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CASE REPORT

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Acral myxoinflammatory fibroblastic sarcoma with unique clonal chromosomal changes

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Abstract Acral myxoinflammatory fibroblastic sarcoma is a rare tumor of the distal extremities. We present the hitherto unreported karyotypic abnormalities of this new entity. The tumor presented as a mass in the dorsum of the foot in a 53-year-old woman and showed the typical virocyte-like and lipoblast-like cells in a myxoid and inflammatory background. Cytogenetic analysis revealed a complex karyotype with a reciprocal translocation t(1;10) (p22;q24) in addition to the loss of chromosomes 3 and 13. Fluorescence in situ hybridization with the 769E11YAC and BAC 31L5 and 2H23 probes showed the breakpoint to be located proximally to BCL10 and distally to GOT1 genes on chromosomes 1p22 and 10q24, respectively. The presence of these clonal chromosomal changes supports the neoplastic nature of acral myxoinflammatory fibroblastic sarcoma and underscores that it represents a separate entity.

Keywords Acral myxoinflammatory fibroblastic sarcoma · Chromosomal changes

Introduction

Mesenchymal tumors of the foot are relatively rare and most tumefactions are non-neoplastic in nature. Ledderhose's disease, Kaposi-sarcoma, and synovial sarcoma are the most frequently occurring cellular spindle cell tumors of the plantar foot. Ganglion cyst, tendinous xanthoma, and giant cell tumors of the tendon sheath are more frequent on the dorsum of the foot [2]. Recently, Montgomery et al. described an unusual lesion of the distal extremities, characterized by large atypical cells, myxoid areas, and an inflammatory background [11]. The descriptive term "inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg-like cells" was proposed. Almost simultaneously, Meis-Kindblom et al. described a similar tumor for which the appellation "acral myxoinflammatory fibroblastic sarcoma" was chosen [7]. In the very same year, Michal reported an "inflammatory myxoid tumor of the soft parts with bizarre giant cells", which basically corresponded to the same entity [6]. In this report, we present hitherto unreported and unique chromosomal changes in this rare tumor, thus supporting its neoplastic nature and the fact that it represents a separate entity.

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Clinical history

A 53-year-old white female had noticed a swelling of the dorsum of the right foot for 5 years. She consulted a surgeon 1 year earlier, because the tumor was slowly growing. Upon physical examination, there was a soft, ill-defined, tender mass extending from the base of the toes to the ankle and to the lateral plantar foot. On the lateral side of the foot, some ecchymoses were seen. Muscle and tendon activity were normal.

Laboratory investigations were noncontributory. Radiologic examination showed no abnormalities. Nuclear magnetic resonance (NMR) showed changes that were compatible with algoneurodystrophy. Based on an arteriography, an arteriovenous malformation was suggested. Subsequently, the tumor was resected. Because of the ill-defined margins and the myxoid appearance, the tumor was removed in a piecemeal fashion.

Materials and methods

The tumor was received fresh. Part of the tissue was fixed in 6% formalin and embedded in paraffin. Sections (5-μm thick) were stained with hematoxylin and eosin. In addition, immunohistochemical stains for keratin [monoclonal (mc), dilution 1/50, Biodesign, Kennebunk, Me.), desmin (mc, dilution 1/20, ICN-Cappel, Costa Mesa, Calif.), CD34 (mc, dilution 1/10, Becton-

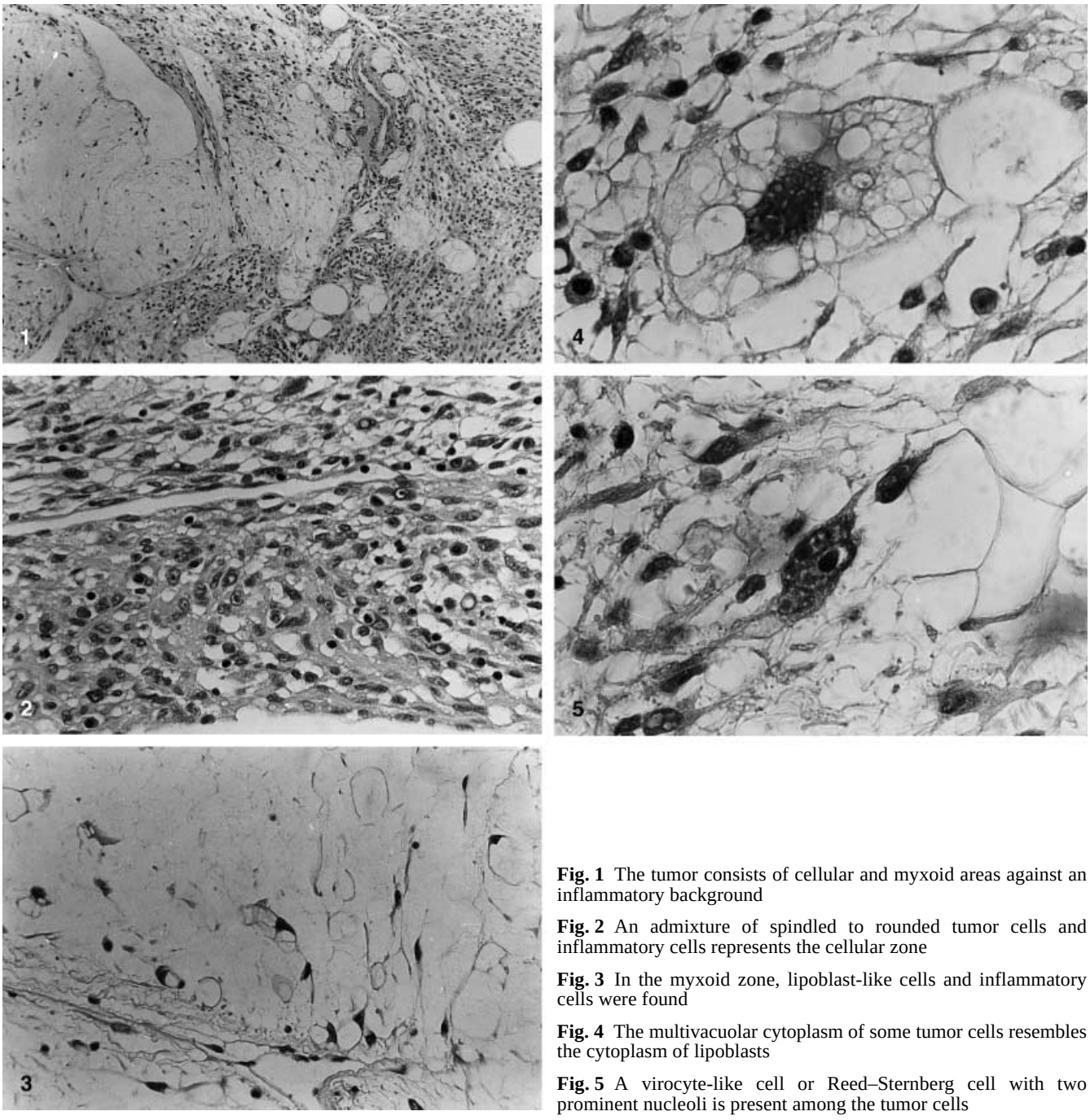

Fig. 1 The tumor consists of cellular and myxoid areas against an inflammatory background

Fig. 2 An admixture of spindled to rounded tumor cells and inflammatory cells represents the cellular zone

Fig. 3 In the myxoid zone, lipoblast-like cells and inflammatory cells were found

Fig. 4 The multivacuolar cytoplasm of some tumor cells resembles the cytoplasm of lipoblasts

Fig. 5 A virocyte-like cell or Reed–Sternberg cell with two prominent nucleoli is present among the tumor cells

Dickinson, Calif.], CD 68 (mc, dilution 1/100, Dako, Denmark), S100 protein (polyclonal, dilution 1/300, Dako) and α-smooth muscle actin (αSMA; mc, dilution 1/400, Sigma, Israel) were performed on paraffin sections using the ABC (avidin–biotin peroxidase complex) technique.

Cytogenetic analysis was performed following standard procedures. A sample of the tissue was disaggregated overnight by means of collagenase treatment and cultured for 7 days according to the method previously described [5]. Chromosome analysis was performed on G-banded metaphases. Karyotypes were described using ISCN (International System for Cytogenetic Nomenclature) criteria [3].

Pathology and laboratory findings

Pathological findings

The tumor consisted of several yellowish and gelatinous nodular fragments. The largest measured 12×4.1×2.3 cm. Some fragments were also covered with skin. The tumor showed an admixture of cellular and myxoid areas upon histological analysis (Fig. 1). The cellular areas consisted of spindled to rounded cells mixed with lymphocytes, plasma cells, mast cells, and hemosiderin-loaded macrophages (Fig. 2). Mitotic figures were rare. The blood

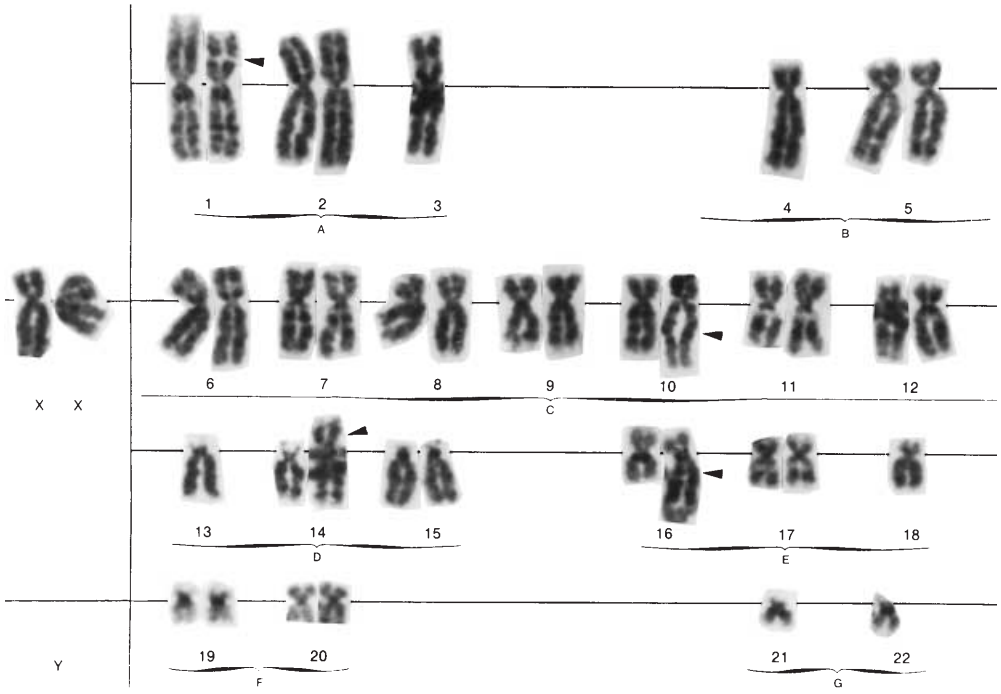

Fig. 6 Representative G-banded metaphase cell from the tumor specimen. *Arrowheads* indicate abnormal chromosomes

vessels were lined with normal endothelial cells and showed only focally a chickenwire or curvilinear pattern. In the myxoid areas, an inflammatory background was mainly noted at the edge. The cells in the myxoid stroma often showed a multivacuolated appearance, resembling lipoblasts or floret-like cells (Fig. 3 and Fig. 4). Nuclear pleomorphism was prominent, but mitotic figures were rare. Virocyte-like cells or Reed–Sternberg cells with prominent eosinophilic nucleoli and a perinuclear halo were not uncommon (Fig. 5). These cells appeared in the myxoid areas and in the cellular areas. Immunohistochemical stains showed that the tumor cells were negative for keratin, desmin, αSMA, and S100 protein. Some CD68-positive cells were present. CD34 decorated the endothelial lining of the vessels and some tumor cells.

Cytogenetic and molecular findings

A complex karyotype was revealed through the analysis of 13 metaphase cells: 39–44, XX, der (1) t (1; 10) (p22; q24) [8], del (1) (p22) [2], –3, del (3) (p11) [4], der (10) t (1;10) (p22; q24), –13, –13 [5], add (14) (p11) [3], der (13; 14) (q10; q10) [2], –16 [3], add (16) (q24) [5], –18 [5], –21 [9], –22 [6], and der (22) t (3; 22) (p11, p11) [6] (cp13; Fig. 6). Two metaphases had a normal karyotype.

For further characterization of translocation breakpoints on chromosomes 1 and 10, digoxigenin-labeled BAC clones 31L5 and 2H23, specific for the GOT1 gene (which maps to 10q24), and the biotin-labeled 769E11YAC probe, specific for the BCL10 gene (1p22), were used in fluorescent in situ hybridization analysis. For chromosome 10, BACs 31L5 and 2H23 mapped proximal to the breakpoint. The 769E11YAC probe hybridized to the homologue chromosome, 1p22, which was not involved in the translocation, and to the derivative chromosome 10, proving the breakpoint on chromosome 1p22 to be proximal to the BCL10 gene.

Discussion

Acral myxoinflammatory fibroblastic sarcoma, "inflammatory myxohyaline tumor of distal extremities with virocyte or Reed–Sternberg-like cells" or inflammatory myxoid tumor of the soft parts with bizarre giant cells, typically presents as a painless, poorly delineated, usually subcutaneous mass that characteristically but not exclusively occurs in the distal extremities. The salient histological features of the 100 previously reported cases and the present case are the inflammatory background, a prominent myxoid component, and the presence of bizarre lipoblast- and virocyte-like cells. Because of the high rate of recurrence (±48%) and a low rate of metastasis, this tumor can be regarded as a low-grade sarcoma [6, 7, 11].

From a morphologic point of view, several differential diagnoses should be kept in mind. There is a great variation depending on whether the inflammatory, myxoid, or bizarre atypical component predominates. Benign differential diagnoses include nodular fasciitis, tenosynovial giant cell tumor, inflammatory myofibroblastic tumor, and infectious lesions. These lesions also show an inflammatory component but lack the atypical, bizarre Reed–Sternberg-like and lipoblast-like cells. Malignant tumors that show some resemblance with acral myxoinflammatory fibroblastic sarcoma are myxoid liposarcoma and myxofibrosarcoma. A liposarcoma is

usually localized in a deeper anatomical level and lacks the inflammatory component. Although there could be some resemblance, myxofibrosarcoma has a propensity to occur in the proximal extremities, has a prominent curvilinear vascular pattern, and is, in its classic presentation, not an inflammatory lesion [2].

Cytogenetic analysis can be of help in discriminating acral myxoinflammatory fibroblastic sarcoma from the above-mentioned entities. Within the myxoid group of tumors, myxoid liposarcoma is associated with classical – t (12; 16) (q13; p11) – or variant – t (12; 22) (q13; p11) – translocations, while ring chromosomes, as the sole structural abnormality, or a normal karyotype appear to be present in myxofibrosarcoma [8, 12].

Furthermore, rearrangements of the short arm of chromosome 1p11–13 and, less frequently, the involvement of chromosome 16q24 are the most common changes observed in localized and diffuse forms of tenosynovial giant cell tumor [14]. Finally, only three reported cases of nodular fasciitis had clonal chromosome changes; two with the 3q21 region involvement as a possibly non-randomly associated anomaly and the third one with a more complex karyotype, including the presence of t (2; 15) (q32; q26) and loss of chromosomes 2 and 13 [1, 13, 15]. Our tumor presented a main stem line with a reciprocal translocation t(1; 10)(p22; q24) and losses of chromosomes 3 and 13 in all abnormal metaphases. The sidelines of the main clone showed a wide spectrum of other structural aberrations, including the loss of chromosome 10q24-qter material from the derivative chromosome 1; all of the latter most likely developed as a result of tumor progression.

Both 1p22 and 10q24 translocation breakpoints in the presented case of acral myxoinflammatory fibroblastic sarcoma are frequently involved in a variety of human neoplasms. Thus, the 1p22 region has previously been reported as a nonrandom site of deletions and rearrangements in malignant melanomas, squamous cell carcinomas of the head and neck, malignant mesotheliomas, esophagus and gastric adenocarcinomas, and lymphomas [4, 9]. Chromosome 10q24 changes have been frequently observed in malignant glial tumors, prostate and urinary bladder cancer, malignant melanomas, small-cell lung cancer, and T-cell lymphomas [10]. Both 1p22 and 10q24 chromosome regions carry some genes that may play an important role in carcinogenesis (namely, BCL10, GLCL, NRAS on 1p22 and MXI1, LGI1, HOX11, LYT-10, APO-1/FAS on 10q24). Nevertheless, no recurrent associations of 1p22 or 10q24 rearrangements with any specific type of soft tissue sarcoma have been reported before. This finding supports that acral myxoinflammatory fibroblastic sarcoma is a separate entity, which can be characterized both histologically and, if our karyotypic analysis will be confirmed, cytogenetically.

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