Granulocytic sarcoma involving the uterus and right fallopian tube with negative endometrial biopsy

G. Kilic[1], *M.D.*; M.C. Boruban[1], *M.D.*; C. Bueco-Ramos[2], *M.D., Ph.D.*; S.N. Konoplev[2], *M.D.*

[1]Departments of Gynecologic Oncology, [2]Deparment of Hematopathology
The University of Texas M. D. Anderson Cancer Center, Houston, Texas (USA)

Summary

Granulocytic sarcoma is an extramedullary tumor associated with acute myelogenous leukemia (AML) and it is rarely seen in the female genital tract. We report an unusual case of granulocytic sarcoma of the uterus and fallopian tube in an AML patient who presented with vaginal bleeding and persistent abdominal pain. She was under chemotherapy. Biopsy did not reveal the diagnosis. After laparoscopic examination, hysterectomy with bilateral salpingo-oophorectomy was performed. Pathology showed atypical myeloid cells infiltrating the muscle bundles which was consistent with granulocytic sarcoma involving the uterus and right fallopian tube. Immunohistochemistry confirmed the diagnosis. The patient is in complete remission for AML and being followed-up for granulocytic sarcoma. Granulocytic sarcoma of the uterus and fallopian tube is very rare, and in AML patients with abnormal uterine bleeding but negative endometrial biopsy it should still be considered in the differential diagnosis.

Key words: Acute Myeloid Leukemia; Abnormal uterine bleeding; Granulocytic Sarcoma; Uterus; Fallopian tube.

Introduction

Granulocytic sarcoma of the female genital tract is a rare occurrence [1]. Granulocytic sarcoma, which is also known as monocytic sarcoma, myeloblastoma or chloroma, is characterized by solid aggregates of malignant myeloid blastic cells and occurs most often in patients with acute myelogenous leukemia (AML) [2]. Granulocytic sarcoma may involve any site outside the bone marrow, including the breast, orbital region, skin, brain, and spinal cord [3]. We present a case of granulocytic sarcoma with involvement of the uterus and right fallopian tube diagnosed during the treatment of AML in whom endometrial biopsy revealed no evidence of malignancy but the surgical specimen after hysterectomy/salpingo-oophorectomy revealed granulocytic sarcoma. Synchronous involvement of the uterus and fallopian tube is a rare situation. Abnormal uterine bleeding in leukemia patients may be due to granulocytic sarcoma even if the biopsy is negative.

Case Report

A 45-year-old female developed increasing fatigue, dyspnea on exercise and low-grade fever which worsened two weeks before her admission to the hospital. She presented to MD Anderson Cancer Center with a total white blood cell count of 43.2 x 10^3/μl (4% neutrophils,18% lymphocytes, 72% monocytes, and 5% blasts), hemoglobin of 8.2 g/l, hematocrit of 21.5%, platelet count of 30 x 10^6/μl, beta-2 microglobulin of 6.1 mg/l, IgG of 2.070 mg/dl, IgA of 475 mg/dl, blood urea nitrogen of 17 mg/dl, and creatinine of 2.8 mg/dl. Her chest X-ray and EKG were negative. After bone marrow aspirate biopsy and genetic examination she was diagnosed with acute myeloid leukemia with inv(16)(p13q22) (WHO classification) with abnormal eosonophils (AML-M4E) (FAB). Flow cytometric analysis of bone marrow aspirate revealed a large blast population with myelomonocytic differentiation. There were two subpopulations of blasts, one with characteristics of myeloblasts expressing CD117 and CD34 and another one showing more monocytic differentiation.

The patient was involved in a protocol with fludarabine and cytarabine. The chemotherapy was complicated by febril neutropenia and she was also complaining of long menstrual periods with heavy bleeding. The complete blood count during this period showed a white blood cell count of 7100/μl, hemoglobin 10.3 g/l, hemotocrit 28.5% and platelets 336,000 K/UL. During physical examination, active vaginal bleeding was observed. Gynecologic exam, pelvic ultrasonography, and a Pap smear revealed dysfunctional uterine bleeding with no evidence of malignancy. Endometrial biopsy revealed weakly proliferative endometrium with marked stromal, glandular breakdown and papillary syncytial metaplasia. As the symptomatic vaginal bleeding was interrupting her chemotherapy, the patient was taken to the operating room for microwave vaginal ablation. Shortly after this management, she was admitted to the emergency room with the complaint of constant pelvic pain. Her pain did not resolve with a conservative approach and she underwent diagnostic laparoscopy. Because of the previous history of pelvic inflammation and multiple omental adhesions an open hysterectomy with bilateral salpingo-oophorectomy was performed.

Pathologic examination of sections of the uterus and right fallopian tube showed atypical myeloid cells. An infiltrate composed of differentiating myeloid cells, with a marked increase in immature cells, was observed between muscle bundles and associated with extensive necrosis and infarction. Immunohistochemical and histochemical stains revealed that the infiltrate was positive for CD117, CD34, myeloperoxidase and naptol AS-D choloacetate (Figure 1).

Twenty months after surgery the patient is in complete remission in terms of both AML and granulocytic sarcoma. She is

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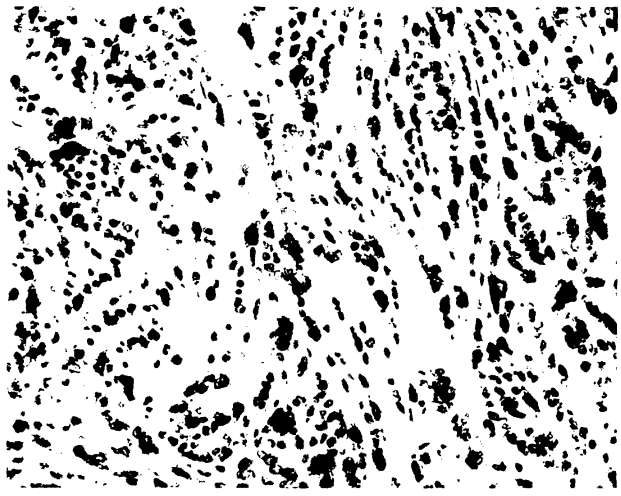

Figure 1. — Myeloperoxidase immunostain showing many positive blasts.

being followed-up annually by physical examination and computed tomography of the abdomen and pelvis for granulocytic sarcoma. At the last control she was in remission.

Discussion

Granulocytic sarcomas are rare extra medullary tumors consisting of myeloid progenitor cells. They usually include diffuse infiltration of myeloid precursor cells along with aggregates of lymphocytes. These cells may be in different maturation stages and in varied percentages; blasts, immature cells or mature differentiated cells [4].

Initially, the term "chloroma" was used in the literature because of the characteristic green tinge of the myeloperoxidase enzyme that can be differentiated grossly. Subsequently, Neiman *et al.* described the clinicopathologic features of a large series of patients with granulocytic sarcoma, but they also included cases with leukemic infiltrates that did not form tumors. Davey *et al.* recommended the term extramedullary myeloid cell tumor to include lesions that formed masses and nondestructive leukemic infiltrates [5, 6].

Granulocytic sarcoma occurs primarily in patients with AML but may also arise in patients with myeloproliferative and myelodysplastic syndromes. The diagnosis of granulocytic sarcoma is appropriate when immature myeloid cells are observed to form a mass in patients with known AML, patients with chronic myeloproliferative disorders, and patients with no additional clinical confirmation of hematologic disease at diagnosis [7, 8].

The mean age at presentation of cervical granulocytic sarcoma in the literature is 47 years, ranging from 26-75 years of age [9].

Extramedullary AML occurs more commonly in the spleen, liver, lymph nodes, central nervous system, testes, gastrointestinal tract, lung and kidneys. Rare sites of relapse include the skin, pancreas, bladder, peritoneal cavity, pleura and thyroid. Involvement of the female genital tract is rare [10].

In our review of the literature we found that the most frequently involved sites of the gynecologic tract with granulocytic sarcoma were the ovary and uterus. Synchronous involvement of the uterus and fallopian tube was rare.

Granulocytic sarcoma may occur in 3-7% of cases of AML during the course of the disease. It is often asymptomatic depending on the site and hence may not be diagnosed [11-13].

However, asymptomatic disease is more common in ovarian involvement with AML. The incidence of clinically evident and significant disease complicating the course of AML is less than one percent [14, 15].

Granulocytic sarcoma can be difficult to diagnose by biopsy. In the case reported here, endometrial biopsy revealed a weakly proliferative endometrium with marked stromal and glandular breakdown of papillary syncytial metaplasia. Granulocytic sarcomas are often undifferentiated and hence may be misdiagnosed on biopsy specimens. In a series of 61 granulocytic sarcoma cases, only 44% of patients were initially given the correct diagnosis of granulocytic sarcoma [16]. The diagnosis of granulocytic sarcoma is especially difficult when the tumor mass precedes the diagnosis of leukemia, has an unusual location, is poorly differentiated, or does not have a green tint (chloroma) [9]. Furthermore, in cases of isolated granulocytic sarcoma following the onset of AML, a misdiagnosis of lymphoma is frequent. For that reason performing immunohistochemistry is recommended in any case where the morphology of the tumor cells suggests the possibility of granulocytic sarcoma [4, 17, 18].

In our case, the diagnosis of granulocytic sarcoma of the uterus and right fallopian tube was established by pathologic assessment of the hysterectomy specimen and immunohistochemical staining.

Granulocytic sarcoma of the female genital tract is infrequent and synchronous involvement of the uterus and fallopian tube is rare. During evaluation of abnormal uterine bleeding in leukemia patients the possibility of granulocytic sarcoma should be considered, even with negative endometrial biopsy. Immunohistochemistry may reduce the risk of misdiagnosis and further evaluation is reasonable.

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Address reprint requests to:
G. KILIC, M.D.
Department of Gynecologic Oncology
P.O. Box 301439,
Houston, Texas 77030 (USA)