

Long period of relative quiescence in distal-type epithelioid sarcoma of the forearm with recurrence after surgery

A case report

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Abstract

Background: Epithelioid sarcoma (ES) is a rare malignant mesenchymal tumor that only accounts for 0.6% to 1.0% of all cases of sarcomas. ES with a relative quiescent state of more than 10 years is extremely rare. Here, we present a rare case of ES in the forearm of a 17-year-old girl. The patient had a congenital mass in her forearm that measured approximately 1 cm; it grew rapidly starting 5 years ago. The mass was not treated until last year when she underwent the first surgery. The mass was located in the middle and lower part of the left forearm and involved the dorsal muscle group, intermuscular space, and subcutaneous tissues without clear boundaries. The patient underwent surgery, and the tumor recurred twice within 1 year postoperatively.

Methods: The tumor samples were examined via hematoxylin-eosin (HE) and immunohistochemistry staining.

Results: Histopathologically, the tumor comprised large polygonal epithelioid cells with abundant eosinophilic cytoplasm arranged in cell nests. Central necrosis and focal myxoid change could be seen in the tumor tissues. Immunostaining showed that the tumor cells were positive for CD34, CK, EMA, and vimentin but negative for CD31, S-100, and INI-1.

Conclusion: Based on these findings, the tumor was diagnosed as ES of distal form. Distal-type ES could have a long period of relative quiescence, after which it could grow rapidly and relapse multiple times over a short duration.

Abbreviations: HE = hematoxylin-eosin, MRI = Magnetic Resonance Imaging.

Keywords: case report, epithelioid sarcoma, forearm, recurrence

1. Introduction

Epithelioid sarcoma (ES) is a rare malignant mesenchymal neoplasm showing epithelioid cytology and only accounts for 0.6% to 1.0% of all cases of sarcomas.^[1] There are 2 clinicopathological subtypes of ES, namely, conventional distal type and proximal type.^[1,2] The patients with distal-type ES are relative younger, with more than 70% of them aged between 10 years and 40 years.^[1] Most distal-type ES involves the distal upper extremities,^[1] and it rarely develops in the proximal extremity, trunk, and head and neck.^[1] Chanplakorn reported an ES in the thoracic spine.^[3] A few cases of ES in the orbit were also

reported.^[4,5] There were also some reports of rare cases that occurred in solid organs, such as the kidney and adrenal gland.^[6] Pathologically, the tumor is characterized by epithelioid cytology^[1] and is mainly composed of epithelioid cells and plump spindle-shaped cells, which both lack marked atypia and may lead to consideration of some benign lesions including inflammation, fibrohistiocytic tumors, and vascular tumors.^[1] Clinically, this kind of tumor usually presents as a slowly growing mass without causing any other obvious symptoms; thus, it is easily mistaken as a benign disease.^[1,7] However, local recurrence and lymph node and distant metastases are common in this malignancy, and it is usually considered as high-grade sarcoma.^[8] The tumors presenting as localized disease usually have better prognosis;^[8] thus, a correct diagnosis in the earliest time possible is essential to improve the prognosis. Here, we present a case of ES in the forearm of a 17-year-old girl. This case is unique in that the patient had a mass in her forearm since she was born. The mass grew very slowly and had a relative quiescent state for more than 10 years. After 16 years, it began to grow faster, and the tumor was resected and confirmed to be distal-type ES via pathological examination. The tumor recurred twice within a year after the surgery.

2. Case report

The patient was a 17-year-old girl who had a skin bulge in her left forearm when she was born. A subcutaneous soft mass measuring approximately 1 cm could be touched under the bulge. No examination and treatment were performed until she was 16 years old. Five years ago, she noticed an obvious enlargement of

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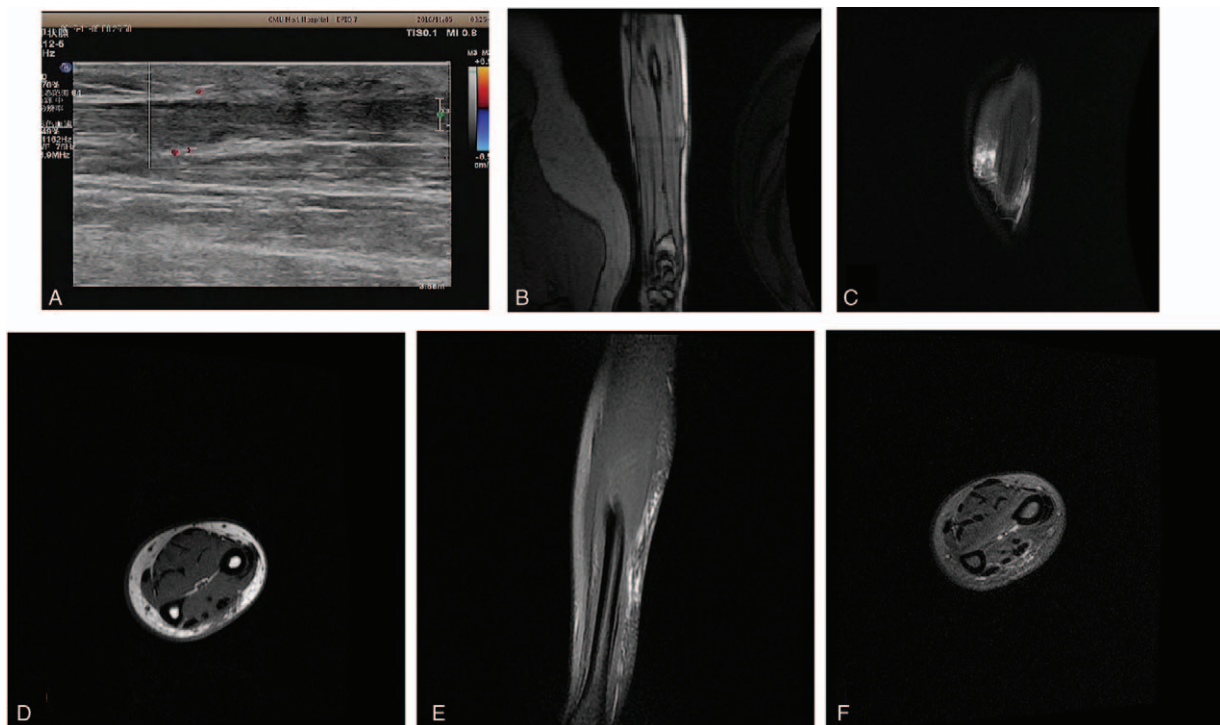


Figure 1. Imaging scans of the tumor. The ultrasonography scan before the second surgery showed low echoes in an area approximately $3.43 \times 0.52 \times 1.07$ cm near the incision (A). MRI showed abnormal signals in the left middle part of the left forearm (B, C) with rough edges. MRI imaging before the third surgery showed abnormal signals in the dorsal muscle group, intermuscular space, and subcutaneous tissues of the left forearm (D, E, F). MRI=Magnetic Resonance Imaging.

the mass. Two years ago, the lump started to become painful but without itching or ulcer in the skin. A subcutaneous mass measuring approximately 3×3 cm in her left forearm was noted upon physical examination in the hospital. Considering that the tumor was congenital, it was pathologically misdiagnosed as cellular hemangioma. She received postoperative radiotherapy. Seven months after this first surgery, the patient noticed an enlargement of the mass near the incision. An irregular subcutaneous mass measuring approximately 2.5×1 cm near the incision was seen on physical examination. Postoperative radiotherapy was continued after the incision healed. Four months later, the patient experienced a second focal recurrence of the tumor and consequently underwent her third surgery. This study was approved by the institutional Ethics Committees of China Medical University and conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Informed consent was obtained from the patient for publication of this case report and accompanying images.

Figure 1 shows the images of the tumor. Before the first surgery, an ultrasonography scan detected a mass measuring approximately 3.06×0.54 cm in the deep fascia layer. Calcification was detected inside the mass. The mass was irregularly shaped without clear boundaries. The deep muscle tissue was compressed and the boundary was clear. She underwent her first surgery, and the medical record showed that the tumor was located in the deep fascia with marked calcification. The ultrasonography scan before the second surgery showed a mass approximately $3.43 \times 0.52 \times 1.07$ cm in size with low echoes (Fig. 1A). Magnetic resonance imaging (MRI) showed abnormal signals in the left middle part of the left forearm (Fig. 1B, C). The edge was rough, and the nearby skin structure was damaged. MRI before the third surgery showed abnormal signals in an area approximately 5.5×8.5 cm in the middle and lower part of

the left forearm, including in the dorsal muscle group, intermuscular space, and subcutaneous tissues (Fig. 1D, E, and F). No abnormalities were found in the left ulna and radius. Grossly, the tumor was white and closely surrounded the extensor tendon of the thumb and ring finger. The mass had no clear capsule, was irregular in shape, and measured approximately 4.5×0.5 cm. Chest x-ray showed no abnormality. Ultrasonography scan showed no abnormalities in the liver, spleen, pancreas, and bladder.

The tumor samples were examined via hematoxylin-eosin (HE) and immunohistochemistry staining as described previously.^[9] Figure 2 shows the histopathological features of the tumor. The tumor cells of the samples obtained during the first surgery were arranged in irregularly cell nests (Fig. 2A, B). There were crack-like structures in the cell nests, and hemorrhage was seen. No classic central necrosis was detected. Most of the tumor cells were large, irregular in shape, and epithelioid with abundant eosinophilic cytoplasm (B). Part of the tumor cells were spindle shaped, and they transitioned to polygonal epithelioid cells. The histopathological features of the samples obtained in the second surgery were similar with those of the first. The tumor cells were also arranged in cell nests, and central necrosis could be seen in the cell nests (Fig. 2C, D). The cell morphology and microscopic features were similar with those of the sample obtained on the first surgery. The tumor cells were arranged in cell nests, and focal myxoid change could be seen in the tumor tissues (Fig. 2E). Most of the tumor cells were the same polygonal epithelioid cells with abundant eosinophilic cytoplasm (Fig. 2F).

Figure 3 shows the immunostaining features of the tumor. The immunostaining pattern of the 3 samples of the tumor was the same. CD31 was negative in the tumor cells and positive in the blood vessels. CD34, CK, and EMA were strongly and diffusely positive in the tumor cells. INI-1 was negative. The Ki-67 index

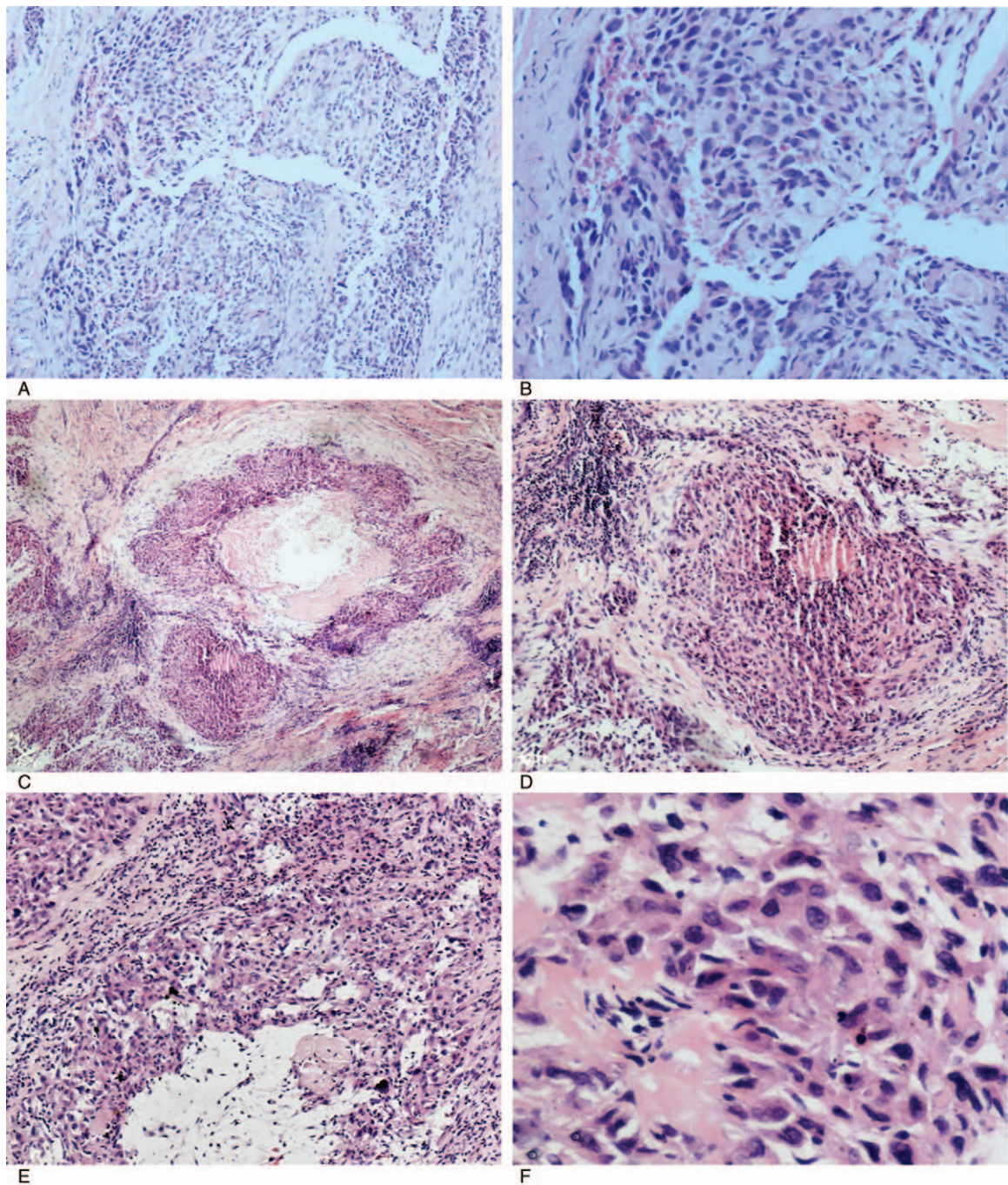


Figure 2. Morphological features of the tumor. In the first sample, the tumor cells were arranged in irregularly shaped cell nests (A, B). There were crack-like structures in the cell nests with hemorrhage. Most of the tumor cells were large, irregular in shape, and epithelioid with abundant eosinophilic cytoplasm (B). Part of the tumor cells were spindle shaped. The histopathological features of the second sample were similar as those of the first. The tumor cells with same morphology were also arranged in cell nests (C, D). Central necrosis could be seen in the cell nests (C, D). The microscopic features of the third tumor samples were also similar with those of the first. The tumor cells were arranged in cell nests with focal myxoid change in the tumor tissues (E). Most of the tumor cells were also polygonal epithelioid cells with abundant eosinophilic cytoplasm (F). (Magnification: A, B, D, E: $\times 200$; C: $\times 100$; F: $\times 400$).

was approximately 5%. S-100 staining was very weak and was negative in the nucleus of the tumor cells. Vimentin was diffusely positive in the tumor cells.

3. Discussion

Distal-type ES is usually superficial and grows slowly.^[1] The tumors in deep sites usually spread along the fascia.^[1] In the

current case, the tumor was located relatively deep, which may be due to the long period of growth and invasion of the deep tissues. Moreover, superficial tumors are usually small, while deep tumors are relatively large.^[1] In some cases, satellite nodules around the tumor can be seen.^[10]

Histopathologically, ES contains 2 types of tumor cells, namely, spindle cell and epithelioid cells, and their proportion varies substantially; thus, the tumor is easily mistaken for many

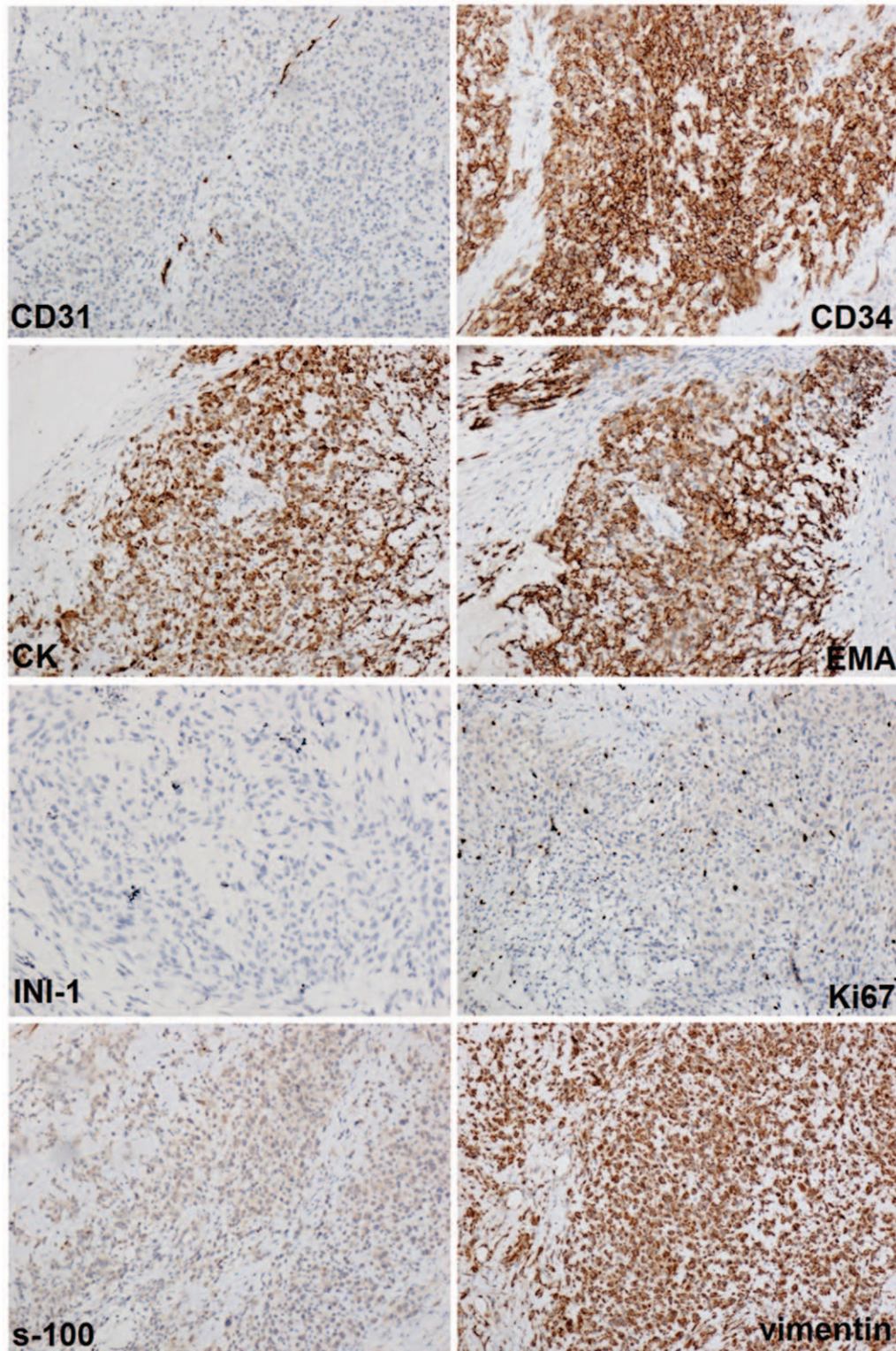


Figure 3. Immunostaining findings of the tumor. CD31 was negative in the tumor cells. CD34, CK, EMA, and vimentin were strongly and diffusely positive in the tumor cells. INI-1 was negative. Ki-67 index was approximately 5%. S-100 was negative in the nucleus of the tumor cells (Magnification: $\times 200$).

other benign or malignant tumors or even inflammatory lesions.^[7] The tumor is at least partly composed of epithelioid cells, which may lead to consideration of metastatic carcinomas. In the distal type, the tumor also contains spindle cells without obvious atypia.

Moreover, as there are usually cystic spaces with blood in the tumor tissues as the current case, it may be mistaken as a vascular neoplasm. In the early stage of the disease, the tumor is often misdiagnosed as a benign tumor.^[10] In the current case, many vascular-like structures but not central necrosis were found in the

primary tumor; thus, it was considered as cellular hemangioma of infancy that was mainly composed of plump endothelial cells forming vascular structures. Another main distinguishing factor is necrotizing granulomas.^[7] In Nishibaba's report, the patient with ES was initially misdiagnosed with fungal infection for the granuloma-like lesion.^[10]

Dystrophic calcification can be seen in approximately 20% of cases.^[11] In the current case, calcification was detected on the first ultrasonography scan. The tumor was initially suspected as lipoma with calcification or vascular lesions with venous stones based on the scan. ES can also histopathologically mimic benign fibrous histiocytoma.^[11] Loss of nuclear expression of INI-1 is a characteristic immunostaining feature of this tumor and is important for its diagnosis.^[1,12,13] CD34 expression is inconsistent,^[14] and more than 50% of the cases are positive.^[11] In the current case, CD34 was positive. CD31 is usually negative in this tumor,^[1,15] as in our case.

MRI is more advantageous than computed tomography and x-ray for the diagnosis of this tumor before pathological examination.^[7] MRI is useful for observing the size and growth pattern of the tumor. In the current case, MRI showed that the tumor was located in the dorsal muscle group, intermuscular space, and subcutaneous tissues of the left forearm without clear boundary, which indicated its aggressive growth pattern. MRI is also used to observe whether there are tumor remnants after surgery.^[7] However, as the tumor frequently invades the intermuscular space and subcutaneous tissue, some small infiltrating foci are difficult to detect before and after the surgery, which cause the difficulty in complete resection of the tumor and may explain the tendency of local recurrence after surgery.

At present, surgery remains the main treatment of ES. Radical resection of the primary tumor is critical to improve patient prognosis.^[3] Postoperative local recurrence is common, and accounts for up to 85% according to Enzinger.^[7] Guzzetta's study showed that there is no significant correlation between the number of recurrences and patient prognosis.^[16] In Guzzetta's study, 35% of patients had multiple recurrence.^[16] In Lee's report, the patient with ES in the cervical spine underwent multiple surgeries and died from respiratory failure due to local invasion in the trachea.^[17] In the current case, the patient experienced 2 recurrences after the surgery.

No unified treatment plan has been established for patients with metastasis.^[18] The effect of chemotherapy and postoperative radiotherapy is inconsistent. Jones reported that although palliative chemotherapy had some effect, the progression-free time was very short.^[19] Meanwhile, the findings of Kim's study indicated that postoperative adjuvant radiotherapy had a beneficial effect on patient prognosis, but postoperative adjuvant chemotherapy had none.^[20] Livi's study also showed that postoperative radiotherapy was helpful in improving the prognosis.^[21] In Viktoras's report, the patient with ES underwent surgery and received radiotherapy and had no recurrence after a 2-year follow-up.^[14] In vitro studies showed that some molecular pathways are involved in the progression of ES.^[22] The molecular mechanism and optimal targeted therapy of this rare tumor are still studied.^[18,22]

Asano's study indicated that the most important factors for prognosis of ES are lymph node and distant metastases.^[23] Like many other sarcomas, the most common organ of distant metastasis is the lung.^[7] Deep tissue involvement is usually an adverse prognostic factor for ES,^[1,8] as well as old age, male sex, proximal extremity location, and large tumor size.^[11] The 10-year

overall survival rate of ES is approximately 42% to 62%.^[11] The prognosis of patients with distal-type ES is usually better than that of patients with proximal type.^[1,23]

The cause of ES is still unknown. Kusum reported a case of ES arising in the burn scar, which indicated an association between burns and the occurrence of the tumor.^[24] To our knowledge, no case of congenital ES has been reported yet. In the current case, the patient had a congenital mass in her left forearm. Although it is possible that the mass was a congenital ES, we are unsure because it was not examined pathologically at that time.

4. Conclusion

ES is rare malignant mesenchymal neoplasm with distinct epithelioid morphology and could be misdiagnosed with a benign tumor. Based on our findings of the current case, we suggest that distal-type ES could be growing slowly for a long time and invade to the deep sites of the extremity. Then, it could grow rapidly at a later time and recur multiple times in a short period after surgery.

Author contributions

Conceptualization: Xiupeng Zhang, Biying Jiang, Xiuying Shi, Chuifeng Fan.

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Supervision: Chuifeng Fan.

Writing – original draft: Xiupeng Zhang, Biying Jiang, Xiuying Shi.

Writing – review & editing: Xiupeng Zhang, Chuifeng Fan.

References

- [1] Fletcher CDM, Bridge JA, Hogendoorn PCW, et al. World health organization classification of tumors of soft tissue and bone. IARC Press, Lyon:2013.
- [2] Han CH, Li X, Khanna N. Epithelioid sarcoma of the vulva and its clinical implication: a case report and review of the literature. *Gynecol Oncol Rep* 2016;15:31–3.
- [3] Chanplakorn P, Chanplakorn N, Pongtippan A, et al. Recurrent epithelioid sarcoma in the thoracic spine successfully treated with multilevel total en bloc spondylectomy. *Eur Spine J* 2011;20(suppl 2): S302–8.
- [4] Alkatan HM, Chaudhry I, Al-Qahtani A. Epithelioid sarcoma of the orbit. *Ann Saudi Med* 2011;31:187–9.
- [5] Tariq Z, Ghose A, Bawany MZ, et al. A case report of complete remission of pulmonary metastases from epithelioid sarcoma to navelbine chemotherapy. *Am J Ther* 2012;19:e95–7.
- [6] Alikhan MB, Pease G, Watkin W, et al. Primary epithelioid sarcoma of the kidney and adrenal gland: report of 2 cases with immunohistochemical and molecular cytogenetic studies. *Hum Pathol* 2017;61:158–63.
- [7] Sobanko JF, Meijer L, Nigra TP. Epithelioid sarcoma: a review and update. *J Clin Aesthet Dermatol* 2009;2:49–54.
- [8] Jawad MU, Extein J, Min ES, et al. Prognostic factors for survival in patients with epithelioid sarcoma: 441 cases from the SEER database. *Clin Orthop Relat Res* 2009;467:2939–48.
- [9] Fan C, Yang L, Lin X, et al. Pseudomyogenic hemangioendothelioma/epithelioid sarcoma-like hemangioendothelioma of the lower limb: report of a rare case. *Diagn Pathol* 2015;10:150.
- [10] Nishibaba R, Higashi Y, Goto Y, et al. Epithelioid sarcoma with multiple lesions on the left arm: a case report. *J Med Case Rep* 2016;10:295.
- [11] Lynch MC, Graber EM, Johnson TS, et al. Epithelioid sarcoma resembling benign fibrous histiocytoma. *Cutis* 2015;95:83–6.
- [12] Sakharpe A, Lahat G, Gulamhusein T, et al. Epithelioid sarcoma and unclassified sarcoma with epithelioid features: clinicopathological variables, molecular markers, and a new experimental model. *Oncologist* 2011;16:512–22.

- [13] Hornick JL, Dal Cin P, Fletcher CD. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. *Am J Surg Pathol* 2009;33:542–50.
- [14] Rudžianskas V, Juozaityte E, Inčiura A, et al. Primary epithelioid sarcoma of the neck: a rare case report. *Medicina (Kaunas)* 2012;48:57–60.
- [15] Chaturvedi M, Khare MS. Epithelioid sarcoma with angiomatous pattern: a diagnostic dilemma. *Indian J Pathol Microbiol* 2010;53:170–1.
- [16] Guzzetta AA, Montgomery EA, Lyu H, et al. Epithelioid sarcoma: one institution's experience with a rare sarcoma. *J Surg Res* 2012;177:116–22.
- [17] Lee C, Choe WJ, Kim N. Epithelioid sarcoma in the cervical spine: a case report. *Korean J Spine* 2015;12:165–8.
- [18] Noujaim J, Thway K, Bajwa Z, et al. Epithelioid sarcoma: opportunities for biology-driven targeted therapy. *Front Oncol* 2015;5:186.
- [19] Jones RL, Constantinidou A, Olmos D, et al. Role of palliative chemotherapy in advanced epithelioid sarcoma. *Am J Clin Oncol* 2012;35:351–7.
- [20] Kim C, Yoo KH, Kim MH, et al. Different subtypes of epithelioid sarcoma and their clinical implication: long-term multi-institutional experience with a rare sarcoma. *APMIS* 2017;125:223–9.
- [21] Livi L, Shah N, Paia F, et al. Treatment of epithelioid sarcoma at the royal marsden hospital. *Sarcoma* 2003;7:149–52.
- [22] Imura Y, Yasui H, Outani H, et al. Combined targeting of mTOR and c-MET signaling pathways for effective management of epithelioid sarcoma. *Mol Cancer* 2014;13:185.
- [23] Asano N, Yoshida A, Ogura K, et al. Prognostic value of relevant clinicopathologic variables in epithelioid sarcoma: a multi-institutional retrospective study of 44 patients. *Ann Surg Oncol* 2015;22:2624–32.
- [24] Jashnani KD, Dhume VM, Bahal NK. Epithelioid sarcoma and squamous cell carcinoma arising in a burn scar. *Indian J Dermatol* 2011;56:585–6.