

A 10-year-old Girl with Metastatic Unclassified Sarcoma with Epithelioid Features

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To the Editor: A 10-year-old girl presented with an asymptomatic ulcerated tumor on her right forearm for 18 months [Figure 1a]. The tumor initially was inconspicuous and then gradually enlarged with painless ulceration in its center [Figure 1b]. Three months later, she developed three nontender new nodules on her right arm, proximal to the initial ulcerated nodule. Her general condition was good. Skin examination revealed a 4 cm × 4 cm tumor, with central ulceration and raised margins. Three diameters in 3–5 cm, round to oval, subcutaneous nodules were palpable over her right forearm. No palpable cervical lymph nodes were detected. Histological examination revealed a tumor composed predominantly of epithelioid cells set in a myxohyaline stroma spanning the entire dermis [Figure 1c]. Aggregates of epithelioid cells were distributed in a palisading pattern around focal areas of dermal degeneration. The epithelioid cells had ample cytoplasm and vesicular nuclei, and some of them also had atypical mitotic figures. Areas of spindle-shaped cells were also present. Immunohistochemical examination revealed that most of the neoplastic cells were weakly positive for vimentin; approximately 5% were positive for Ki-67. The neoplastic cells were completely negative for CD34, CD68, epithelial membrane antigen (EMA), S100, Melan-A, CA125, smooth muscle actin, and pan-cytokeratin. The patient was diagnosed with unclassified sarcoma with epithelioid features (USEF). Chest computed tomography (CT) revealed multiple 40–80 mm nodules on both lungs [Figure 1d]. Her parents refused to consent for surgery or radiotherapy. Examination 4 months later showed enlargement of the ulcerated dermal nodule [Figure 1c], with chest CT showing increases in the nodule numbers and sizes [Figure 1e]. The location and morphological features of these multiple pulmonary nodules were indicative of malignancy. Six months after her initial diagnosis, the patient complained of chest tightness, but her parents still refused any surgery or chemotherapy.

Epithelioid sarcoma (ES) is a rare, slow-growing, soft-tissue sarcoma with granuloma-like appearance. USEF was defined as soft-tissue sarcomas with more epithelioid than spindle cells but not falling within the formal diagnostic category of ES.^[1] USEF represents a heterogeneous cohort of unclassifiable malignancies that exhibit some pathological and immunohistochemical similarities to ES, but to an insufficient degree for a diagnosis of ES. Descriptions of patients with these unclassifiable tumors are still emerging.

These tumors may be more precisely classified using special immunohistochemical markers to differentiate among tumors of epithelial, neurogenic, mesenchymal, and melanocytic cell origin. The cytokeratins are useful screening markers for epithelial differentiation.

Vimentin is the sole intermediate filament expressed by mesenchymal cells. Although the sarcomas in our patient were positive for vimentin, the staining pattern was weak and scattered.

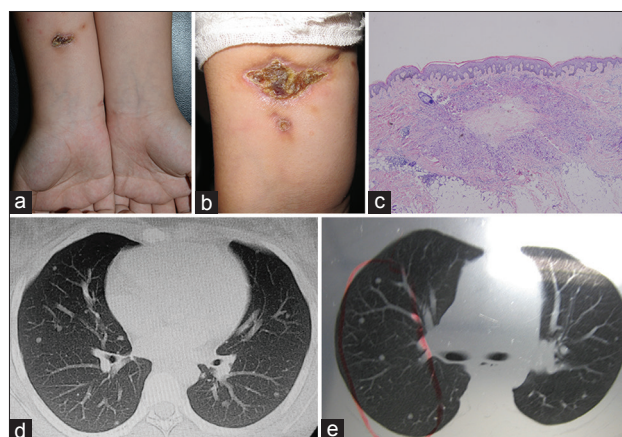


Figure 1: Asymptomatic ulcerated dermal nodule. (a) The ulcerated dermal nodule growing larger 4 months later. (b) A dense infiltrate surrounding a focal area of dermal degeneration was prominent. (c) Aggregates of epithelioid cells with ample cytoplasm and vesicular nuclei were distributed around central area of degeneration, giving an impression of palisading granuloma (H and E, original magnification ×40). (d) Multiple nodules on both sides of the patient's lung. (e) Increased number and size of nodules 4 months later.

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ES was considered in the differential diagnosis, because the tumor had histological characteristics suggesting both mesenchymal and epidermal origin. However, the absence of cytokeratin suggested other diagnoses, because almost all ES are immunohistochemically positive for keratin.^[2] Epithelioid differentiation may also be indicated by positivity for EMA, although the latter is not specific for ES.^[3]

Tumor cells were also assayed for expression of both CD34 and S-100. CD34 immunoreactivity is useful in differentiating sarcomas with epithelioid features from carcinomas. S-100 protein is regarded as a screening marker for melanoma, as it has shown >95% sensitivity in primary and metastatic melanoma. However, the tumor in our patient was negative for both CD34 and S-100. CA125 expression may also be a marker of ES, as most of these tumors are positive for CA125 expression. A previous study found that 12 of 15 USEF samples were negative for CA125 as was the tumor in our patient.^[1]

Follow-up of patients with localized ES found that 35% developed lymphatic metastases.^[1] In contrast to the high rates of local and systemic failure of ES, patient outcomes are relatively favorable, with a 5-year overall survival (OS) rate of 60–75%. Moreover, the 5-year disease-specific survival (DSS) rate for localized ES was 88%. In comparison, 19% of patients with USEF developed lymphatic metastases and 14% developed brain metastases, suggesting the need for a tailored follow-up approach. Patients with USEF had a 5-year DSS rate of 52% and median OS and DSS of 4.7 years each. Although median survival times were shorter among patients with USEF than ES, the differences were not significant.

The 2013 World Health Organization classification of tumors^[4] regards USEF as an unclassified sarcoma due to the absence of a demonstrable line of differentiation and the lack of distinguishing histologic, immunohistochemical, and genetic features. These tumors may have epithelioid, spindled, pleomorphic, and/or round cell morphological features. Further proteomic approaches are required to confirm their origins and classifications, thereby improving clinical outcomes of patients with these unclassified sarcomas.

Similar to other soft-tissue sarcomas, USEF is an aggressive malignancy, making wide and complete surgical resection the

only potentially curative treatment. Wide surgical resection and high-dose chemoradiotherapy can lower the rates of local recurrence and metastases.^[5]

Additional immunohistochemical and morphological investigations would be useful for the exact categorization and standard treatment of these yet unclassified sarcomas.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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