

A comprehensive review of ossifying fibromyxoid tumor: insights into its clinical, pathological, and molecular landscape

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Ossifying fibromyxoid tumor (OFMT) is a rare mesenchymal neoplasm first described in 1989. It typically arises in the superficial soft tissues of the extremities as a slow-growing, painless mass. Histologically, it is commonly characterized by a multilobular architecture composed of uniform epithelioid cells embedded in a fibromyxoid matrix, often surrounded by a rim of metaplastic bone. While classic cases are readily identifiable, the tumor's histopathological heterogeneity can mimic a range of benign and malignant neoplasms, posing significant diagnostic challenges. Molecularly, most OFMTs harbor *PHF1* rearrangements, commonly involving fusion partners such as *EP400*, *MEAF6*, or *TFE3*. This review underscores the importance of an integrated diagnostic approach—incorporating histopathological, immunohistochemical, and molecular data—to accurately classify OFMT and distinguish it from its mimics. Expanding awareness of its morphologic and molecular spectrum is essential for precise diagnosis, optimal patient management, and a deeper understanding of this enigmatic neoplasm.

Keywords: Ossifying fibromyxoid tumor; *PHF1*; Soft tissue neoplasms; Molecular pathology

INTRODUCTION

Ossifying fibromyxoid tumor (OFMT) is a rare soft tissue neoplasm of uncertain histogenesis, typically arising in the soft tissues of the extremities and often in the subcutaneous tissue [1]. First described by Enzinger et al. in 1989 [2], OFMT displays a wide spectrum of morphological findings and biological behavior. While typical histopathological presentations usually pose little diagnostic challenge, the tumor's morphological variability can complicate diagnosis. This includes cases exhibiting chondroid or lipoblastic differentiation [3], clear cell morphology or collagen entrapment [4], which may mimic other soft tissue neoplasms. Furthermore, hypercellular and mitotically active tumors with significant cellular atypia can demonstrate metastatic potential [5], underscoring the importance of accurate and timely diagnosis. The majority of OFMTs have recurrent

molecular alterations, most frequently *PHF1* rearrangements [6], and molecular pathology can serve as a valuable adjunct in diagnosing challenging cases [4]. This review aims to provide a comprehensive overview of the clinical, pathological, and molecular characteristics of OFMT, educating the readers on this enigmatic entity.

EPIDEMIOLOGY AND CLINICAL PRESENTATION

Despite the rarity of OFMT, multiple case series have described its clinical and pathologic findings in thorough detail. In most cases, OFMT presents as a long-existing, slow-growing, painless mass, with a median duration of ~4 years before patients seek medical attention and treatment [7]. In the original case series of 59 patients published by Enzinger et al. in 1989 [2], OFMT

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was diagnosed more frequently in males than females, with age range spanning from 14 to 79 years. In the series of 70 patients published by Folpe and Weiss [5], OFMT was primarily observed in middle-aged adults, with a slight male predominance, and a propensity to arise in the soft tissues of the extremities. These findings were corroborated by a subsequent study of 104 patients from the Armed Forces Institute of Pathology, which highlighted a median age of 50 years at diagnosis, along with a male-to-female-ratio of 1.5:1 [7], as well as the study by Graham et al on 46 patients with a median age of 52 years and male-to-female ratio of 1.7:1 [8]. Apart from the extremities, OFMT frequently arises in various locations of the head and neck region [9-18]. Intracranial involvement [19,20], occasionally with transcranial extension [21], as well as paraspinal [22] or spinal extradural involvement [23] have been described. Other unusual locations include the retroperitoneum [24], the breast [25], and the genitourinary (GU) tract [26]. Pediatric cases, although uncommon, have been reported [27,28], including a 3-week-old male neonate with a left nasal mass [29].

MACROSCOPIC FINDINGS

OFMT typically presents as a well-circumscribed, ovoid, small soft tissue mass, with a rubbery to firm texture, and a glistening, white cut surface. It often features a peripheral hard shell, which can be appreciated on imaging as irregular bone [7,8,30]. Most tumors are small to medium-sized, with a median size of 3–5 cm, although large tumors measuring up to 17 cm or even 21 cm have been reported [5,7,8]. In the appropriate clinico-radiological setting, this finding can occasionally complicate the differential diagnosis with parosteal osteosarcoma [31]. The tumors are most often subcutaneous, although rarely, they may arise within the skeletal muscle, particularly in the head and neck area [7].

MICROSCOPIC FINDINGS

Microscopically, OFMT exhibits a multilobular architecture, with a pressure effect on the superficial component of the overlying skin, occasionally associated with cutaneous ulceration [7]. The tumor is lined by a pseudocapsule with metaplastic lamellar or woven bone, sometimes interspersed with adipocytes between bony trabeculae, but lacking hematopoietic cells. However, it's worth noting that the absence of the peripheral bone shell is reported in ~25%–40% of OFMT [8,32]. Addition-

ally, osteoid material is commonly observed in central regions of the tumor [33], which raises the possibility of osteosarcoma in the differential diagnosis [34]. Pericapsular aggregates of lymphocytes are not uncommon [5,35]. Within a collagenous or myxoid matrix with perivascular hyalinization, the tumor cells are uniform and epithelioid, featuring pale to eosinophilic cytoplasm, round nuclei with even chromatin distribution, delicate nucleoli, inconspicuous clefts or pseudoinclusions, and low mitotic activity [5,7,35] (Fig. 1).

Unusual findings described in OFMT include breakdown of lamellar bone with osteoclasts, central hemorrhagic infarction [7], satellite microscopic nodules, mucinous microscopic cysts, microcalcification, crushing artifact, and paucity or absence of myxoid matrix, as well as chondroid differentiation (Fig. 2) with atypical binucleated cells [36]. Additional unusual findings are predominance of clear cell morphology, extravasated red blood cells, collagen entrapment and interdigitating fibrocollagenous and fibromyxoid stromal bundles [4] (Figs. 3, 4). A recent study also described two OFMTs with prominent lipoblastic differentiation [3].

An OFMT characterized by high nuclear grade or increased cellularity, and mitotic activity exceeding 2 mitoses per 50 high power fields can be classified as malignant [5] (Figs. 5–8). Additionally, necrosis and an infiltrative pattern may be present [8]. Patients with malignant OFMT are more likely to develop distant metastases, most often to the lungs [37]. Although overtly sarcomatous changes in OFMT are uncommon, they have been documented [38], with reported cases including osteosarcoma arising from OFMT after multiple recurrences [39].

HISTOGENESIS

The histogenesis of OFMT remains enigmatic. Initially it was thought to be a neoplasm of Schwannian origin [40] with possible incomplete neural or cartilaginous differentiation, a hypothesis supported by the commonly observed S100 protein immunoreactivity [7]. However, electron microscopy findings largely resemble those seen in pleomorphic adenomas or myoepithelial tumors [41], including paucity of organelles and aggregates of intermediate filaments with reduplicated basal lamina material [41-43]. Therefore, myoepithelial origin or differentiation is a plausible hypothesis, supported by case reports of tumors displaying intermediate characteristics between OFMT and myoepithelial neoplasms, as discussed below.

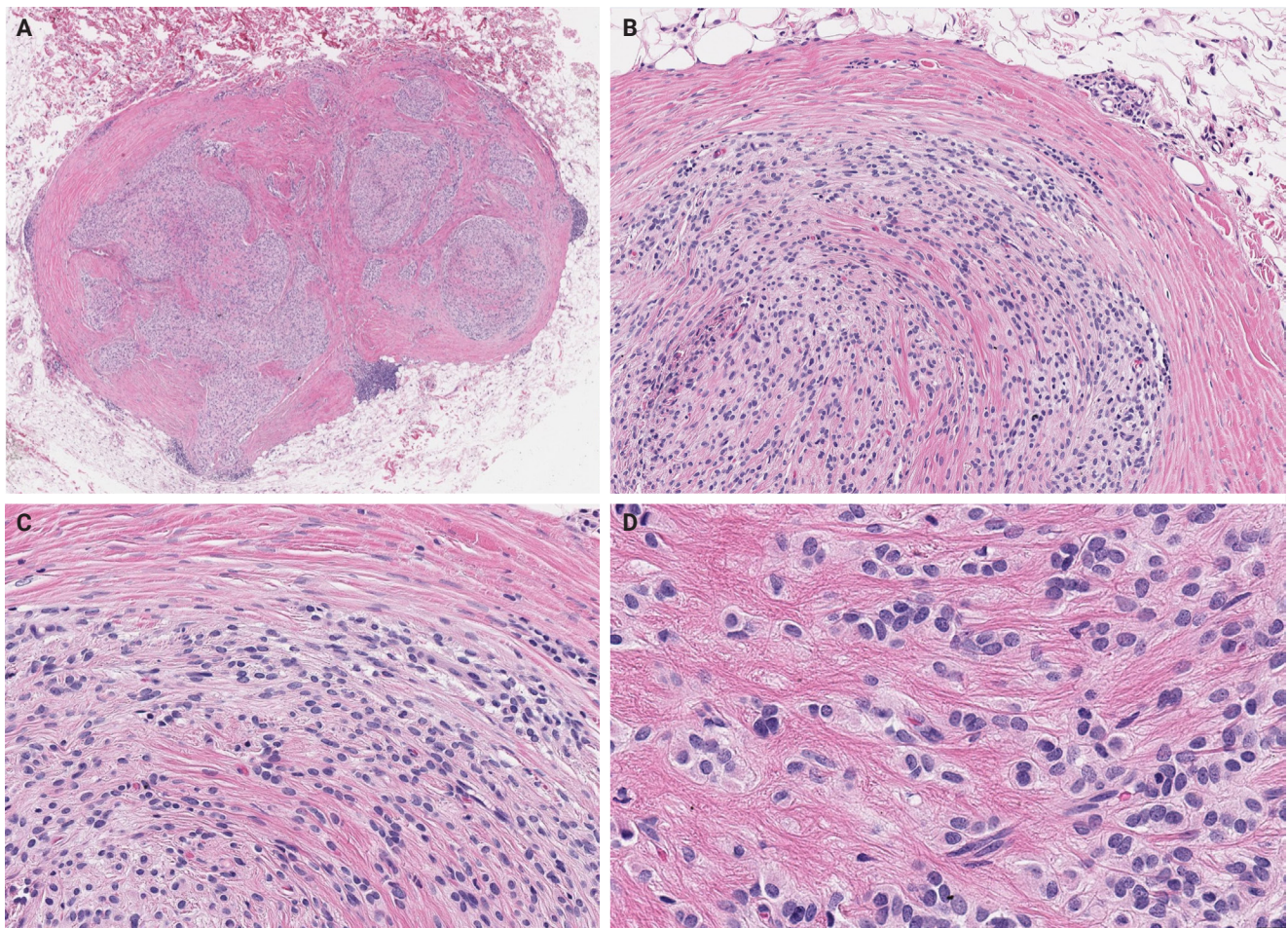


Fig. 1. A right inferior breast ossifying fibromyxoid tumor displaying nearly classic histologic features (except the peripheral metaplastic bone). This case harbors the classic *EP400::PHF1* fusion. (A) At low magnification, the tumor appears as a well-demarcated, multilobulated mass located within the subcutis. (B, C) Tumor cells are arranged in cords and sheets within collagenous stroma. (D) High power view depicting ovoid tumor cells, featuring pale to eosinophilic cytoplasm, and round, regular nuclei.

CYTOPATHOLOGY

The diagnosis of OFMT on cytology specimens is very challenging, both because of its rarity and the non-specific cytomorphology of the cellular component [44]. However, the presence of a fine fibrillary [45] or myxoid matrix [46], with occasional rosette-like structures [44,45] and particularly osteoid-like material [47] can guide cytopathologists to include OFMT in the differential diagnosis of a soft tissue mass. In addition, the presence of nuclear atypia, including features such as prominent nucleoli, chromatin clumping and irregular nuclear contours, may raise the possibility of malignant OFMT [46].

IMMUNOHISTOCHEMISTRY

OFMT typically expresses S100 protein [7,8] and is frequently positive for excitatory amino acid transporter 4 (EAAT4) [8,38], desmin, neurofilament, CD56 [8], CD10 [7], and insulinoma-associated protein 1 (INSM1) [48]. OFMT often displays mosaic expression of integrase interactor 1 (INI1), due to a commonly present underlying alteration of the *SMARCB1* gene, as mentioned in detail below [8,38,49]. Transcription factor E3 (TFE3) nuclear expression is typically seen in OFMT harboring a *PHF1::TFE3* fusion [50,51].

Expression of keratins, collagen IV, glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), smooth muscle actin (SMA) [7], CD99 [52], MUC4 (not diffuse) [8] or

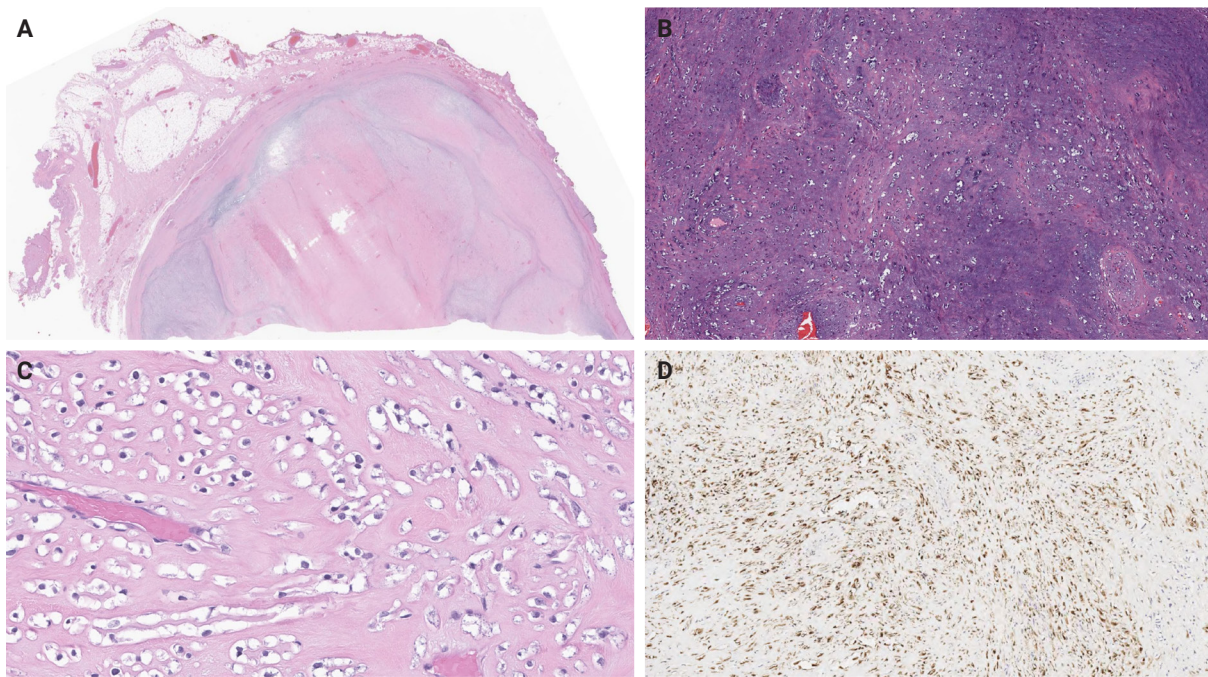


Fig. 2. A lower back ossifying fibromyxoid tumor, harboring a *CREBBP::BCORL1* fusion. (A) Low-power view depicting a well-delineated, pseudoencapsulated tumor, featuring prominent central stromal hyalinization. (B, C) Extensive chondroid differentiation and focal clear cell morphology are appreciated. (D) Tumor cells exhibit positivity for S100 on immunohistochemical staining.

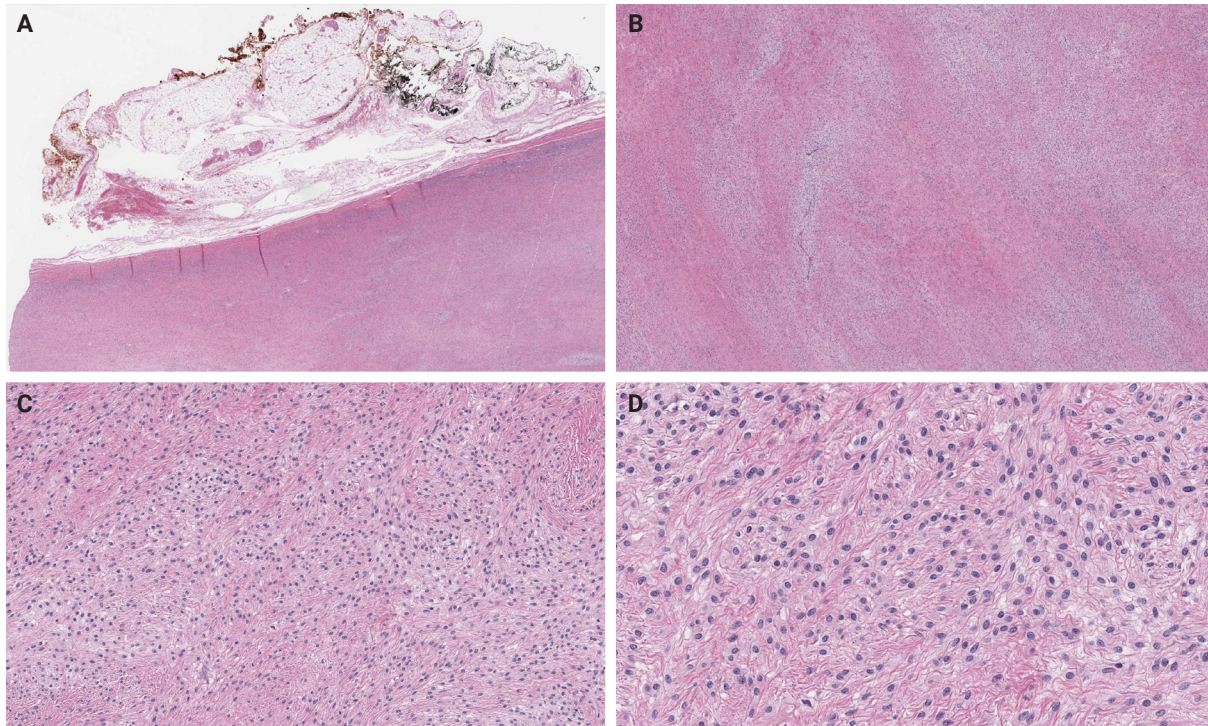


Fig. 3. A left axillary ossifying fibromyxoid tumor harboring an *EP400::PHF1* fusion. (A) At low magnification, the tumor is well-defined and distinctly bordered by adjacent adipose tissue. (B) Tumor cells are set within a stromal matrix that transitions between fibrocollagenous and fibromyxoid areas in a geographically interwoven pattern. (C, D) Cords and sheets of spindle-to-ovoid tumor cells with uniform, ovoid nuclei and pale to eosinophilic cytoplasm are noted.

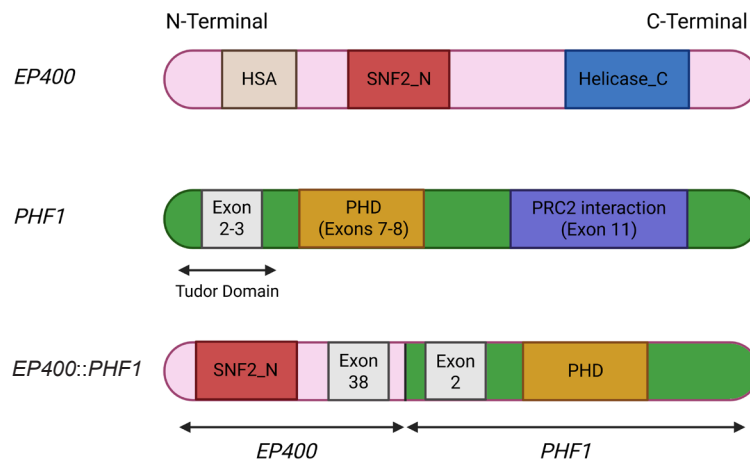


Fig. 4. The *EP400::PHF1* fusion, detected in the case depicted in Fig. 3, preserves SNF2_N from *EP400* and fuses to *PHF1* exon 2 and the PHD domain, altering chromatin regulation via recruitment to new loci [53]. HAS, actin-binding domain in chromatin remodelers; SNF2_N, ATP-binding subdomain of SNF2 helicase; Helicase_C, catalytic helicase subdomain; PHD, zinc finger "reader" domain binding histone marks; PRC2 interaction, region mediating interaction with the PRC2 complex (Illustrations are created by Biorender <https://app.biorender.com>).

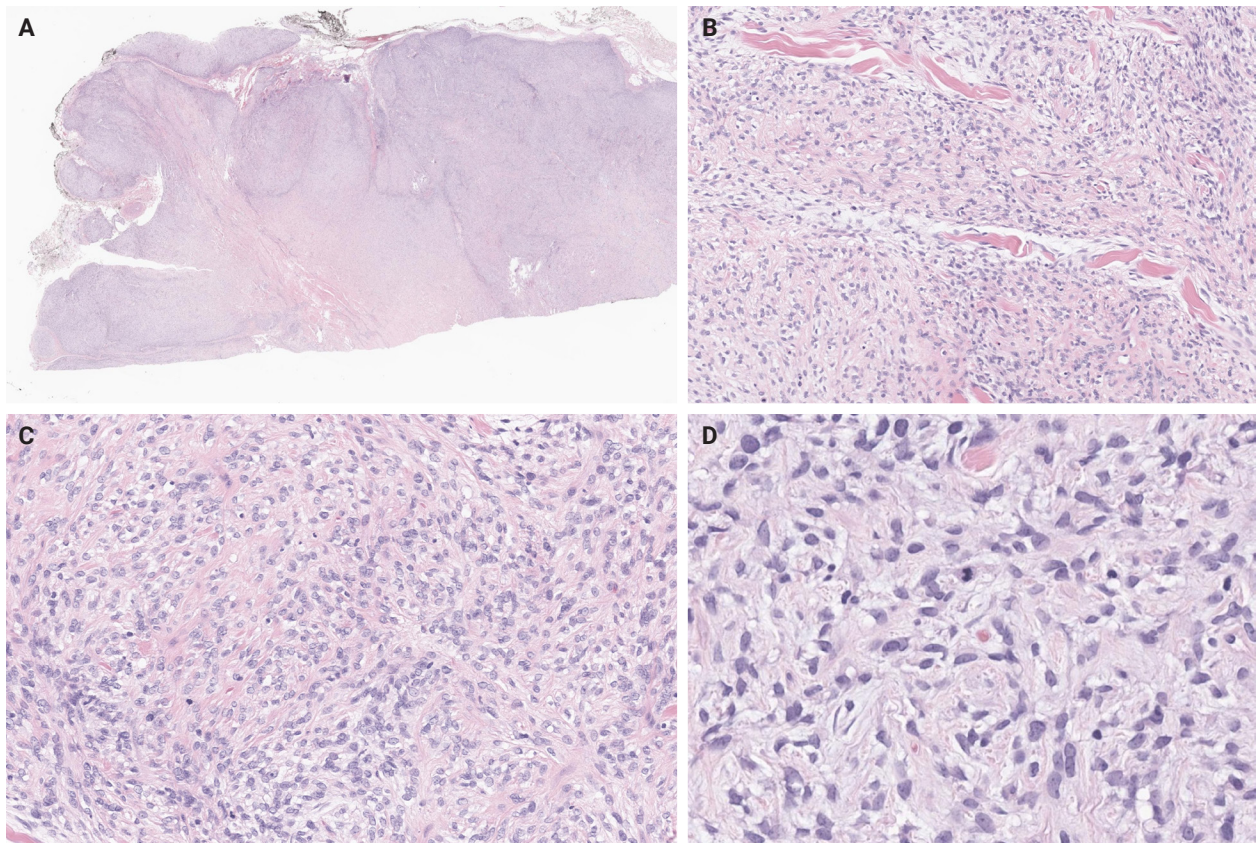


Fig. 5. A malignant, right-back ossifying fibromyxoid tumor harboring an *EPC1::SUZ12* fusion. (A) At low magnification, the tumor appears multilobulated and highly cellular. (B, C) Sheets and trabeculae of tumor cells are seen infiltrating the collagen bundles. (D) Areas of increased mitotic activity are observed, with no evidence of pleomorphism or necrosis.

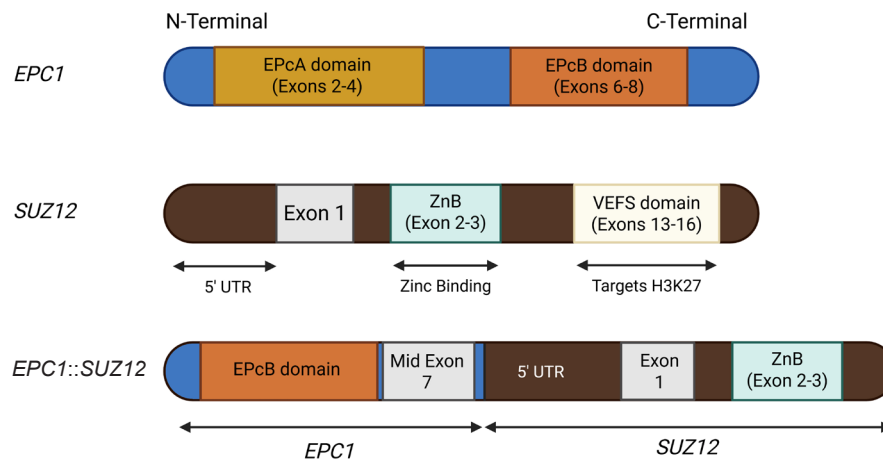


Fig. 6. *EPC1::SUZ12* fusion, detected in the case depicted in Fig. 5, joins the EPcB domain of *EPC1* to *SUZ12* 5'-UTR, reprogramming PRC2 recruitment and function with loss of H3K27 trimethylation [54]. EPcA/EPcB domains, *EPC1* domains that scaffold chromatin modifiers; ZnB, Zinc-binding domain (complex assembly function); VEFS, Domain that interacts with EZH2/EED and targets H3K27 (Illustrations are created by Biorender <https://app.biorender.com>).

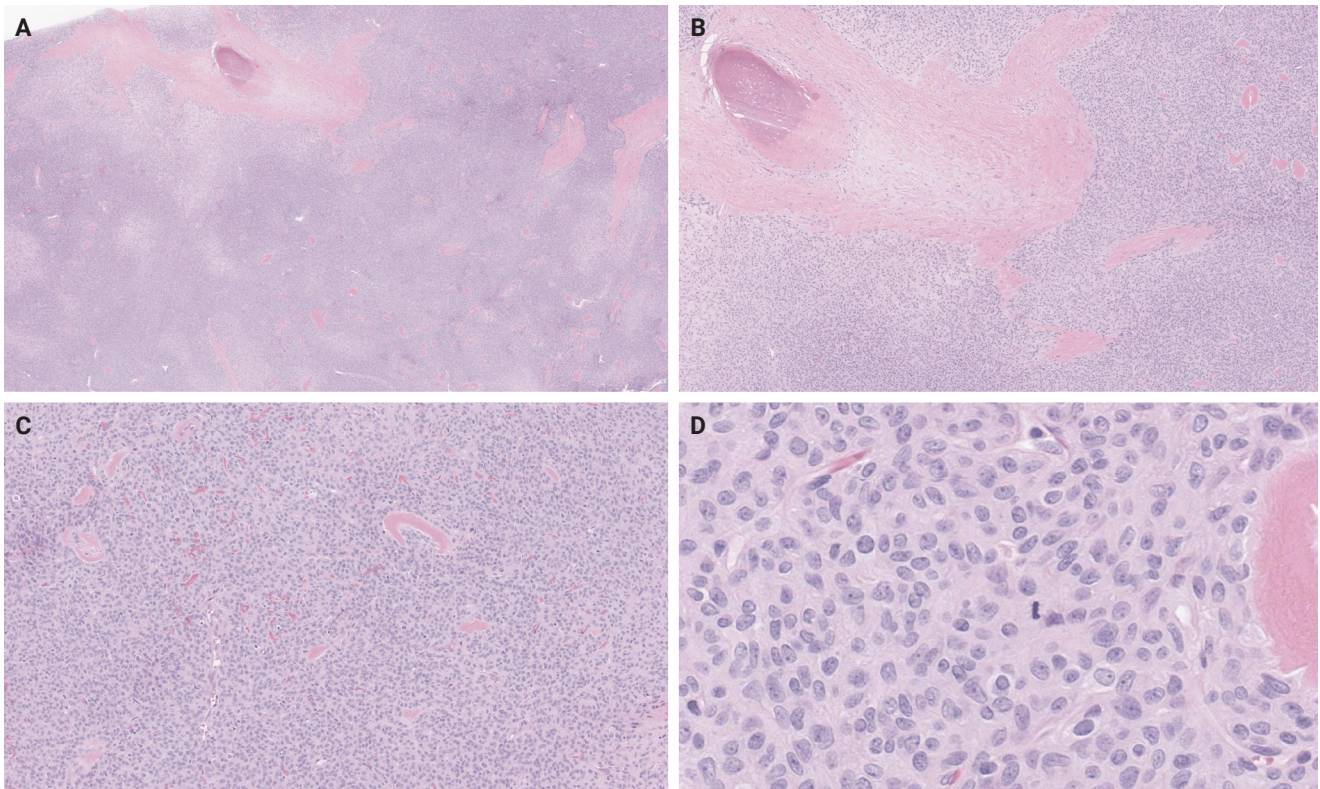


Fig. 7. A malignant right parapharyngeal ossifying fibromyxoid tumor with the very rare *PHF1::FOXQ2* fusion. (A, B) At low magnification, the tumor appears highly cellular, with metaplastic bone present within the fibrous septae. (C) Tumor cells form cords, nests, and sheets, scattered throughout a collagenous to hyalinized background. (D) The tumor cells are predominantly ovoid to spindle-shaped, with a high nucleus-to-cytoplasm ratio, round to ovoid nuclei featuring occasional small nucleoli, and increased mitotic activity. The patient subsequently developed lung metastases.

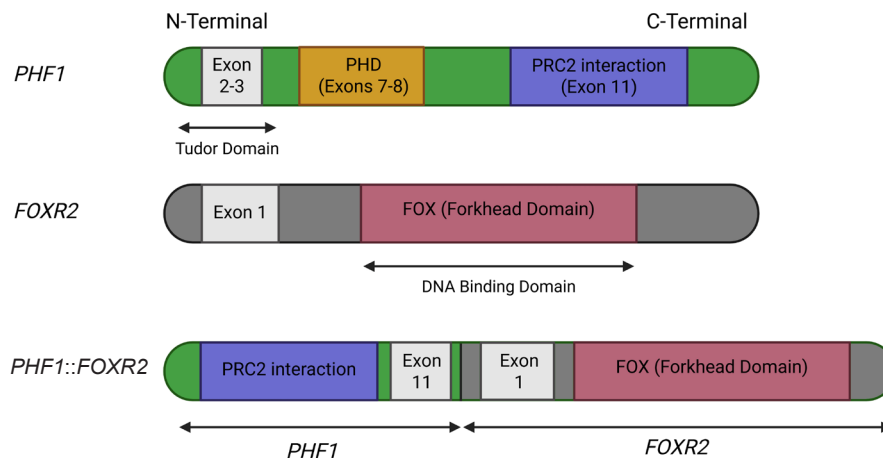


Fig. 8. The *PHF1::FOXR2* fusion, detected in the case depicted in Fig. 7, combines PRC2 recruitment ability (*PHF1*) with the transcriptional targeting domain of *FOXR2*, redirecting epigenetic silencing to FOX-bound genomic loci and mislocalization of chromatin-modifying complexes [55]. PHD, histone reader domain; FOX (Forkhead domain), DNA-binding domain of *FOXR2*, found in FOX transcription factors (Illustrations are created by Biorender <https://app.biorender.com>).

calponin [56] has occasionally been reported, while OFMT is consistently negative for HMB45, CD34 [7], SOX10 [33], and preferentially expressed antigen in melanoma (PRAME) [57]. Interestingly, estrogen receptor and progesterone receptor (PR) expression has been described in a *PHF1*-rearranged OFMT of the breast, which also co-expressed STAT6 [25], as well as in a *PHF1*-rearranged OFMT of the axillary soft tissues [4], while isolated diffuse PR expression was seen in two OFMTs of the extremities with *BCOR* and *TFE3* rearrangements [51].

Of note, expression of pan-tropomyosin receptor kinase (pan-TRK) by immunohistochemistry has been reported in *BCOR*-rearranged OFMT [58,59]. Given the efficacy of targeted neurotrophic tyrosine receptor kinase (NTRK) inhibition for patients with *NTRK*-fused tumors [60], this finding is of potential clinical interest. Although the exact mechanism of pan-TRK expression has not been fully elucidated, it seems that it occurs due to underlying *NTRK3* mRNA overexpression [58].

Finally, it is worth mentioning that malignant OFMT can show an atypical immunophenotype, with attenuation or complete absence of S100 protein expression [61]. Absence of S100 expression was also demonstrated in all four GU OFMTs described by Argani et al. [26], two of which were classified as malignant based on mitotic count.

MOLECULAR GENETICS

The presence of clonal chromosomal alterations such as aneuploidies, unbalanced translocations [62] and complex karyotypes [63], including marker chromosomes [64], was highlighted in early studies. Complex karyotypes have been particularly associated with malignant OFMT cases exhibiting metastases [63]. A relatively recurrent finding is hemizygous deletion of chromosome 22 or 22q, leading to hemizygous loss of *SMARCB1*, an alteration corresponding to the mosaic immunohistochemical pattern of INI1 expression frequently observed, as mentioned above [8]. Another recurrent finding most often seen in atypical and malignant OFMT is loss of the *RB1* tumor suppressor gene, observed in almost a third of cases [55].

The molecular hallmark of OFMT is the presence of recurrent rearrangements of *PHF1*, which are seen in approximately 80%–85% of tumors [6]. The *PHF1* gene encodes a protein which interacts with polycomb-repressive complex 2 (PRC2), an important regulator of chromatin structure and developmental gene expression [65], ultimately controlling histone H3K27 methylation status [66]. Rearrangement of *PHF1* typically occurs in the form of a reciprocal translocation, resulting in gene fusion, with *EP400* being the most common fusion partner (Fig. 4) [67]. Other *PHF1* fusion partners include *EPC1*, *MEAF6* [68], *TFE3* [69], *FOXR1*, *FOXR2* (Fig. 8) [70], *CREBZF* [34], *TP53* [71], and *JAZF1* [3].

Non-*PHF1* fusions have also been described, including *MEAF6::SUZ12* [72], *EPC1::SUZ12* (Fig. 6) [4], *CREBBP::BCORL1*, *KDM2A::WWTR1* [73], *ZC3H7B::BCOR* [59], *CSMD1::MEAF6* [55], and *EPC1::PHC1* [3]. The common denominator of these fusions is that they function as tumor drivers, inducing significant epigenetic changes via histone modification, a process currently regarded as the major molecular mechanism of OFMT pathogenesis [55]. Of note, a non-fused malignant OFMT with a *BCOR* internal tandem duplication has been reported in a pediatric patient with a lateral neck mass and subsequent local and metastatic recurrences [74].

Interestingly, certain of the above mentioned fusions, particularly *JAZF1::PHF1*, *EPC1::PHF1*, *MEAF6::PHF1*, *ZC3H7::BCOR*, and *EPC1::SUZ12* [75,76] have been previously described in low-grade endometrial stromal sarcoma (ESS), a finding explaining why certain OFMT may cluster with ESSs by DNA methylation analysis [4]. The latter fact may limit the utility of DNA methylation assay in the work-up of OFMT.

Given the frequency of *PHF1* rearrangements, a reasonable approach includes morphological assessment with confirmation of *PHF1* alteration by break-apart fluorescent in situ hybridization (FISH) [77]. However, in cases with unusual morphological findings and non-*PHF1* rearrangements, the final diagnosis may need to be deferred until molecular testing by next generation sequencing (NGS) is performed [4].

DIFFERENTIAL DIAGNOSIS

The broad spectrum of the differential diagnosis for OFMT often encompasses myoepithelial neoplasms [78]. In challenging cases, testing for *EWSR1* rearrangements in these neoplasms can provide valuable insights. However, it's essential to acknowledge that *EWSR1* rearrangements are detected in only around 50% of soft tissue myoepithelial neoplasms [79], making the test informative when positive, but less conclusive when negative.

The most frequent pitfall in the differential diagnosis of OFMT is low-grade fibromyxoid sarcoma (LGFMS) [80]. Also known as “Evans tumor” [81], LGFMS is a low-grade sarcoma arising in the extremities of young adults, although as many as 20% of cases occur in patients younger than 18 years old. It consists of spindle to epithelioid cells arranged in alternating hyalinized and myxoid areas, with occasional hyaline rosettes [82]. These morphologic features, along with lack of S100 expression and strong and diffuse MUC4 positivity, usually suf-

fice for distinguishing LGFMS from OFMT. Molecular detection of the characteristic *FUS::CREB3L2* or *EWSR1::CREB3L1* fusions confirms the diagnosis of LGFMS in the appropriate morphologic context [83].

Sclerosing epithelioid fibrosarcoma (SEF) or hybrid SEF-LGFMS tumors are also frequently included in the differential diagnosis. SEF is a rare aggressive variant of fibrosarcoma, characterized by small epithelioid cells arranged in cords and nests within a densely sclerotic stroma [84]. However, unlike OFMT, SEF primarily arises in deep soft tissues and lacks S100 expression [85]. The diagnosis of SEF can be confirmed through molecular studies that identify the characteristic *EWSR1::CREB3L1* fusion [86].

The differential diagnosis also includes the newly described *YAP1::KMT2A*-rearranged sarcoma, an aggressive soft tissue malignancy, notorious for its propensity to mimic benign or low-grade neoplasms, such as schwannoma, fibromatosis or LGFMS [87]. Initially thought to represent a MUC4-negative subtype of SEF, the identification of recurrent *YAP1* and *KMT2A* rearrangements [88,89], along with distinctive morphologic features [89] and a unique DNA methylation profile [87], has established *YAP1::KMT2A* rearranged sarcoma as a novel entity. These tumors usually exhibit an infiltrative growth pattern with areas of variable cellularity, where monomorphic epithelioid or bland, fibroma-like spindle cells are embedded in a densely collagenous matrix. Mitotic activity is generally low and high-grade features, such as necrosis are usually absent [89]. Immunohistochemically, these tumors are consistently negative for MUC4 and usually negative for S100 protein, but may show variable EMA or CD34 expression [86]. Despite its deceptively low-grade histomorphology, *YAP1::KMT2A*-rearranged sarcoma can follow an aggressive clinical course, with local recurrence and metastatic disease developing in up to 50% of patients [86].

Other entities to consider in the differential diagnosis include schwannoma [90], malignant peripheral nerve sheath tumor (MPNST) [78], extraskeletal myxoid chondrosarcoma (EMC) [48], and extraskeletal osteosarcoma [78]. Schwannoma arises from the peripheral nerve sheath and is characteristically strongly and diffusely positive for S100 protein, in contrast to OFMT, where S100 expression may be weak or absent. Schwannomas also lack the peripheral ossification and cytomorphic features typical of OFMT [90]. MPNST typically arises in deep soft tissues, often in association with major nerves, and does not exhibit peripheral ossification. While MPNST may

show attenuated S100 positivity, it can also express other neural markers such as neurofilament and GFAP [78]. Importantly, loss of H3K27me3 expression—frequently seen in MPNST—can help distinguish it from OFMT, in which H3K27me3 expression is consistently retained [91,92]. EMC is characterized by a lobular architecture with fibrous septa and uniform tumor cells showing eosinophilic cytoplasm, occasional spindling, and inconspicuous nucleoli in a myxoid background. EMC typically expresses INSM1, synaptophysin, and sometimes other neuroendocrine or neural markers such as chromogranin, PGP9.5, microtubule-associated protein 2, class III β -tubulin, and peripherin [48]. Genetically, EMC is defined by *NR4A3* rearrangements, most commonly with *EWSR1*, but also involving partners such as *TAF15*, *TCF12*, *TFG*, *FUS*, *HSPA8*, *LSM14A*, or *SMARCA2* [48]. Extraskelatal osteosarcoma is exceedingly rare in the skin or subcutis and typically represents metastatic disease, making clinical history essential. Helpful distinguishing features include lack of S100 expression and the presence of marked nuclear atypia [78].

Notably, primary bone OFMT has also been described, which may be extremely challenging to distinguish from osteosarcoma [93]. In tumors with lipoblastic differentiation, distinction from benign and malignant lipomatous tumors such as chondroid lipoma or myxoid liposarcoma can be challenging [3]. The differential diagnosis can be particularly challenging in tumors with uncommon microscopic features, where the final diagnosis can be confidently rendered only by confirming a characteristic molecular alteration [4].

PRACTICAL DIAGNOSTIC APPROACH

Diagnosing OFMT requires an integrative approach, as the tumor's morphologic and immunophenotypic spectrum is broad and overlaps with several benign and malignant entities. In classic presentations—characterized by uniform ovoid cells embedded in a fibromyxoid matrix and surrounded by a peripheral shell of metaplastic bone—the diagnosis may be straightforward, particularly when supported by strong S100 protein and desmin expression. However, in atypical or malignant variants, these features may be attenuated or absent. For instance, malignant OFMTs frequently lack ossification, exhibit increased cellularity and mitotic activity, and may show reduced or completely lost S100 expression. Ancillary studies are essential in such cases. FISH is widely used and can detect gene rearrangements or amplifications in formalin-fixed paraf-

fin-embedded tissue with good sensitivity, but it is restricted to one locus per assay and, in the case of break-apart probes, cannot identify the fusion partner. Furthermore, cryptic or complex rearrangements may go undetected. Reverse-transcriptase polymerase chain reaction (RT-PCR) offers high sensitivity and relatively low cost for detecting known fusion transcripts, but it requires prior knowledge of the partner genes and thus cannot identify novel fusions. Targeted RNA sequencing and broader NGS panels overcome these limitations by interrogating multiple loci simultaneously, allowing both confirmation of established fusions and discovery of novel ones. Although more resource-intensive, NGS has emerged as the most reliable method for characterizing OFMT at the molecular level, particularly in diagnostically challenging cases [94].

In clinical practice, the diagnostic work-up of a suspected OFMT typically begins with a panel of broad immunohistochemical stains, including S100, SOX10, desmin, SMA, and a broad-spectrum cytokeratin. In tumors with classic morphology, the combination of S100 and desmin positivity is generally sufficient to establish a confident diagnosis. In cases with very suggestive morphology but incomplete immunophenotypic support—for example, when S100 or desmin expression is weak or focal—*PHF1* break-apart FISH is the logical next step, as approximately 80%–85% of OFMTs harbor *PHF1* rearrangements. If *PHF1* testing is negative but the pretest probability remains high, RT-PCR, targeted RNA sequencing or broad-panel NGS can help identify rarer fusions, such as *CREBBP::BCORL1*, *EPC1::SUZ12*, or *ZC3H7B::BCOR* amongst others.

In atypical or malignant cases, where classic immunohistochemical markers such as S100 and desmin are diminished or absent, a diagnosis of OFMT may still be appropriate if the tumor contains areas reminiscent of conventional OFMT. In such instances, *PHF1* FISH remains useful. However, in malignant tumors that lack both morphologic and immunophenotypic features suggestive of OFMT, comprehensive molecular testing via NGS is often the only practical means of confirming the diagnosis.

Emerging evidence supports a correlation between specific gene fusions and atypical or malignant histologic features of OFMT. In a synthesis of reported cases across the literature, approximately 26 OFMTs with non-*PHF1* fusions or *PHF1* fusions involving uncommon partners (e.g., *TP53*, *FOXRI/2*, *CREBZF*, *ZC3H7B*, *EPC1*) have been compiled and analyzed. Of these, 18 tumors (69%) were classified as atypical or malignant, indicating a strong association between rare fusion events

and aggressive histologic behavior. Moreover, certain fusion types—such as *TP53::PHF1*, *PHF1::FOXR2*, *ZC3H7B::BCOR*, and *EPC1::SUZ12*—have been reported almost exclusively in malignant cases, further supporting their potential as molecular indicators of high-grade disease. While these rare fusions do not inherently define malignancy, their frequent occurrence in morphologically aggressive tumors suggests they may play a role in driving dedifferentiation or loss of canonical OFMT features.

These atypical/malignant variants also tend to show marked loss of conventional immunophenotypic markers. In the pooled dataset, S100 expression was retained in only four of 15 cases (27%), often in a focal or patchy distribution, and desmin was expressed in just two of 14 cases (14%). In contrast, classic OFMTs show S100 positivity in ~70% and desmin in ~50% of cases. Additionally, the characteristic peripheral ossified shell was frequently absent in these high-grade tumors, further complicating diagnosis.

Together, these findings highlight the importance of recognizing non-classic morphologic and immunohistochemical presentations and maintaining a low threshold for molecular testing—especially in tumors lacking both classic architecture and marker expression [71].

TREATMENT AND PROGNOSIS

OFMT is treated surgically with local marginal or wide excision and rarely amputation, particularly when a large tumor arises on a digit [7]. Local recurrence is more likely to occur in patients whose tumors show increased mitotic activity [7]. Tumors fulfilling the microscopic criteria of malignancy, should be regarded as sarcomas for treatment purposes, as they tend to display more aggressive clinical behavior, including the potential for distant metastasis [5,95]. These patients may be candidates for adjuvant radiation therapy, particularly after being diagnosed with local recurrence [5]. Similarly, patients with metastatic disease may be eligible for chemotherapy [96]. When malignant OFMT metastasizes, it typically spreads to the lung [8,37,96], although unusual locations such as the thyroid gland have been reported [97].

CONCLUSION

OFMT is a rare mesenchymal neoplasm that can occasionally complicate the differential diagnosis of a soft tissue mass, lead-

ing to diagnostic uncertainty. Given that certain tumors behave in a clinically aggressive manner, pathologists should consider OFMT in the differential diagnosis of an unusual soft tissue tumor and triage cases for molecular testing where appropriate, as rendering an accurate diagnosis is the cornerstone of effective patient management.

Ethics Statement

Not applicable.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Code Availability

Not applicable.

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Conflicts of Interest

The authors declare that they have no potential conflicts of interest.

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REFERENCES

- Endo M, Miettinen M, Mertens F. Ossifying fibromyxoid tumor. In: WHO Classification of Tumours Editorial Board, ed. WHO classification of tumours: soft tissue and bone tumours. 5th ed. Lyon: International Agency for Research on Cancer, 2020; 274-6.

2. Enzinger FM, Weiss SW, Liang CY. Ossifying fibromyxoid tumor of soft parts: a clinicopathological analysis of 59 cases. *Am J Surg Pathol* 1989; 13: 817-27.
3. Klubickova N, Billings S, Dermawan JK, Molligan JF, Fritchie K. Ossifying fibromyxoid tumours with lipomatous and cartilaginous differentiation: a diagnostic pitfall. *Histopathology* 2025; 86: 891-9.
4. Syrnioti A, Chatzopoulos K, Kerr DA, et al. A potential conundrum in dermatopathology: molecularly confirmed superficial ossifying fibromyxoid tumors with unusual histomorphologic findings and a novel fusion. *Virchows Arch* 2024; 485: 1063-73.
5. Folpe AL, Weiss SW. Ossifying fibromyxoid tumor of soft parts: a clinicopathologic study of 70 cases with emphasis on atypical and malignant variants. *Am J Surg Pathol* 2003; 27: 421-31.
6. Pozas J, Thway K, Lindsay D, et al. Ossifying fibromyxoid tumours: a case series. *Eur J Cancer* 2025; 217: 115229.
7. Miettinen M, Finnell V, Fetsch JF. Ossifying fibromyxoid tumor of soft parts: a clinicopathologic and immunohistochemical study of 104 cases with long-term follow-up and a critical review of the literature. *Am J Surg Pathol* 2008; 32: 996-1005.
8. Graham RP, Dry S, Li X, et al. Ossifying fibromyxoid tumor of soft parts: a clinicopathologic, proteomic, and genomic study. *Am J Surg Pathol* 2011; 35: 1615-25.
9. Park DJ, Miller NR, Green WR. Ossifying fibromyxoid tumor of the orbit. *Ophthalmic Plast Reconstr Surg* 2006; 22: 87-91.
10. Blum A, Back W, Naim R, Hormann K, Riedel F. Ossifying fibromyxoid tumor of the nasal septum. *Auris Nasus Larynx* 2006; 33: 325-7.
11. Tanna N, Chadha N, Sharma RR, Goodman JF, Sadeghi N. Malignant ossifying fibromyxoid tumor of the parapharyngeal space. *Ear Nose Throat J* 2012; 91: E15-7.
12. Perez-de-Oliveira ME, Morais TM, Lopes MA, de Almeida OP, van Heerden WF, Vargas PA. Ossifying fibromyxoid tumor of the oral cavity: rare case report and long-term follow-up. *Autops Case Rep* 2021; 11: e2020216.
13. Ohta K, Taki M, Ogawa I, et al. Malignant ossifying fibromyxoid tumor of the tongue: case report and review of the literature. *Head Face Med* 2013; 9: 16.
14. Sharif MA, Mushtaq S, Mamoon N, Khadim MT. Ossifying fibromyxoid tumor of oral cavity. *J Coll Physicians Surg Pak* 2008; 18: 181-2.
15. Nonaka CF, Pacheco DF, Nunes RP, Freitas Rde A, Miguel MC. Ossifying fibromyxoid tumor in the mandibular gingiva: case report and review of the literature. *J Periodontol* 2009; 80: 687-92.
16. Mollaoglu N, Tokman B, Kahraman S, Cetiner S, Yucetas S, Uluoglu O. An unusual presentation of ossifying fibromyxoid tumor of the mandible: a case report. *J Clin Pediatr Dent* 2006; 31: 136-8.
17. Titsinides S, Nikitakis NG, Tasoulas J, Daskalopoulos A, Goutzanis L, Sklavounou A. Ossifying fibromyxoid tumor of the retro-molar trigone: a case report and systematic review of the literature. *Int J Surg Pathol* 2017; 25: 526-32.
18. Mashkova TA, Panchenko IG, Maltsev AB, Shaposhnikova IV. A clinical observation of laryngeal ossifying fibromyxoid tumor. *Vestn Otorinolaringol* 2021; 86: 82-4.
19. Dhawan S, Lal T, Pandey PN, Saran R, Singh A. Synchronous occurrence of colloid cyst with intracranial ossifying fibromyxoid tumor masquerading as meningioma. *Cureus* 2020; 12: e10662.
20. Beyer S, Sebastian NT, Prasad RN, et al. Malignant ossifying fibromyxoid tumor of the brain treated with post-operative fractionated stereotactic radiation therapy: a case report and literature review. *Surg Neurol Int* 2021; 12: 588.
21. Hachmann JT, Graham RS. Malignant ossifying fibromyxoid tumor of the calvaria: illustrative case. *J Neurosurg Case Lessons* 2021; 2: CASE21346.
22. Sangala JR, Park P, Blaivas M, Lamarca F. Paraspinal malignant ossifying fibromyxoid tumor with spinal involvement. *J Clin Neurosci* 2010; 17: 1592-4.
23. Lu Q, Ho CL. A case of an 82-year-old man with a spinal extradural malignant ossifying fibromyxoid tumor. *Am J Case Rep* 2023; 24: e939408.
24. Motoyama T, Ogoe A, Watanabe H. Ossifying fibromyxoid tumor of the retroperitoneum. *Pathol Int* 1996; 46: 79-83.
25. Gajdzis P, Lae M, Choussy O, Lavigne M, Klijanienko J. Fine-needle aspiration features of ossifying fibromyxoid tumor in the breast: a case report and literature review. *Diagn Cytopathol* 2019; 47: 711-5.
26. Argani P, Dickson BC, Gross JM, Matoso A, Baraban E, Antonescu CR. Ossifying fibromyxoid tumor of the genitourinary tract: report of 4 molecularly confirmed cases of a diagnostic pitfall. *Am J Surg Pathol* 2023; 47: 709-16.
27. Aminudin CA, Sharaf I, Hamzaini AH, Salmi A, Aishah MA. Ossifying fibromyxoid tumour in a child. *Med J Malaysia* 2004; 59 Suppl F: 49-51.
28. Ijiri R, Tanaka Y, Misugi K, Sekido K, Nishi T. Ossifying fibromyxoid tumor of soft parts in a child: a case report. *J Pediatr Surg* 1999; 34: 1294-6.
29. Al-Mazrou KA, Mansoor A, Payne M, Richardson MA. Ossifying fibromyxoid tumor of the ethmoid sinus in a newborn: report of a case and literature review. *Int J Pediatr Otorhinolaryngol* 2004;

- 68: 225-30.
30. Schaffler G, Raith J, Ranner G, Weybora W, Jeserschek R. Radiographic appearance of an ossifying fibromyxoid tumor of soft parts. *Skeletal Radiol* 1997; 26: 615-8.
 31. Ogose A, Otsuka H, Morita T, Kobayashi H, Hirata Y. Ossifying fibromyxoid tumor resembling parosteal osteosarcoma. *Skeletal Radiol* 1998; 27: 578-80.
 32. Schneider N, Fisher C, Thway K. Ossifying fibromyxoid tumor: morphology, genetics, and differential diagnosis. *Ann Diagn Pathol* 2016; 20: 52-8.
 33. Carter CS, Patel RM. Ossifying fibromyxoid tumor: a review with emphasis on recent molecular advances and differential diagnosis. *Arch Pathol Lab Med* 2019; 143: 1504-12.
 34. Sharma AE, Dermawan JK, Sherrod AE, Chopra S, Maki RG, Antonescu CR. When molecular outsmarts morphology: malignant ossifying fibromyxoid tumors masquerading as osteosarcomas, including a novel *CREBZF::PHF1* fusion. *Genes Chromosomes Cancer* 2024; 63: e23206.
 35. WHO Classification of Tumours Editorial Board. WHO classification of tumours: soft tissue and bone tumours. 5th ed. Lyon: International Agency for Research on Cancer; 2020.
 36. Zamecnik M, Michal M, Simpson RH, et al. Ossifying fibromyxoid tumor of soft parts: a report of 17 cases with emphasis on unusual histological features. *Ann Diagn Pathol* 1997; 1: 73-81.
 37. Sarraj A, Duarte J, Dominguez L, Pun YW. Resection of metastatic pulmonary lesion of ossifying fibromyxoid tumor extending into the left atrium and ventricle via pulmonary vein. *Eur J Echocardiogr* 2007; 8: 384-6.
 38. Dantey K, Schoedel K, Yergiyev O, McGough R, Palekar A, Rao UN. Ossifying fibromyxoid tumor: a study of 6 cases of atypical and malignant variants. *Hum Pathol* 2017; 60: 174-9.
 39. Shelekhova KV, Kazakov DV, Michal M. Extraosseous osteosarcoma arising in recurrent ossifying fibromyxoid tumor of soft tissue: a case report. *Arkh Patol* 2013; 75: 24-8.
 40. Donner LR. Ossifying fibromyxoid tumor of soft parts: evidence supporting Schwann cell origin. *Hum Pathol* 1992; 23: 200-2.
 41. Min KW, Seo IS, Pitha J. Ossifying fibromyxoid tumor: modified myoepithelial cell tumor? Report of three cases with immunohistochemical and electron microscopic studies. *Ultrastruct Pathol* 2005; 29: 535-48.
 42. Miettinen M. Ossifying fibromyxoid tumor of soft parts: additional observations of a distinctive soft tissue tumor. *Am J Clin Pathol* 1991; 95: 142-9.
 43. Hirose T, Shimada S, Tani T, Hasegawa T. Ossifying fibromyxoid tumor: invariable ultrastructural features and diverse immunophenotypic expression. *Ultrastruct Pathol* 2007; 31: 233-9.
 44. Goyal P, Sehgal S, Agarwal R, Singh S, Gupta R, Kumar A. Ossifying fibromyxoid tumor: diagnostic challenge for a cytopathologist. *Cytojournal* 2012; 9: 17.
 45. Lax S, Langsteger W. Ossifying fibromyxoid tumor misdiagnosed as follicular neoplasia: a case report. *Acta Cytol* 1997; 41: 1261-4.
 46. Minami R, Yamamoto T, Tsukamoto R, Maeda S. Fine needle aspiration cytology of the malignant variant of ossifying fibromyxoid tumor of soft parts: a case report. *Acta Cytol* 2001; 45: 745-55.
 47. Mohanty SK, Srinivasan R, Rajwanshi A, Vasishta RK, Vignesh PS. Cytologic diagnosis of ossifying fibromyxoid tumor of soft tissue: a case report. *Diagn Cytopathol* 2004; 30: 41-5.
 48. Yoshida A, Makise N, Wakai S, Kawai A, Hiraoka N. INSM1 expression and its diagnostic significance in extraskeletal myxoid chondrosarcoma. *Mod Pathol* 2018; 31: 744-52.
 49. Tajima S, Koda K. Atypical ossifying fibromyxoid tumor unusually located in the mediastinum: report of a case showing mosaic loss of INI-1 expression. *Int J Clin Exp Pathol* 2015; 8: 2139-45.
 50. Suurmeijer AJ, Song W, Sung YS, et al. Novel recurrent *PHF1-TFE3* fusions in ossifying fibromyxoid tumors. *Genes Chromosomes Cancer* 2019; 58: 643-9.
 51. Linos K, Kerr DA, Baker M, et al. Superficial malignant ossifying fibromyxoid tumors harboring the rare and recently described *ZC3H7B-BCOR* and *PHF1-TFE3* fusions. *J Cutan Pathol* 2020; 47: 934-45.
 52. Miliaras D, Meditskou S, Ketikidou M. Ossifying fibromyxoid tumor may express CD56 and CD99: a case report. *Int J Surg Pathol* 2007; 15: 437-40.
 53. Sudarshan D, Avvakumov N, Lalonde ME, et al. Recurrent chromosomal translocations in sarcomas create a megacomplex that mislocalizes NuA4/TIP60 to polycomb target loci. *Genes Dev* 2022; 36: 664-83.
 54. Przybyl J, Kidzinski L, Hastie T, Debiec-Rychter M, Nüsse R, van de Rijn M. Gene expression profiling of low-grade endometrial stromal sarcoma indicates fusion protein-mediated activation of the Wnt signaling pathway. *Gynecol Oncol* 2018; 149: 388-93.
 55. Hofvander J, Jo VY, Fletcher CD, et al. PHF1 fusions cause distinct gene expression and chromatin accessibility profiles in ossifying fibromyxoid tumors and mesenchymal cells. *Mod Pathol* 2020; 33: 1331-40.
 56. Squillaci S, Tallarigo F, Cazzaniga R, Capitanio A. Ossifying fibromyxoid tumor with atypical histological features: a case report. *Pathologica* 2009; 101: 248-52.
 57. Cammareri C, Beltzung F, Michal M, et al. PRAME immunohistochemistry in soft tissue tumors and mimics: a study of 350

- cases highlighting its imperfect specificity but potentially useful diagnostic applications. *Virchows Arch* 2023; 483: 145-56.
58. Kao YC, Sung YS, Argani P, et al. NTRK3 overexpression in undifferentiated sarcomas with *YWHAE* and *BCOR* genetic alterations. *Mod Pathol* 2020; 33: 1341-9.
 59. Linos K, Kerr DA, Sumegi J, Bridge JA. Pan-Trk immunoexpression in a superficial malignant ossifying fibromyxoid tumor with *ZC3H7B-BCOR* fusion: A potential obfuscating factor in the era of targeted therapy. *J Cutan Pathol* 2021; 48: 340-2.
 60. Farago AF, Demetri GD. Larotrectinib, a selective tropomyosin receptor kinase inhibitor for adult and pediatric tropomyosin receptor kinase fusion cancers. *Future Oncol* 2020; 16: 417-25.
 61. Foster-Davies H, Jessop ZM, Clancy RM, et al. Reduced S100 protein expression in malignant ossifying fibromyxoid tumors: a case report. *Plast Reconstr Surg Glob Open* 2021; 9: e3482.
 62. Sovani V, Velagaleti GV, Filipowicz E, Gatalica Z, Knisely AS. Ossifying fibromyxoid tumor of soft parts: report of a case with novel cytogenetic findings. *Cancer Genet Cytogenet* 2001; 127: 1-6.
 63. Nishio J, Iwasaki H, Ohjimi Y, et al. Ossifying fibromyxoid tumor of soft parts. Cytogenetic findings. *Cancer Genet Cytogenet* 2002; 133: 124-8.
 64. Kawashima H, Ogose A, Umezue H, et al. Ossifying fibromyxoid tumor of soft parts with clonal chromosomal aberrations. *Cancer Genet Cytogenet* 2007; 176: 156-60.
 65. Gebre-Medhin S, Nord KH, Moller E, et al. Recurrent rearrangement of the *PHF1* gene in ossifying fibromyxoid tumors. *Am J Pathol* 2012; 181: 1069-77.
 66. Sarma K, Margueron R, Ivanov A, Pirrotta V, Reinberg D. Ezh2 requires PHF1 to efficiently catalyze H3 lysine 27 trimethylation in vivo. *Mol Cell Biol* 2008; 28: 2718-31.
 67. Endo M, Kohashi K, Yamamoto H, et al. Ossifying fibromyxoid tumor presenting *EP400-PHF1* fusion gene. *Hum Pathol* 2013; 44: 2603-8.
 68. Antonescu CR, Sung YS, Chen CL, et al. Novel *ZC3H7B-BCOR*, *MEAF6-PHF1*, and *EPC1-PHF1* fusions in ossifying fibromyxoid tumors: molecular characterization shows genetic overlap with endometrial stromal sarcoma. *Genes Chromosomes Cancer* 2014; 53: 183-93.
 69. Zou C, Ru GQ, Zhao M. A *PHF1-TFE3* fusion atypical ossifying fibromyxoid tumor with prominent collagenous rosettes: case report with a brief review. *Exp Mol Pathol* 2021; 123: 104686.
 70. Srivastava P, Zilla ML, Naous R, et al. Expanding the molecular signatures of malignant ossifying fibromyxoid tumours with two novel gene fusions: *PHF1::FOXR1* and *PHF1::FOXR2*. *Histopathology* 2023; 82: 946-52.
 71. Bigot NJ, Neyaz A, Alani A, et al. Malignant ossifying fibromyxoid tumour with *TP53::PHF1* fusion: report of three cases suggesting an association between rare fusions and malignant phenotypes. *Histopathology* 2025; 87: 332-7.
 72. Killian K, Leckey BD, Naous R, McGough RL, Surrey LF, John I. Novel *MEAF6-SUZ12* fusion in ossifying fibromyxoid tumor with unusual features. *Genes Chromosomes Cancer* 2021; 60: 631-4.
 73. Kao YC, Sung YS, Zhang L, Chen CL, Huang SC, Antonescu CR. Expanding the molecular signature of ossifying fibromyxoid tumors with two novel gene fusions: *CREBBP-BCORL1* and *KDM2A-WWTR1*. *Genes Chromosomes Cancer* 2017; 56: 42-50.
 74. McEvoy MT, Blessing MM, Fisher KE, et al. A novel case of malignant ossifying fibromyxoid tumor with a *BCOR* internal tandem duplication in a child. *Pediatr Blood Cancer* 2023; 70: e29972.
 75. Micci F, Panagopoulos I, Bjerkehagen B, Heim S. Consistent rearrangement of chromosomal band 6p21 with generation of fusion genes *JAZF1/PHF1* and *EPC1/PHF1* in endometrial stromal sarcoma. *Cancer Res* 2006; 66: 107-12.
 76. Dickson BC, Lum A, Swanson D, et al. Novel *EPC1* gene fusions in endometrial stromal sarcoma. *Genes Chromosomes Cancer* 2018; 57: 598-603.
 77. Graham RP, Weiss SW, Sukov WR, et al. *PHF1* rearrangements in ossifying fibromyxoid tumors of soft parts: a fluorescence in situ hybridization study of 41 cases with emphasis on the malignant variant. *Am J Surg Pathol* 2013; 37: 1751-5.
 78. Atanaskova Mesinkovska N, Buehler D, McClain CM, Rubin BP, Goldblum JR, Billings SD. Ossifying fibromyxoid tumor: a clinicopathologic analysis of 26 subcutaneous tumors with emphasis on differential diagnosis and prognostic factors. *J Cutan Pathol* 2015; 42: 622-31.
 79. Antonescu CR, Zhang L, Chang NE, et al. *EWSR1-POU5F1* fusion in soft tissue myoepithelial tumors: a molecular analysis of sixty-six cases, including soft tissue, bone, and visceral lesions, showing common involvement of the *EWSR1* gene. *Genes Chromosomes Cancer* 2010; 49: 1114-24.
 80. Thway K, Chisholm J, Hayes A, Swansbury J, Fisher C. Pediatric low-grade fibromyxoid sarcoma mimicking ossifying fibromyxoid tumor: adding to the diagnostic spectrum of soft tissue tumors with a bony shell. *Hum Pathol* 2015; 46: 461-6.
 81. Reid R, de Silva MV, Paterson L, Ryan E, Fisher C. Low-grade fibromyxoid sarcoma and hyalinizing spindle cell tumor with giant rosettes share a common t(7;16)(q34;p11) translocation. *Am J*

- Surg Pathol 2003; 27: 1229-36.
82. Guillou L, Benhattar J, Gengler C, et al. Translocation-positive low-grade fibromyxoid sarcoma: clinicopathologic and molecular analysis of a series expanding the morphologic spectrum and suggesting potential relationship to sclerosing epithelioid fibrosarcoma: a study from the French Sarcoma Group. *Am J Surg Pathol* 2007; 31: 1387-402.
 83. Mohamed M, Fisher C, Thway K. Low-grade fibromyxoid sarcoma: clinical, morphologic and genetic features. *Ann Diagn Pathol* 2017; 28: 60-7.
 84. Meis-Kindblom JM, Kindblom LG, Enzinger FM. Sclerosing epithelioid fibrosarcoma: a variant of fibrosarcoma simulating carcinoma. *Am J Surg Pathol* 1995; 19: 979-93.
 85. Warmke LM, Meis JM. Sclerosing epithelioid fibrosarcoma: a distinct sarcoma with aggressive features. *Am J Surg Pathol* 2021; 45: 317-28.
 86. Arbajian E, Puls F, Magnusson L, et al. Recurrent *EWSR1-CREB3L1* gene fusions in sclerosing epithelioid fibrosarcoma. *Am J Surg Pathol* 2014; 38: 801-8.
 87. Warmke LM, Ameline B, Fritchie KJ, et al. *YAP1::KMT2A*-rearranged sarcomas harbor a unique methylation profile and are distinct from sclerosing epithelioid fibrosarcoma and low-grade fibromyxoid sarcoma. *Virchows Arch* 2025; 486: 457-77.
 88. Kao YC, Lee JC, Zhang L, et al. Recurrent *YAP1* and *KMT2A* gene rearrangements in a subset of MUC4-negative sclerosing epithelioid fibrosarcoma. *Am J Surg Pathol* 2020; 44: 368-77.
 89. Puls F, Agaimy A, Flucke U, et al. Recurrent fusions between *YAP1* and *KMT2A* in morphologically distinct neoplasms within the spectrum of low-grade fibromyxoid sarcoma and sclerosing epithelioid fibrosarcoma. *Am J Surg Pathol* 2020; 44: 594-606.
 90. Martinez-Rodriguez M, Subramaniam MM, Calatayud AM, Ramos D, Navarro S, Llombart-Bosch A. Ossifying fibromyxoid tumor of soft parts mimicking a schwannoma with uncommon histology: a potential diagnostic pitfall. *J Cutan Pathol* 2009; 36: 71-3.
 91. Schaefer IM, Fletcher CD, Hornick JL. Loss of H3K27 trimethylation distinguishes malignant peripheral nerve sheath tumors from histologic mimics. *Mod Pathol* 2016; 29: 4-13.
 92. Prieto-Granada CN, Wiesner T, Messina JL, Jungbluth AA, Chi P, Antonescu CR. Loss of H3K27me3 expression is a highly sensitive marker for sporadic and radiation-induced MPNST. *Am J Surg Pathol* 2016; 40: 479-89.
 93. Sbaraglia M, Bellan E, Gambarotti M, et al. Primary malignant ossifying fibromyxoid tumour of the bone: a clinicopathologic and molecular report of two cases. *Pathologica* 2020; 112: 184-90.
 94. Wang XQ, Goytain A, Dickson BC, Nielsen TO. Advances in sarcoma molecular diagnostics. *Genes Chromosomes Cancer* 2022; 61: 332-45.
 95. Kilpatrick SE, Ward WG, Mozes M, Miettinen M, Fukunaga M, Fletcher CD. Atypical and malignant variants of ossifying fibromyxoid tumor: clinicopathologic analysis of six cases. *Am J Surg Pathol* 1995; 19: 1039-46.
 96. Provenzano S, Raimondi A, Bertulli RM, et al. Response to isolated limb perfusion and chemotherapy with epirubicin plus ifosfamide in a metastatic malignant ossifying fibromyxoid tumor. *Clin Sarcoma Res* 2017; 7: 20.
 97. Lastra RR, Newman JG, Brooks JS, Huang JH. Ossifying fibromyxoid tumor metastatic to the thyroid: a case report and review of the literature. *Ear Nose Throat J* 2014; 93: 221-3.