Case Report
Ovarian granulocytic sarcoma as the primary manifestation of acute myelogenous leukemia

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Abstract: Granulocytic sarcoma (GS) usually occurs concomitantly with or after the onset of acute myeloid leukemia (AML) or other myeloproliferative disorders, however, GS of the ovary as the primary manifestation of AML is exceedingly rare. To the best of our knowledge, eight cases of ovarian GS as the first sign of AML have been reported in the literature. Here, we report the ninth case: a 27-year-old female who presented with an ovarian mass without any underlying hematologic disorder. A high index of suspicion aided by immunohistochemistry established the correct diagnosis of undifferentiated GS that involved the ovary. Simultaneously, laboratory findings indicated that the blood counts continually increased after surgery. Five days after the surgery, bone marrow biopsy confirmed the presence of AML. After establishing the diagnosis, the patient was sent to the hematology department to receive cytosine arabinoside and idarubicin chemotherapy. This report outlines an exceedingly rare case of AML that initially manifested as an ovarian GS. Awareness of this entity will enable earlier diagnosis and appropriate treatment.

Keywords: Ovary neoplasm, granulocytic sarcoma, chloroma, acute myelogenous leukemia

Clinical summary

A 27-year-old female presented with complaints of an abdominal mass and 1-month history of abdominal pain. Routine blood examinations at presentation were normal. Pelvic ultrasound revealed a 10.8 × 10.3 × 8.5 cm solid mass posterior to the uterus. Imaging confirmed the presence of a large, cystic-solid, adnexal mass in the region of the left adnexa measuring 11 × 10 × 8.5 cm (Figure 1) that was likely a malignant ovarian mass. The mass was heterogeneous with several areas of necrosis and involved the left pelvic sidewall. The uterus and right ovary were reported to be normal. The levels of serum tumor markers were normal, and left salpingo-oophorectomy and infracolic omentectomy were performed to confirm that the ovarian mass was malignant.

The mass was encapsulated and its surface was smooth. The sectioned surface showed solid tumor tissue with raised, lobulated areas that were grey-yellow in color. The frozen section was identified as a poorly differentiated sex cord-stromal tumor. Sections of fixed paraffin-embedded tissue revealed diffuse proliferation of small- to moderately-sized cells that were arranged in sheets and at times focally exhibited a cord-like pattern. Focal necrosis was noted. These cells were non-cohesive with an irregular nuclear membrane, and some cells showed angulated nuclei, finely dispersed nuclear chromatin, small nucleoli, and a high nucleocytoplasmic ratio. Mitosis was readily apparent (Figure 2A-E). Due to the appearance of the tumor, multiple immunohistochemical analyses were performed, including staining for CK7, EMA, vimentin, inhabin-α, PLAP, actin, CD99, S-100, CD117, and Ki 67. The tissue was negative for these markers except for vimentin (+), inhabin-α, PLAP and CD99 (weak, + focal), and Ki 67 (40%) (Figure 3A-E). Additional markers (CD45, CD20, pax5, CD3, synaptophysin, and chromogranin) were then examined. The tissue was again negative for these markers except for CD45, which was focally expressed.
Figure 1. Sagittal T1 weighted MRI imaging of the pelvis reveals a large cystic-solid mass (arrow) in the region of the left adnexa.

Figure 2. Diffuse proliferation of small- to moderately-sized cells with abundant mitotic figures, arranged in sheets, and few eosinophilic myelocytes scattered among them (A, 200 ×), occasionally exhibiting a cord-like pattern (B, 200 ×). Focal necrosis was noted (C, 200 ×). These cells were non-cohesive with an irregular nuclear membrane and angulated nuclei (D, 400 ×).

Ultimately, we re-examined the macroscopic and histopathological features of the mass. Interestingly, the sections of the mass were yellow-green in color (Figure 4A), and few eosinophilic myelocytes were scattered in the part of tumor, as identified by microscopy (Figure 2A). The levels of CD68, CD43, and myeloperoxidase (MPO) were then evaluated. Strong MPO and CD43 staining was observed in all cells, while the staining for CD68 was more focal (Figure 4B-D). These findings established a diagnosis of undifferentiated GS that involved the ovary.

Laboratory findings also indicated that the blood counts continually increased after surgery. A blood smear and bone marrow biopsy were performed five days after surgery, and the results of these tests confirmed AML. After establishing the diagnosis, the patient was sent to the hematology department to receive cytosine arabinoside and idarubicin chemotherapy.

Discussion

GS is a localized mass that consists of premature precursors of granulocytic cells or cells of each maturation step in extramedullary sites [1].
GS has also been called chloroma due to its green coloration, which is the result of a high myeloperoxidase content [2]. GS usually occurs concomitantly with or after the onset of acute myeloid leukemia (AML) or other myeloproliferative disorders [3]. On rare occasions, GS evolves before the onset of AML [4]. The bone, lymph nodes, and skin are the favored sites of involvement [3]. The orbit, sacrum, spine, and lung are also frequently involved, and multiple other sites of involvement have been reported [5-7]. However, GS of the ovary as the primary manifestation of AML is exceedingly rare [8].

A review of the literature indicated that the majority of patients with the nonleukemic stage of GS involving the ovary present with abdominal pain and occasionally, other systemic symptoms (Table 1). A single ovary is involved in 88% of cases, predominantly the right ovary. Among the 9 patients with ovarian GS without leukemia, 6 (67%) patients developed AML between 5 days and 27 months (mean: 10 months) after diagnosis [8-12], and patients without leukemia usually developed AML within a mean of 7.4 months [1]. The remaining 3 patients had not developed leukemia or another associated hematological disorder at 84 [13] (n = 1), 12 [14] (n = 1) and 3 [15] (n = 1) months after surgery. These outcomes contradict other reports [1], which indicated...
that patients with GS as a presenting feature of AML did not survive for 60 months. These findings indicate that the prognosis of ovarian GS without leukemia is better than that of GS that involves other organs.

GSs are frequently undifferentiated and consequently are often misdiagnosed, particularly in patients whose tumors precede the appearance of overt leukemia symptoms. Neiman et al [16], reported that a correct initial diagnosis of GS is made in only 44% of GS cases (27/61 cases). When tumors in young females show diffusely proliferating small to moderately sized cells, malignant lymphoma, small cell carcinoma and juvenile granulosa cell tumors may initially be considered in the differential diagnosis. In our case, a GS of the ovary was the first sign of AML and was followed by the appearance of leukocytosis and peripheral blasts. Due to the normal blood cell count pre-surgery and the absence of systemic symptoms, leukemia was not initially suspected. After the GS that involved the ovary was diagnosed, the laboratory tests were repeated, which yielded some alarming results. A subsequent bone marrow biopsy confirmed the presence of AML. This case study illustrates the difficulty of diagnosing GS in an unusual location, such as the ovary. Thus, GS is likely to be under-diagnosed in the absence of a preexisting leukemia.

In conclusion, primary GS of the ovary is a rare presentation of AML and consequently can be easily misdiagnosed on the basis of H&E sections. A high index of suspicion is necessary to differentiate GS from malignant lymphoma and granulosa cell tumors of the ovary, and relevant IHC markers should be evaluated to confirm the diagnosis.

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Disclosure of conflict of interest

None.

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Gynecological pathology


