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CASE REPORT AND LITERATURE REVIEW

From Mystery Mass to Menacing Marrow: Uterine Myeloid Sarcoma Preceding the Diagnosis of Acute Myeloid Leukemia - Case Report and Literature Review

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Abstract

Uterine myeloid sarcoma (MS) is an extramedullary solid tumor composed of leukemic myeloid cells. It is an uncommon tumour usually accompanied by acute myeloid leukaemia (AML). We report a case of a 64-year-old woman with a cervical-uterine mass followed by vaginal postmenopausal bleeding. Initially she was treated with supracervical hysterectomy, bilateral adnexectomy and partial omentectomy and had no systemic sings that could suggest AML. Second postoperative day she developed thrombocytopenia and anemia, followed by febrile neutropenia in the fourth postoperative day. Bone marrow biopsy revealed 68% of blasts consistent with acute myeloid leukaemia with maturation (AML-M2) according to The French-American-British (FAB) classification. Immunohistochemical stains revealed that neoplasm was positive for myeloperoxidase (MPO) and C117, as well as negative for CD20, CD3, CKAE1/AE3, CD34 and CD14. The patient was treated with chemotherapy. Because it is a rare entity, as far as we know, early intensive AML type therapy is the treatment of choice.

Keywords

Myeloid sarcoma, Acute myeloid leukaemia, Postmenopausal bleeding

Introduction

Myeloid sarcoma (MS) is a rare disease, with incidence estimated at 2 per million in adults [1]. Also known as granulocytic sarcoma or chloroma (due to a green colour attributed to the enzyme myeloperoxidase first described by Burns in 1823), it is an extramedullary blasts proliferation of one or more myeloid lineages that disrupt the normal architecture of the tissue in which they are found [2,3]. Initially, it may present as an isolated extramedullary disease (less than 1% of cases), simultaneously with (15-35% of cases) or following (50% of cases) previously diagnosed acute myeloid leukaemia (AML) [3,4]. In 2-8% of cases, it occurs as an AML relapse [5]. Less often, it can be associated with myeloproliferative neoplasm (MPN) or myelodysplastic syndrome (MDS) [2,3]. Regardless of intramedullary disease presence, the most commonly involved sites include skin, bone, and lymph nodes, but it can involve the intestine, mediastinum, breast, and genitourinary tract as well [1-3,5-7]. Depending on the size and location, the most common signs are compression pain and bleeding [2,3,6].

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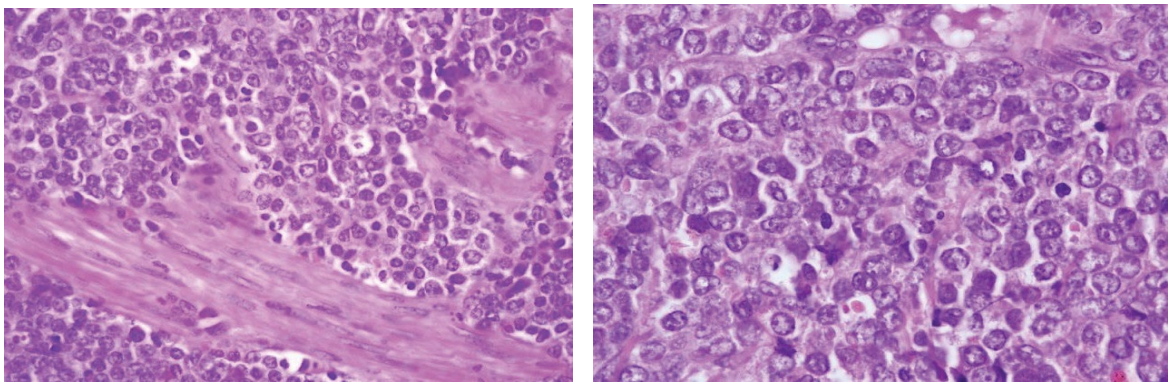

Figure 1: Leukemic cells infiltrating myometrium: (a) HE, 60x; (b) HE, 100x.

The diagnosis is confirmed pathohistologically. Imaging methods, including computerized tomography, magnetic resonances, and positron emission tomography-computed tomography, are also used in diagnostics and follow-up [8]. In this article, we are presenting a case of myeloid sarcoma involving the uterus, with initial postmenopausal bleeding manifestation, followed by the development of AML.

Case Report

A 64-year-old postmenopausal woman (gravida 2, para 2) presented to our institution complaining of vaginal bleeding for 14 days. The bleeding was irregular, small to moderate amount, without clots or pain. She had never had a similar episode for the last 20 years, when she entered menopause respectively. Our patient had experienced subarachnoid haemorrhage 14 years ago which was conservatively treated. For the past decade she has had arterial hypertension. She did not have a family history of bleeding diathesis or malignancy. Her PAP smear was negative for intraepithelial malignancy. Physical examination revealed a 5 cm mass in the vagina, protruding from the cervix, which was fragile and bled easily. The mass was infiltrating, but spared the rectum, the bladder and pelvic wall. Blood counts were normal with a white cell count of 4.9 × 10^9/L, hemoglobin 128 g/dL, platelets 137 × 10^9/L and normal white cell differential. Lactate dehydrogenase (LDH) levels and uric acid levels were within reference ranges suggesting that there wasn't any laboratory sign of tumor lysis syndrome. As the tumor was highly suspicious of carcinoma, she underwent laparotomy with supracervical abdominal hysterectomy, bilateral adnexectomy and partial omentectomy. Despite only minimal lood loss during surgery, in the first postoperative day, the patient had thrombocytopenia (platelets 54 × 10^9/L) and anemia haemoglobin (Hb) 98 g/dL. In the second postoperative day the patient suddenly appeared very pale - thrombocytopenia (platelets 48 × 10^9/L) and anaemia haemoglobin (Hb) 85 g/dL accompanied by vaginal bleeding. The patient was given 8 doses of platelets and 2 red blood cells concentrates. Our first differential diagnosis was heparin induced thrombocytopenia, but we excluded it. Peripheral blood revealed 31% of atypical blast cells, 3% of promyelocytes and 1% of myelocytes, as well as anisocytosis and poikilocytosis. In the fourth postoperative day, the patient had elevated body temperature - max. 38.6 °C, so along with cefazolin sodium 3 × 1g i.v., meropenem 2 × 1g i.v. was introduced. Both wound smear and hemocultures were sterile. Histopathology sections from the sample revealed infiltrating neoplastic lesion composed of sheets of atypical, undifferentiated, uniform large round mononuclear cells (Figure 1). Tumour cells were positive for myeloperoxidase (MPO) (Figure 2) and CD 117 (Figure 3). They were negative for

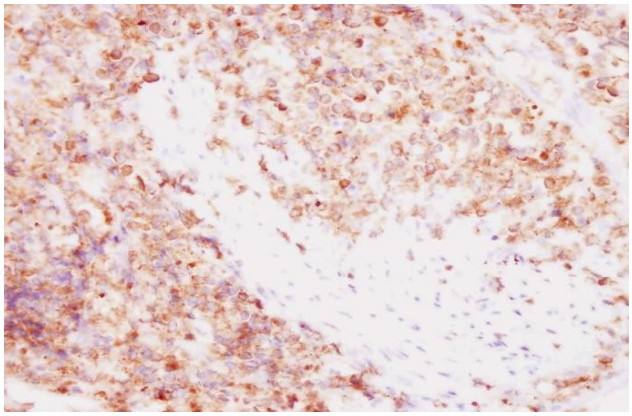

Figure 2: Leukemic cells stained positive for MPO, 60x.

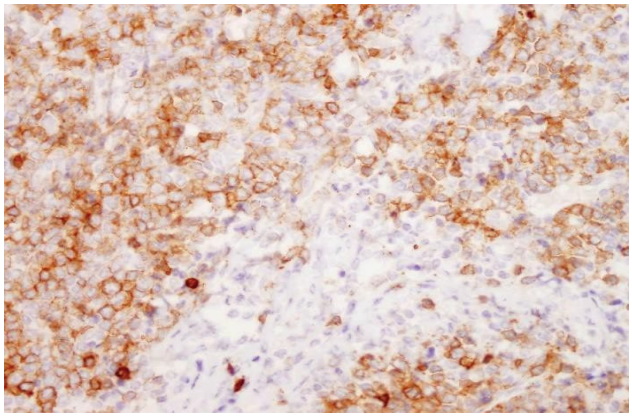

Figure 3: Leukemic cells stained positive for C117, 60x.

CD20, CD3, CKAE1/AE3, CD34 and CD14, consistent with a diagnosis of MS. Bone marrow biopsy revealed 68% of myeloblasts - acute myeloid leukemia with maturation (AML-M2) according to The French-American-British (FAB) classification. The patient was treated with induction therapy: 7 days of citarabyne 100-200 mg/m^2 per day and 3 days of daunorubicine 60 mg/m^2. Since it is newly diagnosed acute myeloid leukemia, positive for FMS-like tyrosine kinase 3 (FLT3) mutations, 4 cycles of intermediate dose cytarabin therapy (IDAC) with midostaurin was administered from 8.0-21.0 day of cycle. Until allogeneic stem cell transplantation (allo-SCT), bridging therapy with azacitidie (AZA) was administered to reduce the incidence of accure Graft-versus-host disease.

Discussion

Due to its rarity, diagnosis of MS can be challenging, and it is often misdiagnosed with malignant lymphoma, undifferentiated carcinoma, sarcomas (particularly Ewing's sarcoma), small cell carcinoma and granulosa cell tumour [8,9]. In the female genital tract, it appears to have a predilection for the ovary estimated up to 36.4% [1,9]. However, in some case series, the uterus was also the site most commonly involved [4,10,11]. Gu Y, et al. [4] reported uterine involvement in 5 out of 8 patients with gynaecological MS. In the report of 11 cases by Garcia MG, et al. [11], the uterus was the site of MS in 8 patients. Uterine cervix tends to be infiltrated in more cases than the uterine body [4,11-13]. Although considered a rare entity, frequent involvement of female reproductive organs in post-mortem studies of AML patients suggests possible under diagnosis of gynecologic MS [6,9]. In ovarian MS, clinically significant symptoms are usually absent, and many of the cases are reported on autopsy [14]. Uterine or cervical MS may be less common, but clinically, it is symptomatic earlier and more easily diagnosed [1-3,5,6,9,14]. Most women present with abdominal pain, abnormal vaginal bleeding, postcoital bleeding, or postmenopausal bleeding [1,2,5,6,9]. Systemic manifestations include fever, night sweats, and weight loss [1]. The mechanism by which myeloid blasts infiltrate the endometrium still remains unclear. Myeloid sarcoma as a first manifestation of the disease is uncommon and most of the women develop acute myeloid leukaemia within 8 days to 28 months (mean 10 months) [1,5]. That is why patients with MS need a close follow-up of their hematologic parameters. Immunophenotype is variable and depends on the stage of the leukemic cells maturation. Most cases stain positive for CD68 KP1, accounting for 92-100% [8]. The expression of other myeloid leukaemia markers, including CD33, CD43, HLA-DR, CD117, and MPO, is reported in 40-95% of cases [7]. Approximately 30% of cases express CD34, particularly more immature profile tumours, while the CD14 expression is documented in only 13% of cases [7,8]. In the presented patient, tumour cells stained positive for C117 and MPO, lacking the expression of CD34, CD14, and leukocyte markers.

Markers of the B- and T-lineage, particularly CD20, may help to exclude lympho proliferative disorders, although aberrant expression in MS is reported [7,8]. FLT3 mutations are detected in about 30% of MS patients [7,8]. In AML, it appears to be associated with an increase of recurrence risk. However, yet there is no study observing prognostic significance in MS [15]. Though clinical preoperative diagnosis is difficult, therapeutic options after the surgery are even more problematic. MS should be looked at as a part of a broader systemic disease, rather than an isolated feature. Possibly induction chemotherapy, associated with an allogenic transplant with an HLA-matched donor, could be a treatment of choice [1,3,6,9]. Radiotherapy may prevent local relapse but is unlikely to change the course of systemic disease [1-3,6,9]. The prognostic impact of MS remains unclarified. According to recent studies, the overall survival and event-free survival appear to be longer or similar in isolated MS patients compared to AML patients with or without extramedullary disease. These findings are contrary to those of previous studies, showing poor outcomes in MS patients. The organ-specific impact has also been reported, with better outcomes in MS involving the gastrointestinal mucosa, urinary tract, and reproductive organs. These findings, however, are not confirmed by other studies [7,8]. Additional studies are necessary for better understanding and treatment of myeloid malignancies.

Conclusion

In conclusion, myeloid sarcoma is a rare and challenging diagnosis with diverse clinical presentations and potential misinterpretations, often mimicking other malignancies. The case of our 64-year-old postmenopausal patient, initially presenting with vaginal bleeding, underscores the importance of considering myeloid sarcoma in the differential diagnosis of gynaecologic masses, particularly when atypical hematologic parameters are observed. We cannot emphasize enough the need for a comprehensive approach in the assessment of unusual gynaecologic symptoms. Management still remains a clinical challenge, requiring a systemic perspective rather than focusing solely on localized treatment. It is essential to recognize that myeloid sarcoma represents a component of a broader systemic disease, necessitating a vigilant follow-up of hematologic parameters for timely detection and management. The prognosis associated with myeloid sarcoma is unfavourable and the overall 2-year survival rate remains low. There is the urgency of further research and exploration of treatment modalities.

Declarations of Interest

None.

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