

Case Report

Articular nodular fasciitis of the right shoulder joint: report of an unusual case with focus on immunohistochemical differential diagnosis

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Abstract: The mesenchymal lesion nodular fasciitis (NF) can affect various sites of the body but usually arises in subcutaneous tissue or occasionally skeletal muscle. NF is not commonly known to arise in joints, and articular NF is extremely rare. Herein, we present a case of a 54-year-old woman with articular NF. No sign of recurrence was observed after surgical piecemeal removal with a suspected positive surgical margin. In our case, a differential diagnosis of NF, desmoid-type fibromatosis, and low-grade myofibroblastic sarcoma was considered. Stromal hyalinization, a characteristic of articular NF, made the diagnosis somewhat difficult, although typical NF morphology was present. Immunohistochemical analysis of α -smooth muscle actin, desmin, β -catenin, and protein gene product 9.5 expression along with close morphological examination provided a reliable distinction.

Keywords: Articular nodular fasciitis, shoulder joint, immunohistochemistry

Introduction

Nodular fasciitis (NF) is a type of mesenchymal lesion that can affect various sites of the body, although it usually arises in subcutaneous tissue or occasionally in skeletal muscle [1-4]. NF is not commonly known to arise in joints, and articular NF is extremely rare [5, 6]. Clinically, NF is characterized by a rapidly (few weeks' duration) growing subcutaneous mass that may exhibit spontaneous regression [1-4]. Histologically, NF occasionally mimics sarcoma because of its high cellularity and mitotic rate, possibly leading to an inappropriate diagnosis [7].

Recently, approximately 90% of NFs were found to harbor rearrangements of the *USP6* gene, and the novel *MYH9-USP6* fusion accounted for two thirds of these rearrangements [8]. Although rearrangements of the *USP6* gene can be detected using fluorescence in situ hybridization or reverse transcription-polymerase chain reaction, these techniques cannot be easily applied in routine pathological prac-

tice. An immunohistochemical method for differentiating between NF and its mimics should be first considered.

Herein, we present the case of a 54-year-old woman with articular NF and an immunohistochemical approach for differentiating articular NF from its morphological mimics such as desmoid-type fibromatosis (DF) [9] and low-grade myofibroblastic sarcoma (LGMS) [10].

Clinical summary

A 54-year-old Japanese woman visited an outpatient clinic because of a lump on the ventral side of her right shoulder that was causing shoulder pain and decreased range of motion. The patient reported that she had not noticed the mass on her shoulder until approximately 2 months before presentation. Soon after detection, she noticed that the mass increased in size and began to feel right shoulder pain; she reported no fever, fatigue, numbness, or other specific complaints. During a physical examination, a 5-cm x 6-cm solid mass without mobility

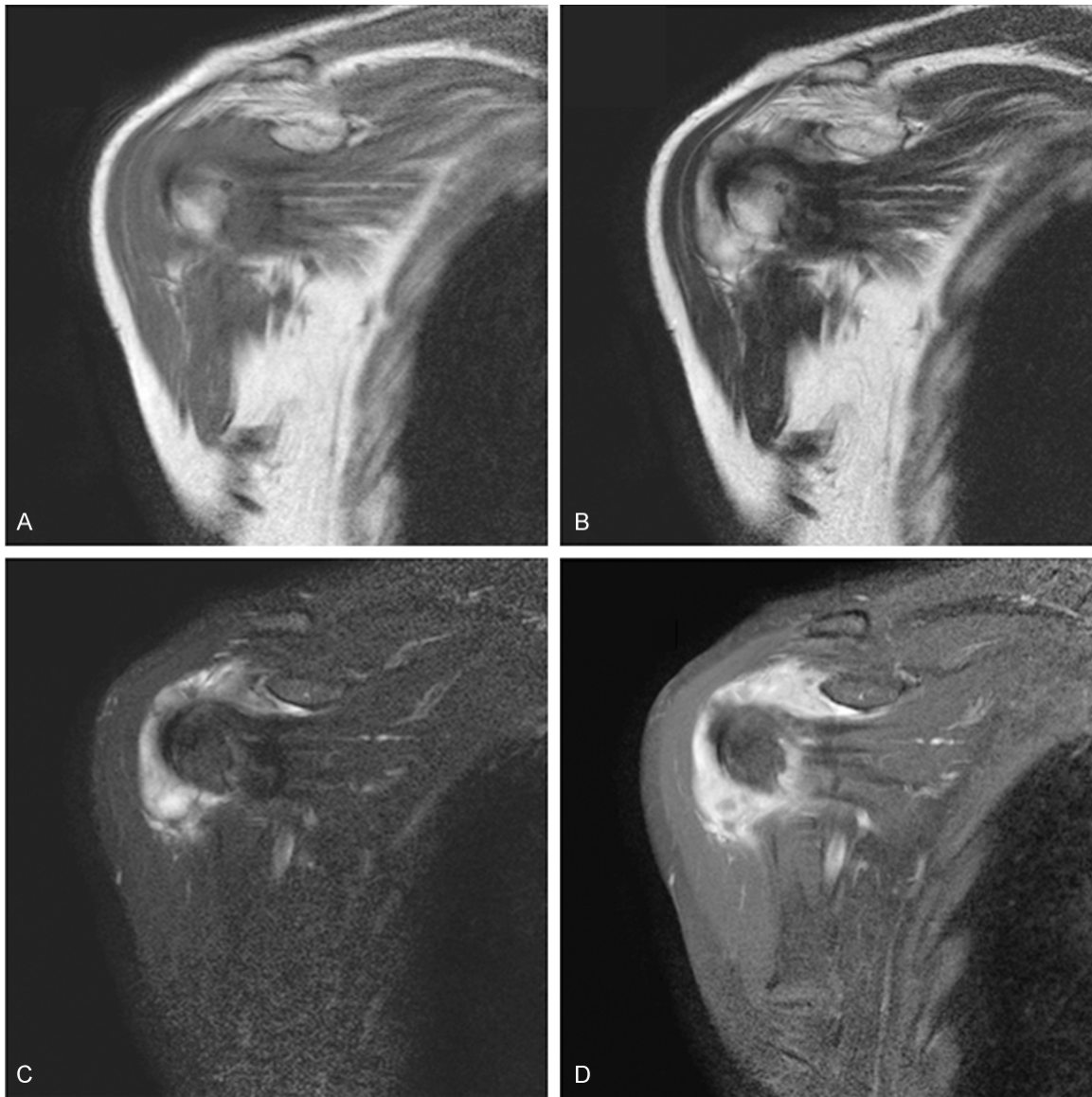


Figure 1. Magnetic resonance imaging of the mass at the right shoulder joint. A. T1-weighted imaging showed low signal intensity. B. T2-weighted imaging revealed high signal intensity. C. T2-weighted fat-suppressed imaging displayed pronounced high signal intensity. D. Contrast enhancement was observed with T1-weighted fat-suppressed imaging.

or tenderness was found on the ventral side of her right shoulder. The range of shoulder joint motion, including flexion, abduction, and external rotation, was limited. X-ray of the right shoulder did not find any abnormality. Magnetic resonance imaging revealed an irregularly shaped mass at the right shoulder joint. The articular mass exhibited relatively low signal intensity on T1-weighted images (**Figure 1A**), high signal intensity on T2-weighted images (**Figure 1B**), and pronounced high signal intensity on T2-weighted fat-suppressed images (**Figure 1C**). Contrast enhancement was observed on T1-weighted fat-suppressed images

(**Figure 1D**). The patient was subsequently hospitalized. Shoulder arthroscopy was performed and the soft-tissue mass was resected in a piecemeal manner. Her postoperative course was uneventful, and she recovered shoulder joint motion. She has remained recurrence-free for 3 months.

Pathological findings

The surgical specimens were removed in a piecemeal manner. Given the method of lesion removal, the surgical margin was considered to be positive.

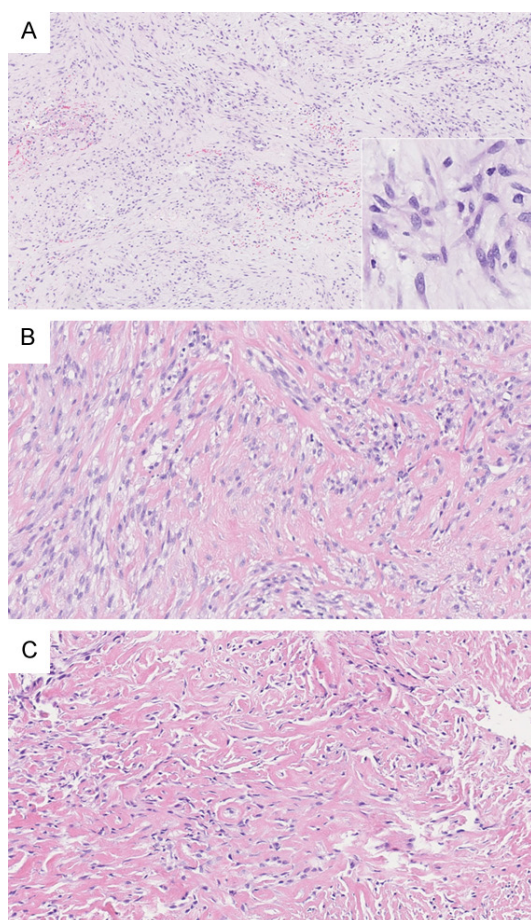


Figure 2. Microscopic findings. A. Lesional cells were observed to proliferate haphazardly or form fascicles within a myxoid background, accompanied by focal areas of extravasated red blood cells; inflammatory cell infiltration was modest (40× magnification). Inset: lesional cells were spindle-shaped with weakly eosinophilic cytoplasm and focally presented a tissue-culture-like growth pattern; nuclei exhibited mild enlargement without obvious atypia (600×). B. Older changes accompanied by collagen fiber deposition were observed (200×). C. The oldest part of the lesion contained abundant hyalinized collagen fibers (200×).

In fact, microscopically, nearly the entire areas of all specimens contained lesional cells, and remaining lesional cells were suspected. Lesional cells were observed to proliferate haphazardly or form fascicles within a myxoid background, accompanied by focal areas of extravasated red blood cells; inflammatory cell infiltration was modest (**Figure 2A**). The lesional cells exhibited a spindle shape with weakly eosinophilic cytoplasm and presented focally in a tissue-culture-like growth pattern; their nuclei exhibited mild enlargement without obvious

atypia (**Figure 2A**, inset). Two mitotic figures per 10 high-power fields were detected in the most affected area. In some areas, older changes accompanied by the deposition of collagen fibers (**Figure 2B**) were observed along with the oldest part of the lesion, which contained abundant hyalinized collagen fibers (**Figure 2C**).

Immunohistochemistry (IHC) revealed that the spindle cells were positive for α -smooth muscle actin (SMA; 1A4, 1:100; Dako, Glostrup, Denmark) (**Figure 3A**) and negative for desmin (D33, 1:100; Dako) (data not shown). β -catenin (β -Catenin-1, 1:100; Dako) positivity was observed in the cytoplasm but not in the nuclei (**Figure 3B**). Protein gene product (PGP) 9.5 (13C4, 1:50; Abcam, Cambridge, UK) expression was observed in the spindle cells (**Figure 3C**). A stain for anaplastic lymphoma kinase 1 (ALK1, 1:25; Dako) was negative (data not shown).

A diagnosis of articular NF was rendered after considering the IHC results together with the morphological findings.

After making the diagnosis, additional IHC using matrix metalloproteinase 3 (EP1186Y, 1:100; Epitomics, Burlingame, CA) was performed and spindle cells were positive for it (**Figure 3D**).

Discussion

The differential diagnosis of articular NF in the shoulder joint included two types of lesions: spindle cell lesions occurring near the joint and lesions with close morphological similarity to NF, which is not usually seen near the joint. Examples of the former type include fibroma of the tendon sheath [11] and juxta-articular myxoma [12]. Examples of the latter type include DF [9], LGMS [10], and inflammatory myofibroblastic tumor [13]. As fibroma of the tendon sheath nearly always occurs in the hands [11] and juxta-articular myxoma nearly always occurs in the knee [12], both of these lesions could be almost excluded. Given the modest inflammatory background along with ALK negativity, this case did not match the definition of an inflammatory myofibroblastic tumor [13, 14]. The remaining differential diagnosis included DF and LGMS. The typical IHC patterns of NF, DF, and LGMS are summarized in **Table 1**; α SMA expression is common feature among all

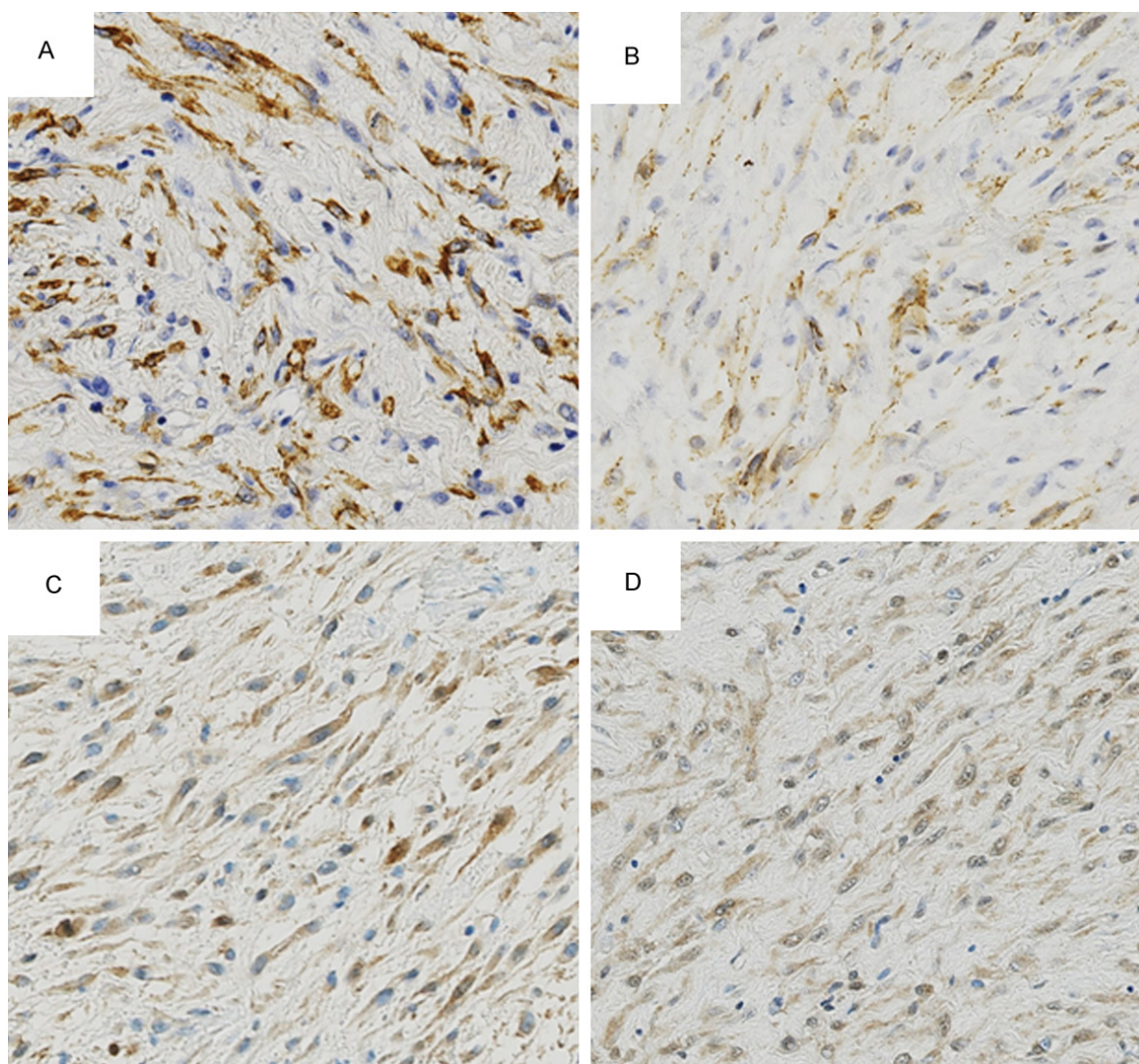


Figure 3. Immunohistochemical findings. A. Positivity for α -smooth muscle actin (400 \times magnification). B. Positivity for β -catenin was observed in the cytoplasm but not in the nuclei (400 \times). C. Positivity for protein gene product 9.5 (400 \times). D. Positivity for matrix metalloproteinase 3 (400 \times).

Table 1. Typical immunohistochemical characteristics of nodular fasciitis (NF), desmoid-type fibromatosis (DF), and low-grade myofibroblastic sarcoma (LGMS)

	α SMA	Desmin	nuclear β -catenin	PGP 9.5
NF	+	-	-	+
DF	+	-	+	NA
LGMS	+	+	-	NA

NA: reliable data is not available.

three lesions [10, 15]. DF usually presents as proliferating spindle cells on a collagenous background with nuclear β -catenin expression; the myxoid background observed in this case is

not usually encountered except for cases in the mesentery [5, 9, 16, 17]. DF usually does not express desmin, similar to NF [15]. One noticeable characteristic of articular NF in this case that introduced possible confusion regarding DF was stromal hyalinization, which could be attributed to the longer clinical history prior to surgery when compared to NF at other sites (history range of articular NF: 2 months to 1 year) [5]. LGMS usually comprises spindle cells with more hyperchromatic nuclei and higher cellularity than NF, and LGMS lesions tend to express α SMA and desmin [10]. Unlike NF, some cases of LGMS may unexpectedly express nuclear β -catenin [17]. Last but not least, PGP9.5, a known neuron- and neuroendocrine-

specific ubiquitin carboxyl terminal hydrolase, is expressed in NF [18] and other mesenchymal tumors, although this expression is possibly aberrant [19]; no reliable data is available for DF and LGMS.

From a genetic viewpoint, an important difference between NF and DF involves the expression pattern of genes related to inflammation and remodeling of the extracellular matrix. NF is associated with a more elevated expression of genes encoding proteases that participate in extracellular matrix degradation, such as matrix metalloprotease 1, 3, 9, and 13 [20]. Recently, approximately 90% of NFs were found to harbor rearrangements of the *USP6* gene [8]; *USP6* protein participates in inflammatory signaling and induces the expression of matrix metalloproteases through the activation of NF- κ B, a transcription factor involved in inflammation [21]. In contrast, DF exhibits increased expression of genes encoding members of the TGF- β signaling pathway [20]. TGF- β promotes fibroblast/myofibroblast proliferation and extracellular matrix protein synthesis [22, 23]. These signaling pathway differences between NF and DF could explain the respective myxoid and collagenous backgrounds typical of these lesions.

Articular NF tends not to recur, although the number of cases has been limited [5]. In our case, the surgical margin was considered positive, but no sign of recurrence was observed. However, careful follow-up is still required because of the lack of proof regarding the biological nature of articular NF.

In conclusion, we have presented an extremely rare case of articular NF. In contrast to DF, *USP6* gene rearrangement leads to matrix metalloprotease upregulation and extracellular matrix degradation in NF. However, articular NF in particular tends to exhibit stromal hyalinization in addition to typical morphological features, thus rendering differential diagnosis somewhat difficult. For this differential diagnosis, IHC was a useful ancillary method along with close morphological examination.

Disclosure of conflict of interest

None.

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