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Case Report

An Exceptional Vulvar Tumor: Myeloid Sarcoma of the Labia Majora

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Summary: Vulvar malignancies are rare and have diverse origins and presentations. The majority of these tumors are squamous cell carcinoma. An ulcerating vulvar tumor was found in a 74-yr-old woman presenting with fatigue and leukocytosis. Tumor biopsy revealed infiltration of blastoid cells from myeloid origin. Through bone marrow aspiration chronic myelomonocytic leukemia was diagnosed, of which the vulvar tumor was a rare extramedullary disease manifestation termed myeloid sarcoma. Limited palliative treatment was instated with a focus on the patient's quality of life. Myeloid sarcoma (chloroma; granulocytic sarcoma) is a mass of myeloblasts occurring in cases of myeloid disease. Manifestations in most organ systems have been described. Presentation in gynecologic areas is reported in a few case reports, to which we now add our experience. **Key Words:** Myeloid sarcoma—Granulocytic sarcoma—Vulvar malignancy—Myeloid leukemia—Chronic myelomonocytic leukemia.

Malignancies of the vulva are rare and will not be every gynecologist's subject of expertise. They make up for only 0.7% of all cancers in women and 2% to 6% of gynecologic cancers. As such, care is often specialized. Premalignant and malignant vulvar tumors are, however, among the cancers with most rapidly increasing incidence rates (1). Even though treatment remains primarily surgical, it is important to recognize different subtypes of vulvar cancer, as prognosis and survival rates may vary. These also depend on staging, tumor thickness, and classification of disease progression.

Squamous cell carcinoma accounts for $>90\%$ of all vulva malignancies. It most often presents as a solitary lesion, either endophytic and ulcerated or exophytic and nodular (2). Two main types can be identified. The keratinizing type (78%) is associated with higher age and pre-existing chronic dermatoses such as lichen sclerosus. The non-keratinizing type, which may be warty or basaloid, is less common and occurs in younger women. It may be associated with HPV-infection. Five-year survival varies between 90% and 40% on the basis of extensiveness of disease (1,2).

Malignant melanoma is the second most common vulvar tumor, with the reported incidence ranging from 3% to 10%. It can be recognized by the same characteristics as cutaneous melanoma. Unlike cutaneous melanoma, its carcinogenesis is unrelated to ultraviolet radiation. It most often manifests on the labia minora or clitoris. An acral-lentiginous form and a superficial spreading form can be differentiated. Prognosis is poor, 5-yr survival ranging from 27% to 60%, partly caused by typically late diagnosis (1,2).

Basal cell carcinoma, the most common type of skin cancer, rarely manifests on the female genitalia due to its strong association with exposition to UV rays. It accounts for 2% to 3% of vulvar cancers and has the same appearance as elsewhere on the body: nodular or ulcerated lesions with raised margins.

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Adenocarcinoma of the vulva is rare (incidence 2%) and diverse, originating from inter alia the mammary-like glands of the vulva, the Bartholin glands, or the apocrine sweat glands. Examples are extramammary Paget disease or breast-like vulvar adenocarcinomas. These tumors are aggressive, and prognosis is extremely poor, with 5-yr survival rate at 0% (1).

There is obviously a great diversity among vulvar malignancies, some manifestations being only described in case series. In this manuscript, we present an even more unusual tumor of the vulva.

CASE REPORT

A 74-yr-old woman was referred by the general practitioner to our secondary care center in Dordrecht, the Netherlands, with unexplained leukocytosis. The patient's past medical history included diabetes mellitus type II and osteopenia. She presented with progressive fatigue for 5 mo and dyspnea without a cough for the past month. Within the last month she had also experienced significant unexplained weight loss of 8 kg. The patient consulted the general practitioner because chest pains had started to accompany her breathing problems.

Physical examination revealed a solitary ulcerated tumor on the caudal side of the labium majus dextrum, 2×2 cm in size (Fig. 1). It had a crater-like appearance with raised, sharply defined margins and green-yellow slough in the center. There were multiple ecchymoses and petechiae on her back. Differential blood count demonstrated hemoglobin of 9.8 g/dL (normal range: 11.7–13.8 g/dL), thrombocytopenia of 43×10^9/L (normal range: 150–450×10^9/L), and leukocytosis of 21.5×10^9/L (normal range: 4–11×10^9/L) with 21% monocytes and 12% blasts. A high-grade myeloid leukemic disorder was suspected. Bone marrow morphology by aspiration showed trilineage dysplasia with 15% blasts and 24% monocytes. Splenomegaly with a midclavicular length of 17 cm without focal pathology was reported on abdominal ultrasound. No explanation for the dyspnea was found on pulmonary CT.

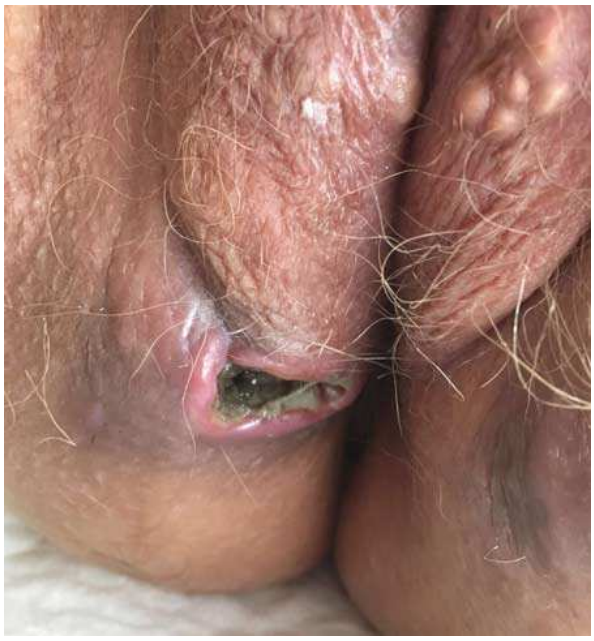

FIG. 1. Myeloid sarcoma of the labium majus dextrum.

Biopsy of the vulva showed a diffuse infiltrate of medium-sized cells in the dermis and underlying fat, with little cytoplasm and blastoid features (Fig. 2). Between these larger cells were small lymphocytes, plasma cells, and some neutrophils present. Immunohistochemistry showed strong positivity of the blastoid cells for myeloid peroxidase, demonstrating that the cells are derived from the myeloid lineage (3). The cells were also positive for CD68 and partially positive for CD4. The blastoid cells stained negative for CD34, CD56, and CD117. Ki-67 showed a high proliferation index in these cells (> 90%). A bone marrow biopsy was not performed. Flowcytometry of the bone marrow aspirate showed that the blasts were positive for myeloid peroxidase, but also for CD34 and CD117. Although the blast cells in the vulvar biopsy did not show staining for CD34 or CD117 histologically, the morphology of the tumor cells, expression of myeloid peroxidase, and high proliferation index are consistent with an extramedullary manifestation of a myeloid leukemia. Cytogenetic analysis showed a normal karyotype.

On the basis of these findings, myeloid sarcoma was diagnosed: an extramedullary manifestation of the underlying chronic myelomonocytic leukemia. Considering the low life expectancy of myeloid sarcoma associated with chronic myelomonocytic leukemia at this age, after extensive deliberation with the patient, the decision was made to abstain from further intensive treatment (3,4). The patient was discharged from the hospital after 6 d with morphine and hydroxyurea. The general practitioner supervised further palliative care. The patient passed away 2 mo after initial presentation.

DISCUSSION

Myeloid sarcoma, also known as granulocytic sarcoma, is a rare potential manifestation of several myeloid disorders. It is defined as a tumor mass of myeloblasts,

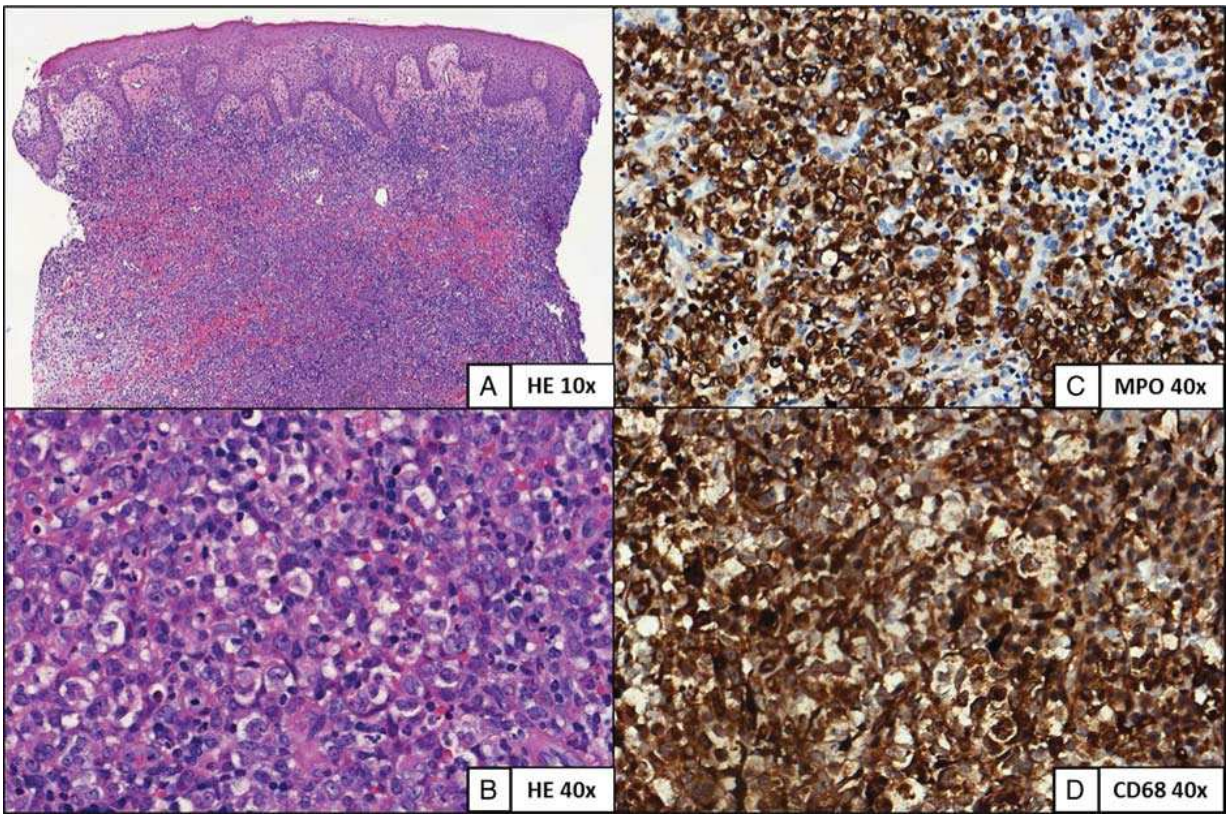

FIG. 2. Immunohistochemical staining on tumor biopsy. (A and B) Lymphoid cells with blastoid features. (C) Immunohistochemical staining result is positive for myeloid perixodase. (D) Immunohistochemical staining result is positive for CD68.

immature myeloid cells, in an extramedullary location (5). Myeloid sarcoma most often either precedes or accompanies acute myeloid leukemia (AML). Less often, it presents in relation to other myeloid disorders like myelodysplastic disorder, myeloproliferative neoplasm, or chronic myelomonocytic leukemia—as in this case (5).

Although it is a rare phenomenon, multiple isolated reports of manifestations in most organ systems are described in the literature (6). Incidence rates are unknown, but skin, bone, and lymphatic tissue appear to be affected most often (7). Occurrence in the female genital tract has thus far been reported in case reports and reviews of the literature, most often concerning the uterus (8). Only a handful of cases involve manifestations in the lower genital tract. Lee et al. (9), Pathak et al. (10), Kilic et al. (11), and Henes et al. (12) described myeloid sarcoma of the cervix. All these patients presented with abnormal vaginal bleeding. In half of the cases, AML was diagnosed concurrently to analysis of the gynecologic pathology; in the other half, there already was a history of myeloid leukemia. One patient died within days of initial presentation, the other 3 went in remission after chemotherapy. Policarpio-Nicolas and colleagues and Skeete and colleagues present 3 cases of vaginal myeloid sarcoma, all patients first presenting with palpable masses of the vaginal walls. In one 16-yr-old patient, there was no accompanying leukemic involvement found despite additional examnations including bone marrow biopsy, making this a rare isolated myeloid sarcoma (7). After chemotherapy she went into remission. The other 2 patients with vaginal myeloid sarcoma passed away due to complications of AML within 6 mo after presentation (7,13).

To our knowledge, only 3 case reports of myeloid sarcoma of the vulva have been published, making this an extremely unusual finding (8,14,15). Ersahin and colleagues reported a similar case in 2007, involving a 73-yr-old woman with an ulcerating tumor of the labium majus, after which AML was diagnosed. In this case, chemotherapy was chosen instead of palliative care, but the patient also did not survive past 6 months after diagnosis (8). Yu and colleagues describe a younger patient, 45-yr old, presenting with vaginal blood loss and masses of the vulva, vagina, and cervix (15). No leukemic disorder could be diagnosed on bone marrow biopsy at that point.

The patient received one cycle of chemotherapy, but refused all examination and treatment thereafter. She died 4 mo later. The last case report, by Hu and colleagues in 2016, involves a 40-yr-old woman with a history of myelodysplastic syndrome. Two weeks after consultation for a vulvar tumor she developed AML. She passed away after neutropenic fever during chemotherapy, 3 mo after diagnosis (14).

The literature shows poor survival for myeloid sarcoma in the lower female genital tract, as is illustrated in our own case report. This is most often the result of rapid progression of underlying leukemic disease. The literature warns of delays and misdiagnosis (12). We advise a thorough history and physical examination when confronted with leukemic disease. When a patient first presents with a tumor mass that is identified as myeloid sarcoma, additional examinations like a complete blood count, bone marrow aspiration and/or bone marrow biopsy should be performed because of the high probability of concurrent leukemic disease. This determines the prognosis. As leukemic disease may develop even months after initial presentation, strict follow-up is crucial (10). In our patient, recognizing this exceptional vulvar tumor as myeloid sarcoma was aided by the simultaneous diagnosis of underlying leukemic disease. However, it definitely is a rarity even among the very diverse range of vulvar tumors that we can currently distinguish.

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