Myoepithelioma-like tumor of the vulvar region: a SMARCB1-deficient epithelioid tumor in the vulva with indolent behavior

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Introduction

Myoepithelioma-like tumor of the vulvar region (MELTVR) is a rare and recently described entity of spindle cell neoplasm in the vulvar region with aggressive microscopic features and characteristic loss of INI-1 nuclear expression. MELTVR was firstly described by Yoshida et al. in 2015 and, to our best knowledge, only 17 cases have been reported in English journals. It morphologically resembles myoepithelioma but worrisome histology features, including cellular atypia, brisk mitosis, necrosis, and vascular invasion have been reported. It presents with a distinct immuno-profile (EMA, ER, PR positive) and a characteristic loss of INI-1 nuclear expression. SMARCB1/INI-1-deficient tumors are predominantly sarcoma with poor prognosis. However, the behavior of MELTVR was reported to be indolent and metastasis has not been documented. We would like to report a rare case of MELTVR, which is an important differential diagnosis of spindle cell neoplasm with high-grade histology features but indolent behavior.

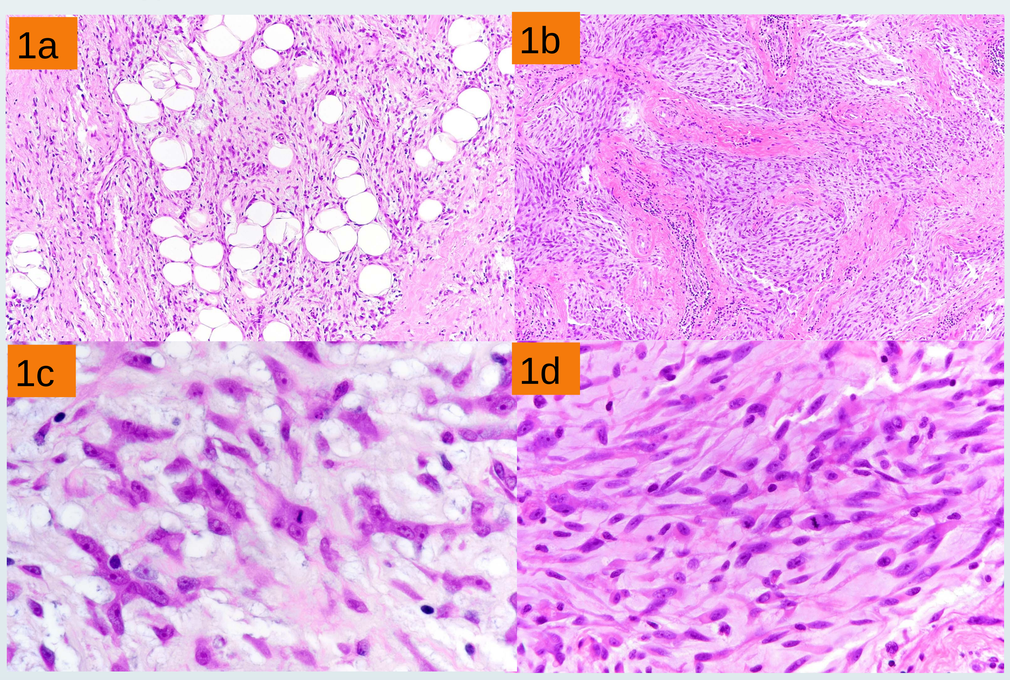
Case presentation

Clinical findings

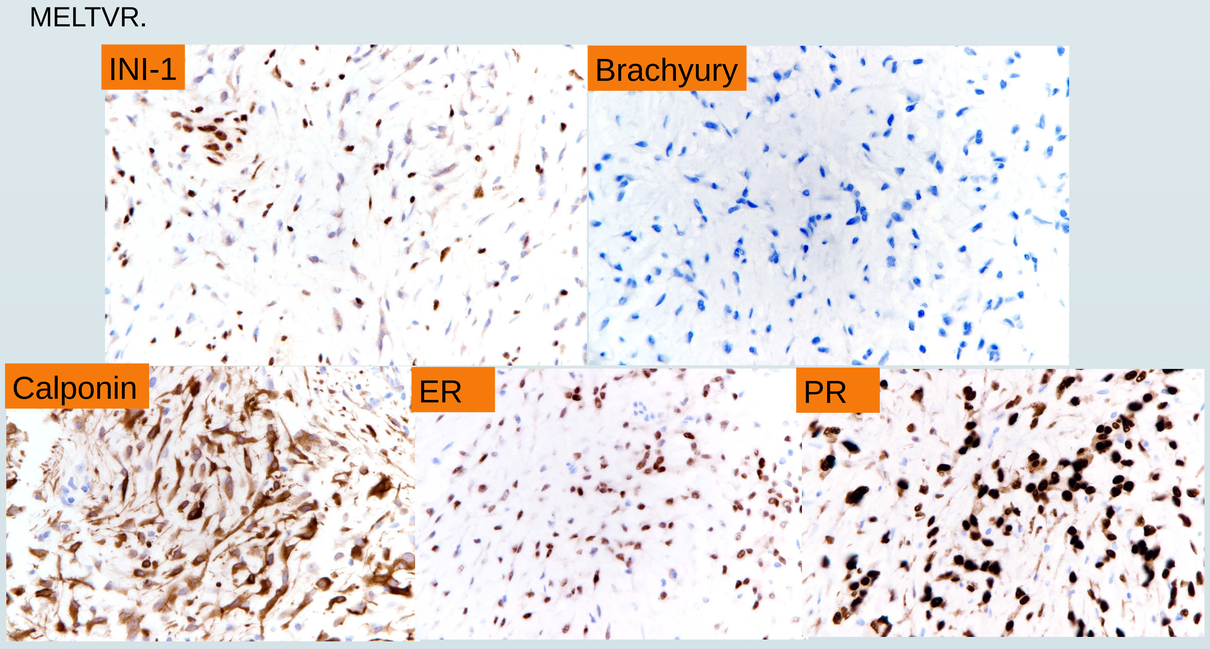
A 48 years old female presented with a gradual onset of painless vulvar swelling over 12 months. She enjoyed good past health. Physical examination revealed an elongated subcutaneous vulvar mass sized 9 cm long and 4 cm wide arising from the right anterior labia majora, extending to the mons pubis. The provisional diagnosis was vulvar leiomyoma. The mass has been excised by a gynecologist. Macroscopically, the mass was encapsulated with a smooth outer surface.

Microscopic findings

The mass was well-demarcated with a focal infiltrative border(Figure 1a). The internal histology was heterogeneous with variable myxoid and non-myxoid tumor areas. The tumor was cellular and comprised epithelioid and spindle cells in sheet, fascicular, storiform, and reticular arrangement with variable myxoid stroma (Figure 1b). The tumor cells possessed characteristic uniformly atypical nuclei, with enlarged vesicular chromatin, distinct nucleoli, and amphophilic cytoplasm (Figure 1c-1d). Mitotic count measured up to 3 per 10 high power fields. Atypical mitosis was not seen. Necrosis or vascular invasion was absent.



On immunohistochemical studies, the tumor cells were diffusely positive for EMA, ER, and PR; variably positive for calponin, and SMA; negative for cytokeratin (CAM5.2, AE1/AE3), p40, CD34, S100, GFAP, desmin, STAT6, and brachyury. Immunostaining for INI-1 shows loss of nuclear stain. The morphology and the immuno-profile were compatible with MELTVR.



Discussion

SMARCE1/INI-1 is one of the core subunit proteins of the ATP-dependent SWI/SNF chromatin remodeling complex, taking part in tumor progression and often correlating with poor prognosis.(1) Complete loss of INI-1 expression has been reported in the malignant rhabdoid tumor, epithelioid sarcoma, epithelioid malignant peripheral nerve sheath tumor, a subset of myoepithelial carcinoma, and extra-skeletal myxoid chondrosarcoma.(1) However, the behavior of MELTVR is reported to be indolent. Local recurrence was reported but metastasis was not found. Clinical, morphologic, and molecular correlation is needed to differentiate the indolent MELTVR from other aggressive SMARCE1/INI-1-deficient spindle cell tumors. The proximal variant of the epithelioid sarcomas can present in the vulva and inguinal region. It usually shows infiltrative growth, more pleomorphic nuclei, and lacks myxoid stroma. Cytokeratin and CD34 are positive while ER is negative. (2) Myoepithelial tumor, which might be morphologically undistinguishable from MELTVR, is usually located in the limbs or limb girdles. Cytokeratin, S100, and GFAP are usually positive. EWSR1 and PLAG1 gene rearrangement can be demonstrated.(2) Extra-skeletal myxoid chondrosarcomas are usually located in the deep soft tissue of extremities and show scanty stromal vasculature. EMA and ER are negative and NR4A3 gene rearrangement can be demonstrated.(2) However, these associated genetic rearrangement has not been identified in MELTVR.

MELTVR is a rare spindle cell neoplasm in the vulvar region in females; to our best knowledge, only 17 cases have been reported in English journals.(2-11) They usually present with a well-circumscribed growth pattern with at least a focal fibrous pseudocapsule and are often lobulated.(2-11) Three cases reported focal infiltrative growth.(4,8-9) Majority of the cases are composed of epithelioid and spindle cells in sheet, fascicular, reticular, and storiform patterns with at least focal myxoid stroma.(2-11) High-grade features including high-grade nuclear atypia, vascular invasion, necrosis, and increased mitotic activity up to 12 per 10 HPF have been reported but atypical mitosis is absent.(2-11) The tumor cells are diffusely or focally positive for ER, PR, and EMA but negative or rarely positive for cytokeratin, CD34, S100, GFAP. The INI-1 nuclear stain is typically lost.(2-11) Local recurrence has been reported in 3 cases but metastasis was not documented.(2-11) Our reported case showed typical morphology and immuno-profile as in the literature.

Myxoepithelioid tumor with chordoid features(METC) is a newly described SMARCA1/INI-1 loss soft tissue neoplasm, which shares similar morphology, immuno-profile, and genetic presentation as MELTVR. Kinoshita et al. described 14 cases of METC, involving 2 males and 12 females in 2021. The tumor was located in the vulva, groin, thigh, and pelvic cavity. The tumor was composed of relatively uniform epithelioid to spindle cells with at least focal myxoid stroma and variable mitotic activity. EMA, ER, and PR were positive. SMA, S100, GFAP, and cytokeratin were variable or negative. All 14 cases presented with distinctive focal brachyury positivity, which was sensitive and specific to chordoma and rarely reported in other soft tissue tumors. NR4A3 or EWSR1 gene rearrangement was absent. The behavior was intermediate, where there were 3 cases of local recurrence and 2 cases of metastasis.(12) MELC and MELTVR share almost identical morphologic and immunohistochemical presentation, except for the focal brachyury positivity. However, brachyury was not mentioned in the 17 reported cases and the result was uncertain. Our case is the first MELTVR case stained with brachyury, which was negative. More cases are needed to further study the relationship between the MELC and MELTV, which can possibly be a spectrum of the same tumor. MELTV might be found out of the vulvar region, in males and show metastasis.

Conclusion

MELTVR is a rare and newly described group of spindle cell neoplasm in the vulvar region with atypical histology features and characteristic INI-1 loss but indolent behavior. Pathologists should be aware of this indolent tumor among the other aggressive INI-1-deficient tumors.

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