

# Pathological Observation and Literature Clinical Review of Ossifyingfasciitis

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**Abstract:** *Objective* To investigate the clinicopathological features of ossifyingfasciitis. *Methods* The clinical, imaging and pathological data of a case of ossifying fasciitis diagnosed in Aikang Pathology Department of Huangshi in June 2023 were collected, and the relevant literature was reviewed. *Results* A 36-year-old male patient with ossifying fasciitis was located in the elbow of the right upper limb. The lesion was relatively clear and consisted of chaotic proliferation of fibroblasts/myofibroblasts and osteoid tissues with varying degrees of maturity. The fusiform fibroblasts are mild in form and occasionally have mitotic signs, which are morphologically similar to myositis ossificans. Osteoid tissues were of varying maturity and irregular shape. Osteoblasts could be seen around them and were randomly distributed in fibrous tissues in the form of cords. *Immunohistochemistry:* Vimentin spindle cells (+), SMA (+) and caldesmon (-), desmin (-) and B - catenin (-), S - 100 (-) and CD34 (-). CK (-). *Conclusion* Fasciitis ossificans is a rare benign lesion, its clinicopathological features are very similar to myositis ossificans, and the prognosis is good after complete resection. No metastasis or malignant transformation has been reported.

**Keywords:** *ossifying fasciitis; Myositis ossificans; Parosteosarcoma*

## 1. Introduction

Ossifyingfasciitis is a form of heterotopicbone nodular fasciitis fibroblastosis with heterotopicbone formation with varying degrees of maturity, which can eventually develop into more mature lamellar bone. Unlike myositis ossificans, fasciitis ossificans is often irregularly zoned, with bone-like tissue randomly distributed within the fibrous interstitium [2]. Recent studies have shown that fasciitis ossificans and myositis ossificans have similar molecular genetic changes, that is, COL1A1-USP6 gene rearrangement can occur in both. Ossifyingfasciitis is rare and more likely to be misdiagnosed as paracortical osteosarcoma or extraosseous osteosarcoma. This article reports a case of ossifying fasciitis, and reviews the relevant literature to discuss the diagnosis and differential diagnosis of the disease, in order to further deepen the understanding of the disease.

## 2. Materials and Methods

The clinical, imaging and pathological data of a case of ossifying fasciitis diagnosed in the Department of Pathology of Huangshi Aikang Hospital in June 2023 were collected. Specimens were fixed with 10% neutral formalin solution, paraffin embedded, and 3 μ m thick sections were examined by routine HE, immunohistochemistry and FISH. *Immunohistochemistry:* Performed by Envision two-step method with negative and positive controls. The anti-SMA, calponin, caldesmon, desmin, β -catenin, S-100, vimentin, CD34, CK, EMA, Ki-67 and other primary antibodies used in the experiment were purchased from Fuzhou Maixin Biotechnology Co., LTD., and the steps were carried out according to the instructions. *FISH test:* Specimens were sliced continuously with a thickness of 5μm, and USP6 gene rearrangement was performed for the cases. USP6 two-color separation signal. The probe was purchased from Guangzhou Ambipin Medical Technology . The red fluorescent probe was bound to the 5' end of USP6 gene, and the green fluorescent probe was bound to the 3' end of USP6 gene. When the red and green signals were separated by more than 1 signal point distance, they were interpreted as positive cells. 100 tumor cells were counted, and the ratio of red and green separation signal was more than 15%, which was interpreted as positive.

### 3. Results

Clinical features A 36-year-old male patient with right elbow mass was admitted to hospital more than 1 month ago. X-ray examination showed a strong echo mass in the volar of the right elbow joint (FIG. 1A), which was considered to be lymph node calcification. Right elbow joint tumor was considered clinically. Intraoperative findings: The tumor was round and regular, with obvious adhesion to surrounding tissues, blood vessels and nerves.

A grayish-brown mass of 2cm×1.5cm×1cm was observed in general, and the gray-white-gray brown gravel on the cut surface seemed to have ossification.

HE staining showed a clear lesion boundary, consisting of chaotic proliferation of fibroblasts and bone-like tissues with varying degrees of maturity (FIG. 1B). The fusiform fibroblasts/myofibroblasts had varied density, loose edema or mucous degeneration, and local collagen. The plasma of the fusiform cells was eosinophilic, the nuclei were oval or slender and fusiform, and the morphology was mild. Occasionally, mitotic images could be seen, similar in morphology to nodular fasciitis, and multinuclear giant cells could be seen locally (FIG. 1C). The osteoid tissues varied in maturity, irregular in shape and random in stringy shape. Distributed in the fibrous tissue, osteoblasts can be seen around the osteoid tissue or bone trabecular surface changes, osteoblasts are more mature differentiation, no atypia, no mitotic signs.

Immunohistochemical phenotypic spindle cells vimentin(+), calponin (+), sma(+) Figure 1D), caldes ossified myossitis n(-), Desmin(-),  $\beta$ -catenin(-), s-100(-), cd34(-), ck(-), ema(-), The proportion of cells with IUSP6 break signal in about 10% of Ki-67 hotspots (Figure 1E)

Molecular biological phenotype cases was about 48%, indicating that the sample detected a USP6 gene break (Figure 1F). The proportion of cells with the USP6 break signal in case 2 was about 5%, indicating that no USP6 gene break was detected in the sample.

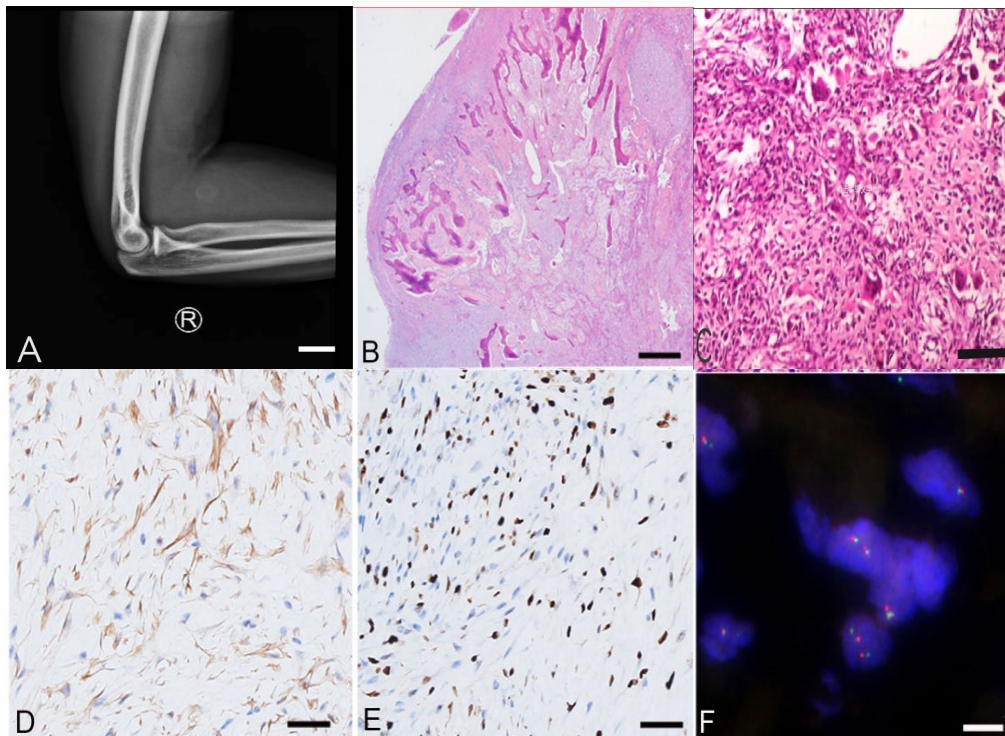


Figure 1 shows the image and pathological features of ossifying fasciitis. A) X-ray images; B, the tumor is composed of fibroblasts and bone-like tissue; C, multi-nucleated giant cells can be seen in the fusiform cell region; D, SMA(+); E, the proliferation index of Ki-67 was about 20%; F, USP6 gene break; Scale: B, 250 $\mu$ m; C, D, E, 50 $\mu$ m; F, 25 $\mu$ m

### 4. Discussion

Ossifying fasciitis is a benign lesion with osteogenic fibroblast/myofibroblast proliferation [1], a

specific subtype of nodular fasciitis, and a classic pseudosarcomatous lesion. Previous literature reports such as popular on sexual response tomorrow (florid reactive periostitis), soft tissue fake malignant bone tumor (pseudomalignant osseous tumor of soft tissue), bone fasciitis (parosteal fasciitis), etc. With histological changes similar to those seen in ossifying fasciitis, these names are used interchangeably, but the classification of specific lesions remains controversial. Fasciitis ossificans is a lesion associated with ossification and may cause periosteal reaction of adjacent bones. However, it does not originate from bone tumors, but is closely related to myositis ossificans and has similar histological changes and molecular genetic characteristics to myositis ossificans, so it can be considered as a superficial variant of myositis ossificans [2]. Ossifying fasciitis tends to occur in soft tissues, especially in the proximal joints, and in rare cases may involve the adjacent periosteum. Fasciitis ossificans is generally small, about 0.8cm~5.6cm in diameter, with an average of 1cm. It can occur at any age, but it is more common in young people around 20-30 years old, and more women. Clinically, ossifying fasciitis is generally characterized by local swelling or mass, which may be accompanied by pain or swelling and functional dysfunction of different degrees. The skin on the surface of the mass may show erythema, ulcer, epithelial hyperplasia and pale skin [3, 4]. Some cases have a history of trauma, but it is uncertain whether it is related to trauma. The growth of the lesions is relatively rapid, and the history of the disease generally ranges from a few weeks to several months, with a few cases having a disease history of several years [8]. The typical imaging manifestation of ossifying fasciitis is a bony mass with clear parosseous boundary, uniform or uneven density, which does not surround the adjacent bone tissue, and in a few cases can erode the bone cortex, and there may be periosteal reaction near the periosteal membrane. The lesion ossification was not obvious and presented as isodense soft tissue mass. X-ray and CT only showed the swollen soft tissue and periosteal reaction of adjacent bone, and MRI was required to show the mass [9, 10]. Imaging needs to distinguish from osteochondroma, parosteosarcoma, extraosseous chondroma, osteomyelitis, etc.

In general, the boundary of the lesion was clear, with nodular shape, gray section, medium texture or tough quality, and gritty feeling during incision. The microscopic lesions were composed of chaotic proliferation of fibroblasts and osteoid tissues with varying degrees of maturity. The fusiform fibroblast area is variously dense, the interstitial is loose and edema or mucous change, map collagen can be seen, and scattered lymphocyte infiltration can be seen in the lesion. The plasma of fusiform cells is eosinophilic, the nuclei are oval or slender fusiform, the shape is mild, occasionally visible mitosis, the morphology is similar to nodular fasciitis. Osteoid tissues varied in maturity, including mature bone trabeculae, braided bone without calcium deposition, and amorphous bone tissues. The osteoid tissues were randomly distributed in the fibrous tissues, and the osteoblasts were uniformly "beaded" around them. Osteoblasts were differentiated and mature, with abundant cytoplasm, no atypia, and no mitotic signs. Compared with myositis ossificans, osteoid tissues of fasciitis ossificans are disordered with no obvious zonal phenomenon. Immunohistochemical spindles can express SMA, suggesting fibroblast/myofibroblast differentiation in ossifying fasciitis, and S-100, CD34, H-caldes n and CK in ossifying myositis were negative. The immunophenotype of ossifying fasciitis was the same as that reported in the literature. USP6, also known as TRE17, is the encoding gene of ubiquitin-specific PeptiDase6, which is mainly involved in the ubiquitination and transport of cargo protein [11]. Currently, USP6 gene rearrangement has been found in nodular fasciitis, ossificomyositis, cranial fasciitis, aneurysmal bone cyst, and cellular-rich tenosynovial fibroma [12,13,14,], which is known as USP6-induced tumor [15]. Such lesions have long been considered as reactive changes. However, the presence of repeated USP6 gene rearrangement supports its tumor characteristics. In addition to the similar molecular background, their clinicopathological features also have certain similarities, such as a tendency to self-limited growth and relapse. The rate is low, and there is fiber/myofibroblast proliferation and may be accompanied by bone-like tissue formation. In this study, USP6 gene rearrangement test was performed and USP6 gene break was detected. USP6 gene rearrangement test can be used as a useful method to distinguish ossifying fasciitis from other similar lesions. Ossifying fasciitis is a classic pseudosarcomatous lesion, which is clinically manifested as a rapidly growing mass. Imaging cortical destruction and periosteal reaction can be seen, pathological cell density and active proliferation, Ki-67 proliferation activity is high, imaging and pathological examination are more likely to be misdiagnosed as malignant mesenchymal tumors, especially parosteosarcoma or extraosseous osteosarcoma. ① Parosteosarcoma: it usually occurs in young adults and is more common in the epiphyses of long diaphysials, and rarely occurs in the fingers and toes.

Imaging findings show that the boundary of parosteosarcoma is unclear, and the tumor can wrap around the involved bone when enlarged. "Line sign" can be seen in typical parosteosarcoma X, and bone destruction can occur near the bone cortex; fibroskeletal pseudotumor has clear edges and does not grow around the bone, and bone destruction rarely occurs. Endoscopic paraspecial osteosarcoma is

composed of bone trabeculae and fusiform fibroblasts that tend to be arranged in parallel. Fibroblasts have only mild atypia, few mitotic images can be seen, and MDM2 gene amplification can be seen. Diagnosis should be combined with medical history and imaging examination. ② Extrasosseous osteosarcoma: It is a highly malignant osteosarcoma, mainly occurring in older patients, mostly in the proximal extremities of the lower limbs. The tumor cell atypia is obvious, pathological nuclear mitosis can be seen, and the osteoid tissue is thin grid or lace-like, with no surrounding osteoblastic lining. ③ Periosteal osteosarcoma: moderate malignant osteosarcoma, usually occurs in the long bone shaft, is chondrogenic osteosarcoma, but there is obvious neoplastic osteoid tissue formation, the cartilage is generally grade II-III chondrosarcoma, a small number of ossifying fasciitis can appear cartilage, but the cartilage is not deformed. ④ Paracortical singular osteochondroplasia (Nora disease) : It usually occurs near the bones of the hands and feet and is more common in young people. The lesions are composed of spindle cells, bone and cartilage, and the histological morphology overlates with ossifying fasciitis. Some scholars believe that Nora disease is a state between ossifying fasciitis and acquired osteochondroma . Differentiating the disease by imaging, Nora's disease is associated with the bone surface and ossifying fasciitis is located in the parosteal soft tissue. ⑤ ossifying myositis: Both are characterized by nodular fasciitis like fibroblast/myofibroblast proliferation, accompanied by osteoid tissue formation with varying maturity, and COL1A1-USP6 fusion genes can appear. Myositis ossificans usually occurs in the extremities and trunk at a deep location, and the typical zonal phenomenon can be seen under the microscope, that is, the disordered spindle cells in the center of the lesion gradually transition to the peripheral bone components, while fasciitis ossificans tends to occur in soft tissues, without obvious zonal phenomenon, and the disordered distribution of bone-like tissues. Studies have shown that bone Myositis chemosificans and fasciitis ossificans have similar clinicopathological features and molecular genetic changes, and the differences between the two are very subtle, which may only be the difference in the location of the lesions .

## 5. Conclusions

Ossifying fasciitis is a benign lesion with a good prognosis. Most cases can be cured after complete resection, and a few cases can recur. No metastasis or malignant transformation has been reported. The ossifying fasciitis reported in this paper did not recur after local resection for 2 months.

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