes and rare bony trabeculae [1,25]. Similar features were also showed in our cases (Fig. 3A–C). Although morphology of EAMs is similar with that of the normal bone marrow tissue, the key point of identification between the two tissues is that the trabecular bone and thin-walled sinuses are commonly observed in normal bone marrow (Fig. 3D–E), but rare in EAMs. Malignant degeneration of EAMs has never been reported so far.

There is no consensus regarding the EAMS management [3,21]. Given the rarity of EAMs, there is limited knowledge about their natural history, long-term prognostic outcomes and treatment recommendations. Treatment of EAMs is either observational or surgical. Several factors should be taken into consideration comprehensively to determine whether surgical intervention is indicated, including the general condition of the patient with or without symptoms, the risk of surgical intervention, and location and size of the tumor. In thoracic EAMS, quite a few studies suggest surgical therapy as the first option because the tumor has the capacity of continuous growth [5,26,27]. However, Shen C et al. argued that symptomatic patients with a tumor size larger than 7 cm should be candidates of surgery, and asymptomatic patients with smaller tumors should be followed up closely [26]. In intraosseous and presacral EAMs, surgery is indicated, especially for patients with clinical symptoms, and the masses greater than 7 cm [12,28,29]. It is generally suggested that surgical intervention may be necessary if the mass is larger than 4 cm in diameter [3,21]. In our report, all patients underwent surgeries, because most patients had clinical symptoms and malignancy of the tumor could not be excluded by imaging examinations. The treatment strategies for Case 3 and 6 were discussed in depth and surgery was eventually decided on with the consideration of the potential progression and unpredictable prognosis of the tumor. Postoperative follow-up observation demonstrated excellent prognoses in all our patients as represented by an overall improvement in the quality of life of the patients, and no recurrence and metastasis occurred during the follow-up period. Therefore, we recommend that surgical resection should be the choice of treatment for EAMs with large size, clinical symptoms, imaging diagnoses suspected as malignant tumors, and involvement in the spine and thorax.

5. Conclusions

EAMs are rare benign tumors with good prognosis but limited cases have been reported so far, especially those involving the spinal and intraosseous regions. Conventional imaging differential diagnosis of EAMs remains a big clinical challenge. Our study has demonstrated that the total surgical resection can serve as a radical method for spinal and intraosseous EAMs. For those with no clinical symptoms and small tumor size, dynamic observation is suggested. At present, no study has indicated that the tumor has the tendency of postoperative recurrence, malignant transformation and metastasis. More multi-institutional and larger-sample studies are required to gain more insights into etiologies and clinical characteristics of spinal and intraosseous EAMs.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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