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Case Report

Pediatric Interdigitating Dendritic Cell Sarcoma and High-Grade Myxoinflammatory Fibroblastic Sarcoma: Case Reports

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Abstract

Rare soft tissue sarcomas such as interdigitating dendritic cell sarcoma (IDCS) and high-grade myxoinflammatory fibroblastic sarcoma (MIFS) are diagnostically challenging due to their rarity and overlapping histopathologic features with other neoplasms. We report two unusual cases diagnosed at the Histopathology Department, King Fahad Specialty Hospital, Tabuk, KSA. The first involved a 2-year-old male presenting with a maxillary sinus mass, an unprecedented location for pediatric IDCS. To our knowledge, this is the first reported pediatric IDCS in the maxillary sinus. Histology revealed spindle to ovoid tumor cells with variable nuclear atypia arranged in fascicles and storiform patterns. Immunohistochemistry showed positivity for S100, CD68, CD63, EGFR, and cyclin D1, confirming the diagnosis with the latter two staining results suggesting potential activation of the MAPK/ERK signaling pathway. The second case involved a 70-year-old woman with a high-grade MIFS of the lower limb. Histopathology demonstrated aggressive features, including necrosis, infiltrative growth, and high mitotic activity, with tumor cells positive for CD10 and D2-40. The IDCS patient followed an aggressive course and patient died before surgical intervention, while the MIFS patient received wide local excision with close follow-up. Both cases underscore the importance of thorough clinicopathologic correlation and immunohistochemical analysis for accurate diagnosis. Identifying rare sarcomas in unusual locations or age groups, utilizing specific immunohistochemical markers to distinguish them from histologically similar tumors, and applying precise grading are all critical for guiding prognosis and ensuring appropriate management.

Keywords: *Interdigitating Dendritic Cell Sarcoma, Myxoinflammatory fibroblastic sarcoma, Pediatric.*

Introduction

Rare soft tissue sarcomas pose significant diagnostic and therapeutic challenges due to their diverse histopathology and limited clinical data. Interdigitating Dendritic Cell Sarcoma (IDCS) is a rare, aggressive neoplasm of dendritic cells, primarily involving lymph nodes, with fewer than 200 cases reported and pediatric presentations being exceptional [1–4]. Extranodal involvement, including head and neck sites, is uncommon, and only about 18% of head and neck IDCS cases involved extranodal sites such as the brain, parotid , nasopharynx, and nasal cavity [4]. While MAPK/ERK pathway activation has been suggested, no consistent genetic alterations have been identified [5]

MIFS is another rare, predominantly low-grade, and locally aggressive malignant soft tissue tumor first characterized in 1998 [6]. High-grade variant—often referred to as dedifferentiated or high-grade component—is rare, accounting for approximately 2% of cases. It typically affects adults in the fourth to sixth decades and most often arises in the distal extremities, particularly the foot and ankle [7]. MIFS has a high local recurrence rate and rare potential for metastasis [7].

Genetic studies have identified characteristic chromosomal rearrangements involving the TGFBR3 and MGEA5 genes, which may aid in diagnosis, although molecular testing is not widely available [8].

Case reports

The reported cases were presented to King Fahad Specialist Hospital, Tabuk, Saudi Arabia. Clinical and radiological data were retrieved from the hospital information system (HIS). All immunohistochemical stains were performed on a Leica automated platform using monoclonal antibodies.

Case 1:

A 2-year-old boy presented with a rapidly enlarging, painless left facial swelling over two weeks. A contrast-enhanced computed tomography (CT) scan revealed a large, highly vascular, lytic lesion in the left maxillary sinus with destructive features and strong enhancement [Fig 1].

Incisional biopsy was performed, and an extended IHC panel covering pediatric soft tissue, histiocytic, and dendritic cell markers was applied.

Microscopic examination revealed a cellular neoplasm composed predominantly of spindle-shaped cells arranged in interlacing fascicles with whorled pattern. The tumor cells displayed elongated, vesicular nuclei with occasional nucleoli, occasional nuclear grooves with moderate amounts of eosinophilic cytoplasm and

ill-defined borders. Nuclear pleomorphism was noted, and mitotic figures were readily observed [Fig. 2]. The stroma was scant, with scattered small vascular proliferations and dispersed lymphocytes and plasma cells among the tumor cells.

Immunohistochemically, the tumor showed diffuse and strong positivity for S100 protein, cyclin D1 and EGFR . The Ki-67 proliferation index was elevated at 40–50%, indicating high proliferative activity. CD45 positivity was limited to scattered intratumoral lymphocytes. CD68 and CD163 showed scattered positive cells [Fig 3].

Markers typically associated with myogenic (SMA, Desmin, Myogenin, MyoD1), epithelial (pan-cytokeratin, EMA), melanocytic and peripheral nerve sheath (Melan A, HMB45, SOX10), follicular dendritic (CD21, CD23), histiocytic (CD1a, Langerin), and some pediatric and other sarcomas (WT-1, CD34, CD31, ERG, Pan-TRK, STAT6, CD99, FLI-1, and BCL2) were negative with appropriate controls.

The diagnosis of IDCS was confirmed through multidisciplinary pathology consultation and expert second opinion. Unfortunately, the patient's condition deteriorated rapidly, and he died two weeks after diagnosis, highlighting the aggressive nature of pediatric IDCS in atypical locations.

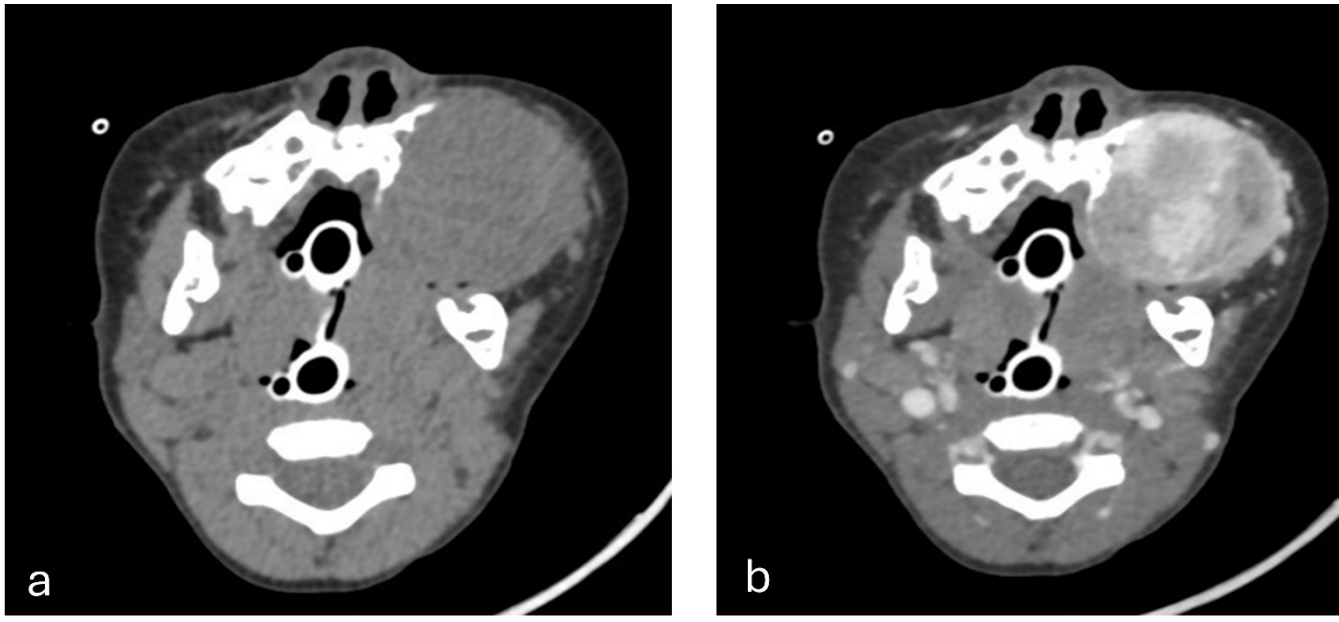

Fig 1: Axial pre-contrast CT image at the level of the maxilla

(a), axial post contrast CT image at the same level

(b) and coronal post contrast PNS CT image show contrast enhancing large soft tissue mass lesion occupying the left maxillary sinus and causing bony destruction of the maxilla.

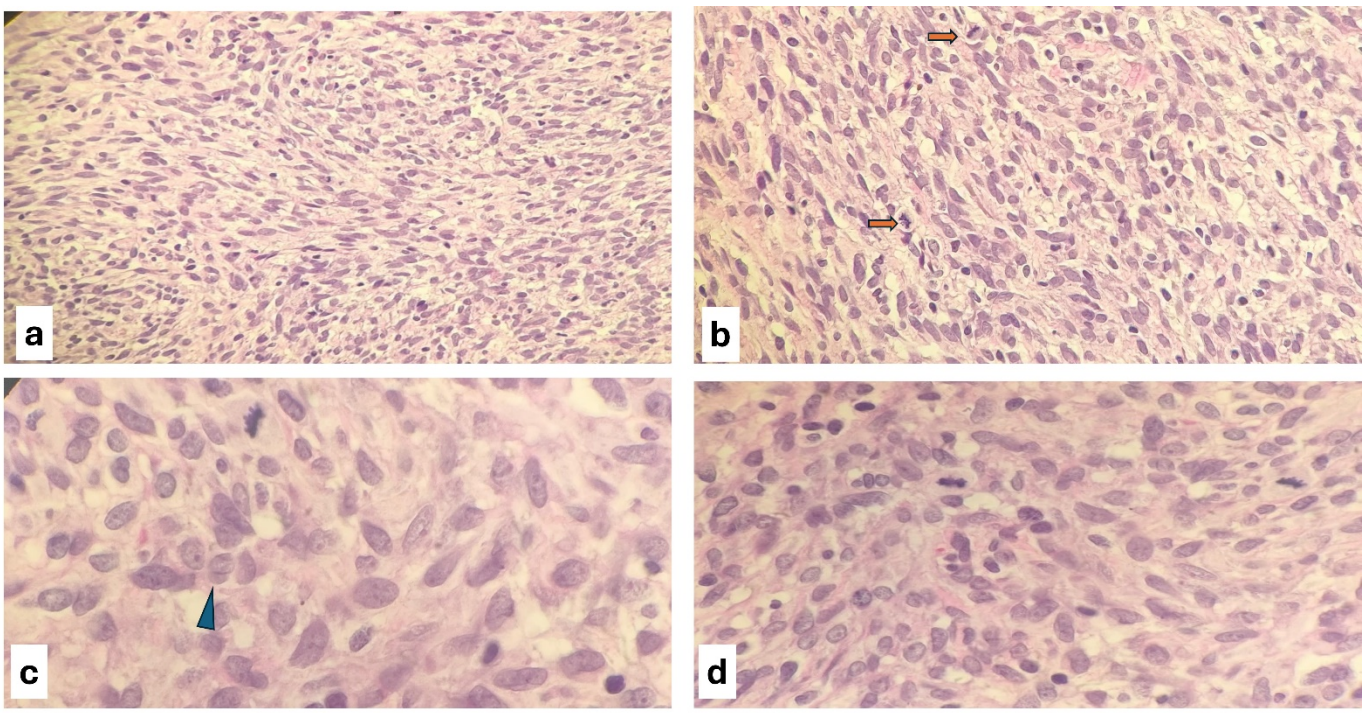

Fig 2: Hematoxylin and eosin (H&E)–stained sections of IDCS composed predominantly of spindle-shaped cells arranged in interlacing fascicles with a whorled pattern (a). Nuclear pleomorphism is present, and mitotic figures are readily observed (b, red arrows; d). The tumor cells exhibit elongated, vesicular nuclei with occasional nucleoli and nuclear grooves (c, blue arrow head) (a, b: ×200; c, d: higher magnification, ×400).

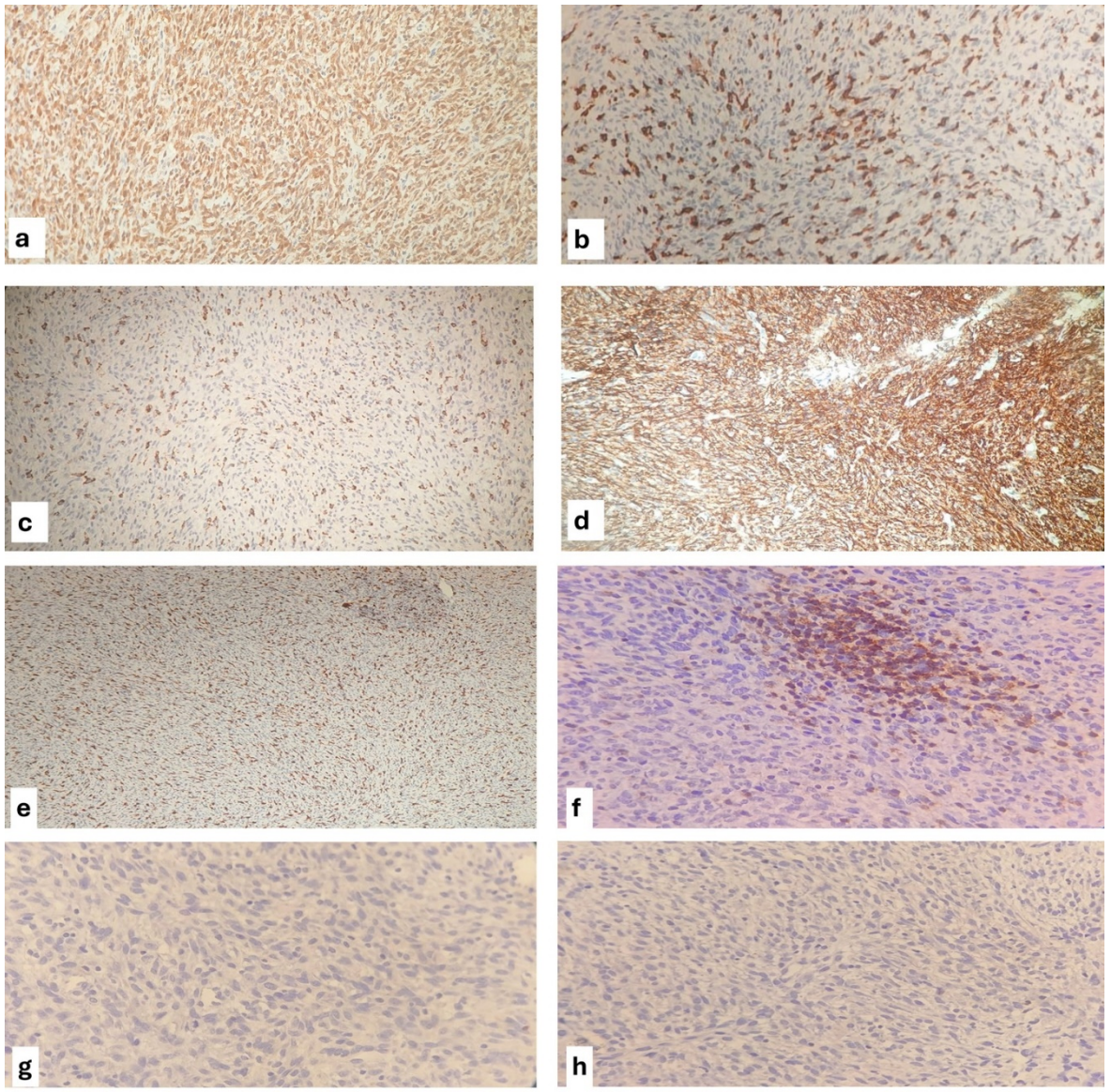

Fig 3: Immunohistochemical profile of interdigitating dendritic cell sarcoma (IDCS): (a) diffuse nuclear and cytoplasmic S100 positivity; (b) scattered CD68 positivity; (c) scattered CD163 positivity; (d) diffuse membranous EGFR positivity; (e) diffuse nuclear Cyclin D1 positivity; (f) CD45 negativity in tumor cells with positive staining in lymphocyte clusters; (g) CD1a negativity; and (h) SOX10 negativity (all ×400).

Case 2

A 70-year-old woman presented with a 3.5 cm subcutaneous mass in the left lower limb, abutting underlying muscle. Imaging showed a well-defined but infiltrative lesion.

Microscopically, the subcutaneous tumor consisted of sheets of spindle to polygonal cells with vesicular nuclei and moderate cytoplasm, admixed with larger atypical multinucleated cells resembling virocyte- or Reed–Sternberg–like forms, > 19 mitosis /10 HPF, and necrosis [Fig. 4]. The tumor shows focal skeletal muscle invasion, and a mixed inflammatory background with focal myxoid change and fibrosis. Margins were clear

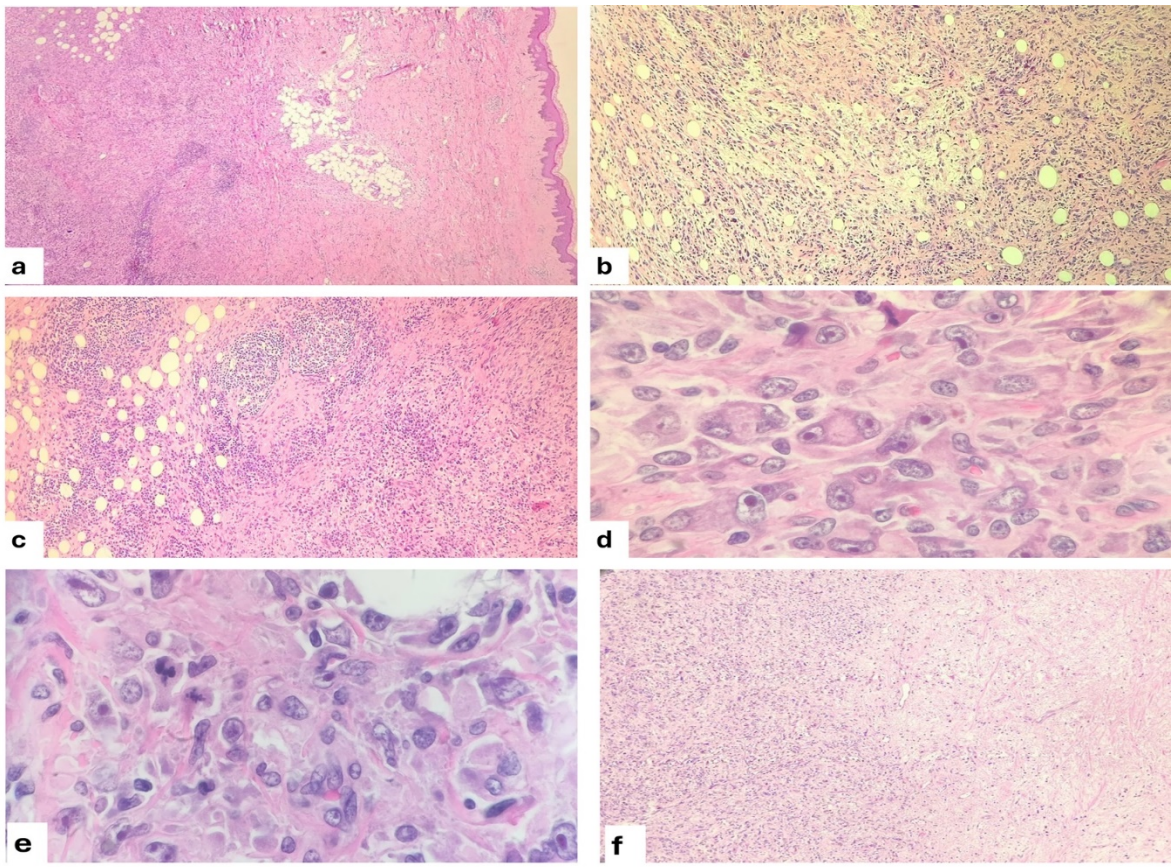

Fig 4: Hematoxylin and eosin (H&E)–stained sections of high-grade myxoinflammatory fibroblastic sarcoma: (a, ×100) tumor located in the subcutaneous tissue; (b, c ×200) neoplasm composed of sheets of spindle to polygonal cells with vesicular nuclei, moderate cytoplasm, and myxoid areas (b), with a background rich in mixed inflammatory infiltrates predominantly plasma cells and lymphocytes with lymphoid aggregates (c); (d, e, ×400) scattered larger atypical cells with prominent nucleoli, nuclear irregularities, multinucleation, and features reminiscent of virocyte-like or Reed–Sternberg–like cells (d), tumor cell pleomorphism with frequent mitoses (e); (f, ×200) necrosis evident on the right side of the field.

Immunohistochemistry showed diffuse CD10 and patchy D2-40 positivity [Fig. 5]. Tumor cells were negative for myogenic (Actin, Desmin), melanocytic (S100, SOX10), epithelial (cytokeratin), vascular (CD34, CD31), lymphoid (CD68, CD45, CD3, CD30, CD15), and other lineage-specific markers (ALK, MDM2, FLI1, TLE1, CD99, BCL2), effectively excluding a broad differential and supporting the diagnosis of high-grade MIFS.

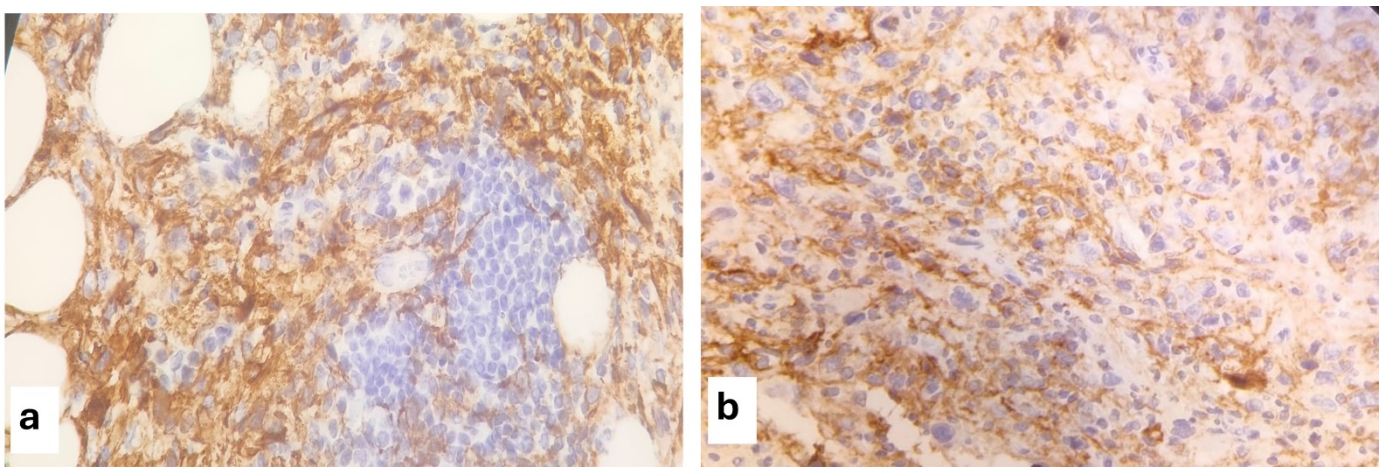

Fig 5: Immunohistochemical staining of high-grade myxoinflammatory fibroblastic sarcoma showing tumor cell positivity for CD10, sparing the infiltrating lymphocytes (a), and diffuse positivity for D240 (b) (both ×400).

Discussion

We report two rare and diagnostically challenging soft tissue sarcomas: an IDCS in a 2-year-old male involving the maxillary sinus—the first such case reported—and a high-grade MIFS in the lower limb of an adult female. These cases underscore the substantial clinical and pathological complexity of both entities.

IDCS most frequently presents in adults with a slight male predominance and commonly involves lymph nodes. It can arise de novo or less commonly in association with lymphoid malignancies such as Hodgkin or non-Hodgkin lymphoma. This suggests a potential clonal relationship or transformation in some cases [9]. Primary presentations in the head and neck remain rare, and pediatric cases are extremely uncommon [1,4]. The maxillary sinus involvement in our patient represents the first reported pediatric case at this site.

Microscopically, the tumor exhibited a storiform pattern composed of neoplastic cells with vesicular spindle to ovoid shaped nuclei and occasional nuclear grooves, consistent with the described morphological features [10].

Given the patient's young age and the tumor's unusual maxillary sinus location, a broad differential diagnosis was considered and systematically excluded using IHC: Histiocytic sarcoma was ruled out based on diffuse S100 positivity in our case. Langerhans cell sarcoma (CD1a, Langerin negative), follicular dendritic cell sarcoma (CD21, CD23 negative; CD68, CD163 positive), rhabdomyosarcoma (Desmin, Myogenin, MYO D1 negative), malignant peripheral nerve sheath tumor and melanoma (SOX10, Melan-A negative), epithelioid sarcoma (CK, CD34, ERG negative), solitary fibrous tumor (STAT6 negative), and synovial sarcoma (EMA, CD99, BCL2 negative). Other pediatric sarcomas, including Ewing and NTRK- or CIC-rearranged tumors, were also excluded [2,4,10].

Diffuse EGFR and cyclin D1 expression in our case suggests active cell cycle progression, likely via EGFR–MAPK signaling, reflecting the tumor's proliferative potential with possible diagnostic and therapeutic relevance. Although genetic testing was not performed, reported NRAS, KRAS, and MAPK pathway alterations in IDCS support a mechanistic link to these markers and a shared oncogenic profile with other hematopoietic and myeloid neoplasms [5,9].

Management of IDCS is not standardized; complete surgical excision remains the primary approach, with chemotherapy and radiotherapy reserved for advanced or recurrent disease [2]. Our pediatric case had a fulminant course, with death occurring within weeks of diagnosis, highlighting the tumor's aggressive nature and poor prognosis in children. Although pediatric IDCS is exceedingly rare with limited survival data, pooled data suggest that young age, advanced stage, intra-abdominal involvement, and adverse histologic features are associated with worse outcomes [1,2,11].

High-grade variants of MIFS, as in our second case, are uncommon and pose significant diagnostic and prognostic challenges due to their more aggressive histologic features and broader differential diagnosis [7]. Very few cases of high-grade MIFS have been clearly documented in the literature [7,12], and many were initially misclassified due to overlapping features with other high-grade sarcomas.

Our patient, a 70-year-old woman, presented with a 3.5 cm subcutaneous mass in the lower limb. Histologically, the tumor exhibited hallmark features of high-grade MIFS, including increased cellularity, infiltrative margins extending into skeletal muscle, frequent mitoses (>19/10 HPFs), and necrosis [7].

Immunohistochemically, the tumor showed strong CD10 and patchy D2-40 positivity, while negative for lineage-specific markers, effectively excluding high-grade differentials such as leiomyosarcoma (SMA+), rhabdomyosarcoma (Desmin+), epithelioid sarcoma (keratin+), melanoma (S100+), inflammatory myofibroblastic tumor (variable SMA/Desmin+, ALK rearrangement), and dedifferentiated liposarcoma (MDM2+) [13]. Undifferentiated pleomorphic sarcoma and myxofibrosarcoma are important entities in the

differential diagnosis; but typically arise proximally, are deeply seated, and display marked pleomorphism, storiform patterns, and lack the inflammation-rich background characteristic of MIFS [13]

Most reported cases involve the distal extremities, often confined to subcutis; however, infiltration into skeletal muscle, as seen in our patient, has been reported and is associated with more aggressive behavior [7,12]. The presence of high mitotic activity, necrosis, and deep tissue invasion are established poor prognostic indicators [14].

To date, no targeted treatments are approved for high-grade MIFS; management relies on wide surgical excision and may include radiotherapy when margins are inadequate. The role of adjuvant therapy is not well defined, but may be considered in recurrent or metastatic cases [7].

Molecular studies in MIFS have identified TGFBR3–MGEA5 rearrangements, VGLL3 amplifications, and occasional BRAF alterations, suggesting a shared genetic pathway with related tumors and potential for targeted approaches, including MEK inhibitors in high-grade or refractory cases [7,8].

Compared to the classical low-grade form, high-grade MIFS is associated with a higher risk of local recurrence and potential for distant metastasis [7]. Some studies reported metastasis in up to 40–50% of cases and a correspondingly higher mortality risk. Accurate histopathologic grading is therefore essential to guide prognosis and management decisions [7,14].

Conclusion

The reported two cases highlight the need for a broad differential diagnosis in rare soft tissue tumors, especially in unusual sites or age groups. Accurate diagnosis depends on integrated histopathologic, immunohistochemical, and molecular assessment. Given MAPK/ERK pathway involvement in IDCS and potential drivers in MIFS, targeted therapies may be worth exploring for unresectable or recurrent disease when conventional options are limited.

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