

Acral Myxoinflammatory Fibroblastic Sarcoma: Cytopathologic Findings on Fine-Needle Aspiration

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Key Words

Fine-needle aspiration · Cytopathology · Sarcoma

Abstract

Background: Acral myxoinflammatory fibroblastic sarcoma (AMFS) is a rare low-grade sarcoma with somewhat unique morphologic characteristics. While recurrences are relatively common, distant metastases are infrequent. Cytopathologic descriptions of AMFS are limited, prompting the current study. **Methods:** A retrospective review was performed at two tertiary-care hospitals, and 3 patients with this diagnosis were identified. The cytopathologic and clinical features were reviewed. The following clinical data was collected for each case: age, gender, site of lesion, treatment, and follow-up information. **Results:** Pertinent cytologic features included large atypical epithelioid cells with occasional macronucleoli and lipoblast-like features in a background of bland spindle cells, myxoid stroma, and inflammation. All patients presented with acral mass lesions. Metastatic disease to an inguinal lymph node was found in 1 patient. **Conclusions:** AMFS is a low-grade sarcoma which shows some characteristic cytologic features. However, due to the presence of occasional bizarre and pleomorphic giant cells, there can be overlap with higher-grade sarcomas, and correlation with histology, immunohistochemistry, and imaging are required to make this diagnosis.

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Introduction

Acral myxoinflammatory fibroblastic sarcoma (AMFS) is a rare low-grade sarcoma first described by two groups of investigators around 1998 under several names including: ‘inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg-like cells’, and ‘inflammatory myxoid tumor of the soft parts with bizarre giant cells’ [1, 2]. The World Health Organization describes AMFS as a ‘unique low-grade sarcoma with myxoid stroma, inflammatory infiltrate, and virocyte-like cells that predominately involves the hands and feet’ [3]. There are over 100 reported cases of this characteristically painless tumor that shows ill-defined borders and involves the subcutaneous/dermal tissue of distal extremities [4–9]. Despite the name, AMFS has also been reported in the legs and arms [1]. Cases have been reported over a wide age range; however, the typical presentation is in the fourth to sixth decade of life, with no gender predilection. While recurrences are relatively common (20–30%), distant metastases are infrequent (3–5%) [1, 2]. The clinical differential includes the more commonly encountered ganglion cyst, tenosynovitis, or giant cell tumor of the tendon sheath [3, 4, 7]. The greatest importance of this lesion is to distinguish it from a more aggressive sarcoma, as AMFS is characterized by often bizarre cytologic atypia. Numerous large atypical epithelioid and spindle cells are present with

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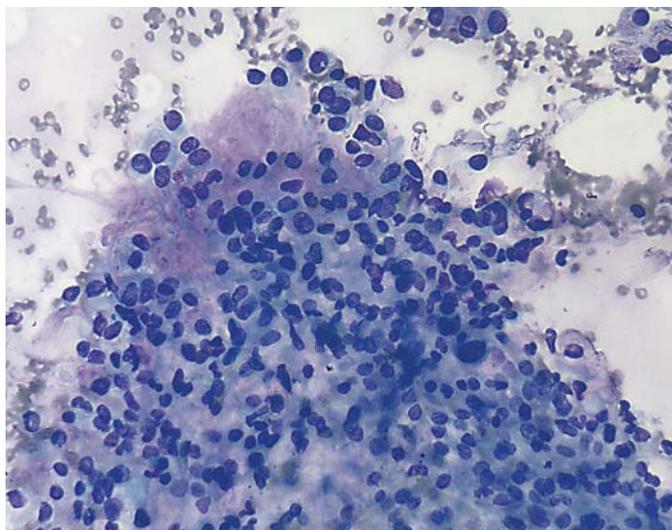


Fig. 1. AMFS. FNA. A tissue fragment of neoplastic cells with uniform, round to oval nuclei embedded in a prominent loose myxoid stroma. Diff-Quik stain. $\times 200$.

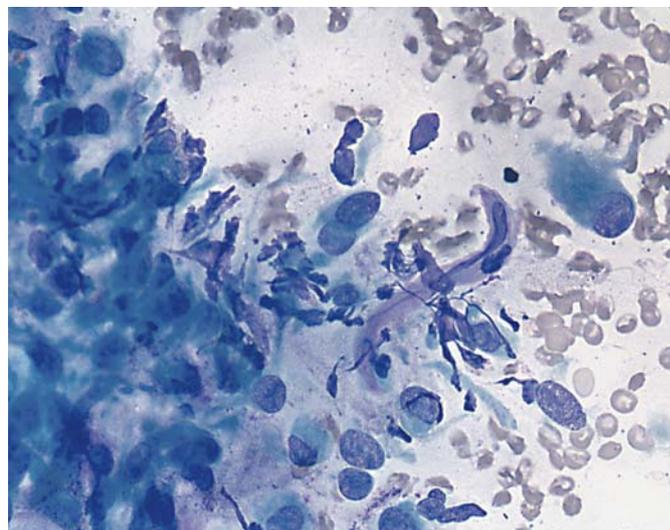


Fig. 2. AMFS. FNA. Malignant cells with round to occasionally spindled nuclei. Also evident is an eccentric nuclear placement of the epithelioid cells, prominent nucleoli, and focal anisonucleosis. Diff-Quik stain. $\times 400$.

vesicular nuclei and macronucleoli in a prominent myxoid matrix with marked inflammation [7, 8, 10]. Prior work has described the management, differential diagnosis, and immunohistochemical features of this entity. This study was designed to focus on cytologic specimens of AMFS from two institutions in an effort to describe the numerous cytologic features and potential pitfalls of this diagnosis.

Methods

A retrospective search of all cytologic cases of AFMS from the previous 20 years was performed at 2 major tertiary-care academic institutions (Johns Hopkins and Ohio State). A total of 3 cases of AMFS were retrieved, all material reviewed, and cytomorphologic features analyzed. Material was obtained by FNA performed under radiologic guidance using a 22-gauge needle, and direct smears were prepared and stained with Diff-Quik and Papanicolaou methods. The following clinical data was collected for each case: age, gender, site of lesion, treatment, and follow-up information.

Results

Patient 1

A 40-year-old female presented with a mass on the right foot. An ultrasound-guided FNA was performed and the diagnosis of a 'spindle cell neoplasm' was rendered (similar diagnosis made in each case). She under-

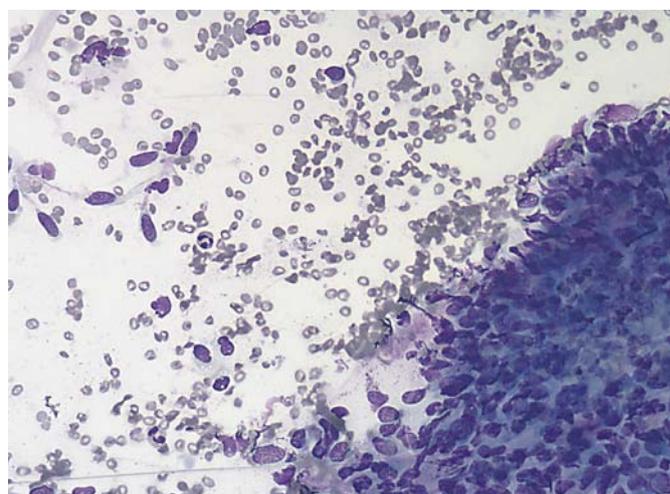


Fig. 3. AMFS. FNA. A tightly cohesive tissue fragment is present. Also seen is a more spindled appearance of the malignant cells with fine wispy cytoplasmic processes. Diff-Quik stain. $\times 200$.

went local resection and has not developed recurrence or metastasis with 4 years of follow-up. Prominent cytologic features (fig. 1–3) included hypercellularity comprising tissue fragments of varying sizes and some single cells. The predominant cytologic pattern was a rather uniform neoplastic cell population with round to oval nuclei. Scattered among these tissue fragments were

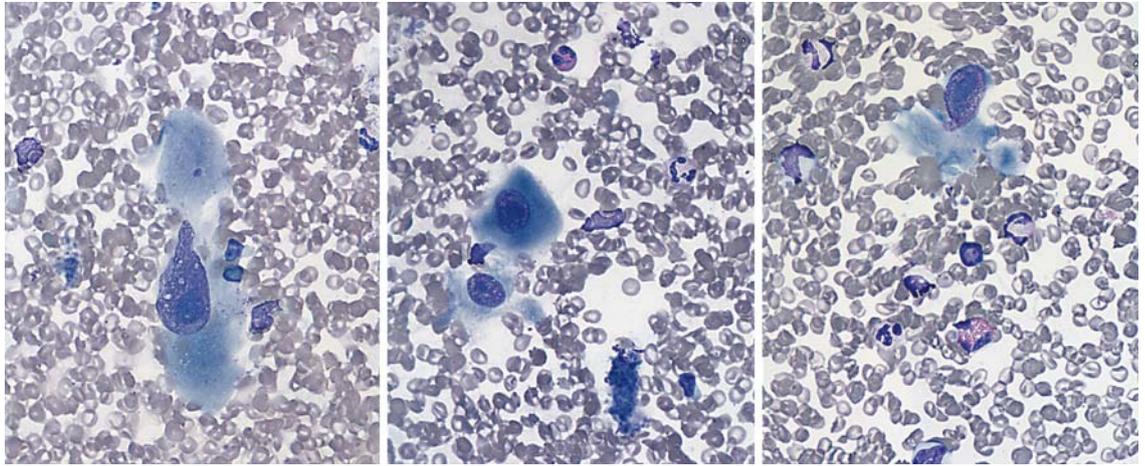


Fig. 4. AMFS. FNA. Pleomorphic and bizarre giant cells with fragile cytoplasm, large nuclei, and macronucleoli resembling R-S or ganglion-type cells. Diff-Quik stain. $\times 400$.

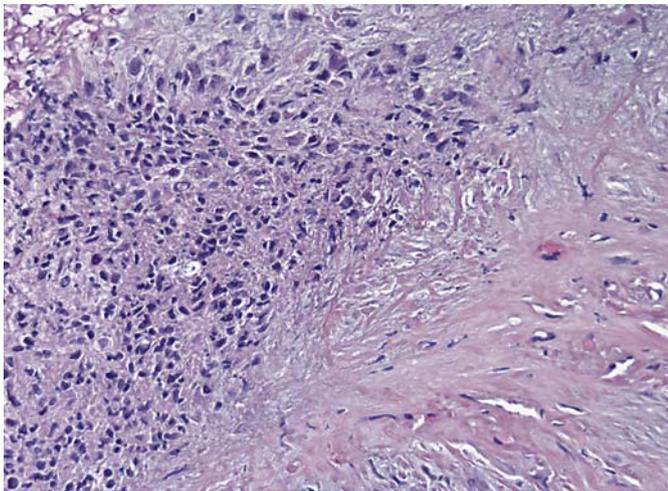


Fig. 5. AMFS. Core biopsy. Round to oval malignant cells as well as scattered large, hyperchromatic epithelioid cells are seen associated with myxoid stroma and hyalinized collagen. H&E stain. $\times 200$.

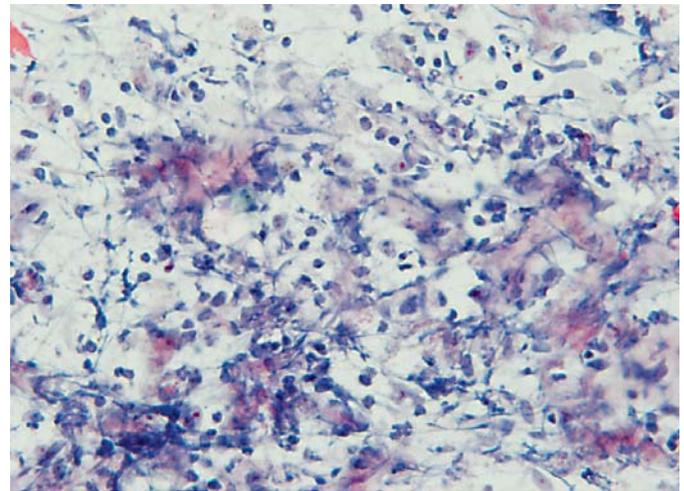


Fig. 6. AMFS. FNA. Prominent myxoid matrix and inflammatory cells. Pap stain. $\times 200$.

large irregular and pleomorphic epithelioid cells with poorly delineated cytoplasm, eccentrically placed nuclei, and macronucleoli. Also observed were occasional lipoblast-like cells in a myxoid background, spindle cells with bipolar cytoplasmic extensions, and bizarre giant cells with pleomorphic macronucleoli mimicking Reed-Sternberg (R-S) or ganglion type cells (fig. 4). Histologic sections of the tumor demonstrated a multinodular growth pattern with round to oval malignant cells displaying mild to moderate pleomorphism and occasional large and irregular hyperchromatic epithelioid cells

(fig. 5). Foci of myxoid stroma as well as hyalinized collagen were readily apparent.

Patient 2

A 60-year-old male presented with a mass on the right ankle. He underwent a below-the-knee amputation and has not developed recurrence or metastasis with 7 years of follow-up. Prominent cytologic features included an inflammatory background composed of lymphocytes and neutrophils. In contrast to patient 1, there was a minimal amount of myxoid stroma. Similar to patient 1, large

atypical epithelioid cells were present mimicking R-S cells, and cytologically bland spindle cells with ovoid to elongated nuclei were noted.

Patient 3

A 70-year-old male presented with a recurrent mass on the right lower leg. He underwent local resection with aspiration and was found to have metastatic disease in an inguinal lymph node 1 year later. Following resection of the inguinal node, the patient has been disease-free for 2 years. Prominent cytologic features included an abundant amount of myxoid stroma (fig. 6) with cytologically bland spindle cells, rare R-S like cells, and a minimal inflammatory infiltrate.

Discussion

The findings of our study correlate with previously reported cytologic descriptions, and should assist in differentiating AMFS from other lesions with potentially overlapping cytology. The classic cytologic features of AMFS include myxoid material, spindle cells with bipolar extensions, epithelioid cells with extracellular matrix, ganglion/lipoblast-like cells, and an inflammatory infiltrate [11]. Further, our clinical follow-up illustrates the propensity of AMFS to manifest local recurrences, and occasionally distant metastases including lymph node involvement [4, 5, 8, 10].

The cytologic differential is broad and includes both benign and malignant neoplasms. The clinical differential may include long-standing infections or inflammatory conditions such as tenosynovitis; however, these would be readily excluded upon cytologic review [6, 12]. Location is unhelpful in excluding other lesions, and although AMFS rarely occurs in proximal/axial sites, the converse is not true as numerous soft tissue neoplasms occur in acral locations.

The main cytologic differential of AMFS includes:

- (1) Myxofibrosarcoma (myxoid malignant fibrous histiocytoma): while both tumors involve the dermis and subcutaneous tissue, myxofibrosarcoma rarely involves acral sites. AMFS shows a considerably lower proliferation index and also contains ganglion-like cells with larger amounts of inflammation [11]. Curvilinear blood vessels with alternating fibrosclerotic and myxoid areas seen in myxofibrosarcoma are often best appreciated on histologic sections [7, 13].
- (2) Fibromyxoid sarcoma: contains little to no inflammation relative to AMFS [11].

(3) Myxoid liposarcoma: while AMFS contains lipoblast-like cells, cytoplasmic vacuoles present in AMFS contain mucin rather than fat [6]. AMFS also contains spindle cells with bipolar cytoplasmic extensions [11].

(4) Inflammatory myofibroblastic tumor (IMT): AMFS contains spindle and epithelioid cells with marked atypia precluding a diagnosis of IMT [8].

The immunohistochemical features of AMFS are relatively nonspecific and have been reported to include: +vimentin, +CD68, +smooth muscle actin, +CD34, +keratin (variable), Ki-67 < 5%, and +EGFR [6, 8]. Strong keratin expression would favor epithelioid sarcoma, while CD15+ and CD30+ large atypical cells would be consistent with Hodgkin lymphoma [13].

The cytogenetic and ultrastructural features have also been previously studied. Reciprocal translocations at t(1;10)(p22;q24), as well as loss of chromosomes 3 and 13, have been reported in AMFS [12, 14]. Additional abnormalities of chromosomes 7, 8, and 13 have been identified [4, 15]. The ultrastructural features confirm fibroblastic derivation with prominent rough endoplasmic reticulum, mitochondria, and intermediate filaments [10, 16].

Treatment with resection and wide margins has been suggested; if margins cannot be obtained amputation may be considered [6]. Radiation is commonly administered either pre-, intra-, or postoperatively [5]. Postsurgical follow-up at 4- to 6-month intervals with evaluation of the primary site and systemic imaging have been recommended [6].

In summary, we have presented a cytologic case series of a rare low-grade sarcoma which may show overlapping features with more common, higher-grade, sarcomas. While the diagnosis may be favored on cytologic grounds in the appropriate clinical context, correlation with immunohistochemistry, histology, and imaging studies should be included given the significant implications for patient management.

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