

Case Report

Ovarian granulocytic sarcoma as the primary manifestation of acute myelogenous leukemia

Jun Ding¹, Hua Li², Yu-Kai Qi¹, Jian Wu¹, Ze-Bin Liu³, Bin-Cang Huang⁴, Wei-Xiang Chen¹

¹Department of Pathology, Shanghai Gongli Hospital, Shanghai, People's Republic of China; ²Department of Pathology, Hua Bei Oil Field Total Hospital, Hebei, People's Republic of China; ³Department of Pathology, Fudan University Shanghai Cancer Center, Shanghai, People's Republic of China; ⁴Department of Radiology, Shanghai Gongli Hospital, Shanghai, People's Republic of China

Received July 2, 2015; Accepted August 20, 2015; Epub October 1, 2015; Published October 15, 2015

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 sec-

tion 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, inhibin- α , PLAP, actin, CD99, S-100, CD117, and Ki 67. The tissue was negative for these markers except for vimentin (+), inhibin- 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.

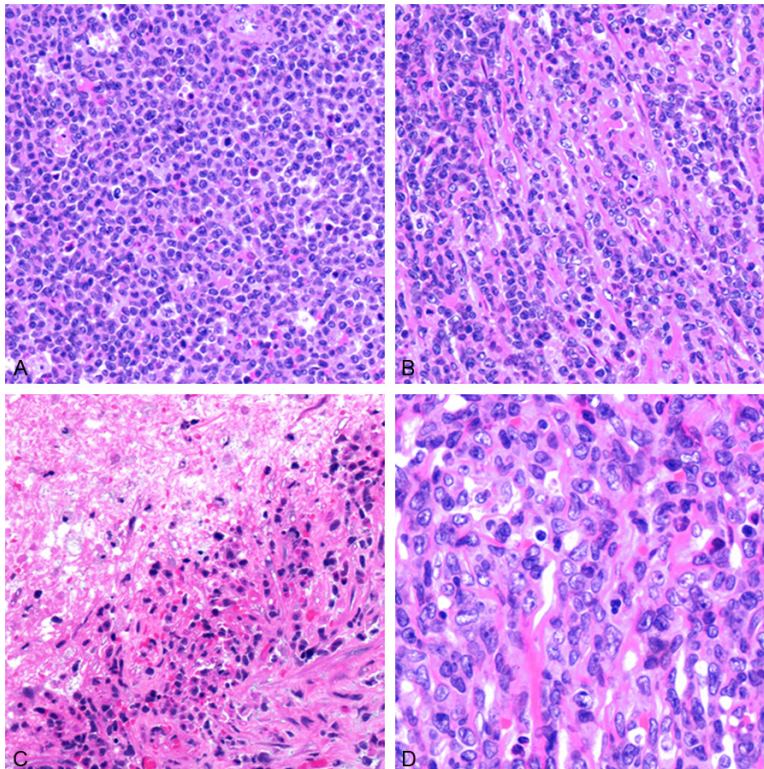


Figure 2. Diffuse proliferation of small- to moderately-sized cells with abundant mitotic figures, arranged in sheets, and few eosinophilic myelocytes scattered among them (A, 200 \times), occasionally exhibiting a cord-like pattern (B, 200 \times). Focal necrosis was noted (C, 200 \times). These cells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

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].

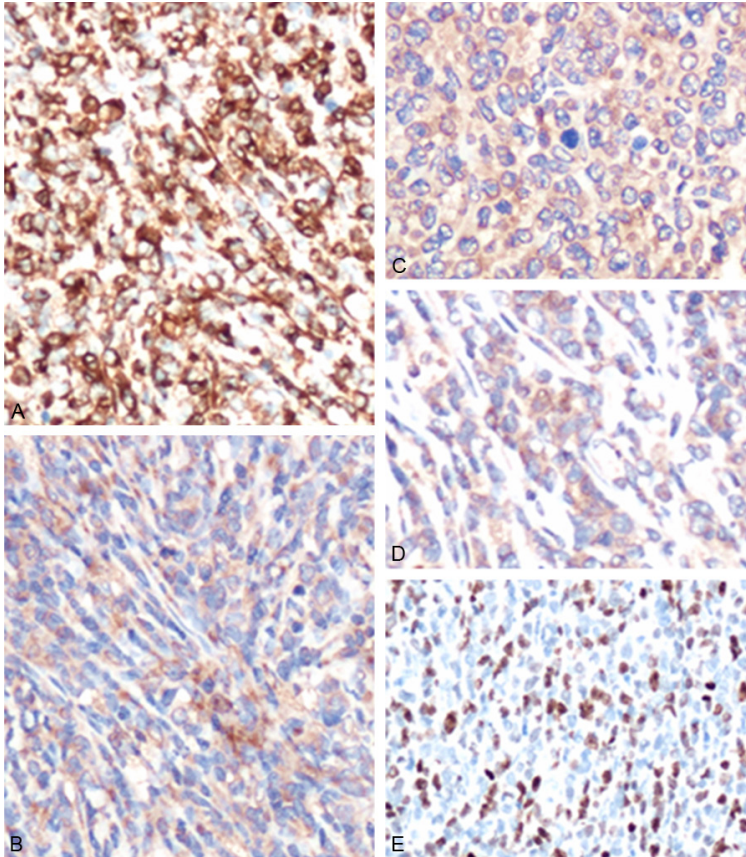


Figure 3. Immunohistochemical staining of the mass, showing diffuse positive staining for vimentin (A) and weak and focal positive staining for inhibin- α (B), PLAP (C) and CD99 (D), 400 \times . The Ki67 proliferation index was high (E, 200 \times).

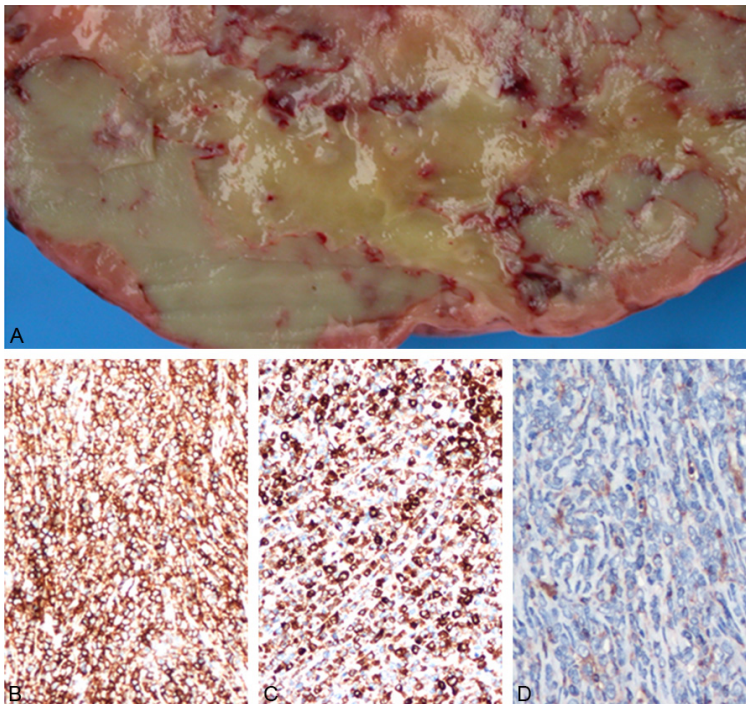


Figure 4. The sectioned surface shows solid tumor tissue with lobulated areas and a yellow-green color (A). Strong cytoplasmic immunoreactivity for CD43 (B) and myeloperoxidase (C) and focal staining for CD68 (D), 400 \times .

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

Table 1. Literature review of the clinical characteristics of patients with granulocytic sarcoma of the ovary without history of AML (with negative PBT and unknown BMB results at presentation)

No	Age	Manifesting symptoms	Physical findings (ovarian mass)	Progression	Treatment	Literature
1	3 m	Anemia/abdominal mass	Bilateral	AML	NS	[9]
2	NS	NS	Right	None after 7 y	High-dose Polychemo/RXT	[13]
3	49 y	NS	Right	AML after 12 m; GS recurrent	Right oophorectomy/Chemo	[12]
4	43 y	Routine pelvic examination	Right	AML after 18 m	Right oophorectomy/Chemo	[10]
5	26 y	Abdominal pain	Right	None after 12 m	Right oophorectomy/Chemo	[14]
6	19 y	Abdominal pain	Right	AML after 3 m	Right oophorectomy/Chemo	[8]
7	26 y	Abdominal pain	Right	AML after 27 m	Right SO/Chemo	[11]
8	30 y	Abdominal pain	Left	None after 3 m	Left SO/infracolic omentectomy/Chemo	[15]
Our case	27 y	Abdominal pain	Right	AML after 5 d	Right SO/infracolic omentectomy/Chemo	

AML: acute myelogenous leukemia, PBT: peripheral blood test, BMB: bone marrow biopsy, SO: salpingo-oophorectomy, RXT: radiation therapy, NS: not stated.

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.

Acknowledgements

This work was supported by the Shanghai Pudong New Area science and technology development innovation fund (Grant No. PKJ2013-Y08), Excellent Academic Leaders of Shanghai Pudong New Area (Grant No. PWRd2013-01). We also thank American Journal Experts for providing language help.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Weixiang Chen, Department of Pathology, Shanghai Gongli Hospital, 219 Miaopu Road, Shanghai 200135, People's Republic of China. E-mail: cwx7511@sohu.com

References

- [1] Pathak B, Bruchim I, Brisson ML, Hammouda W, Bloom C, Gotlieb WH. Granulocytic sarcoma presenting as tumors of the cervix. *Gynecol Oncol* 2005; 98: 493-497.
- [2] Oliva E, Ferry JA, Young RH, Prat J, Srigley JR, Scully RE. Granulocytic sarcoma of the female genital tract: a clinicopathologic study of 11 cases. *Am J Surg Pathol* 1997; 21: 1156-1165.
- [3] Paydas S, Zorludemir S, Ergin M. Granulocytic sarcoma: 32 cases and review of the literature. *Leuk Lymphoma* 2006; 47: 2527-2541.
- [4] Uchiyama A, Motegi S, Yamada K, Amano H, Ishikawa O. Primary Granulocytic Sarcoma of the Skin without Hematologic Disorders. *Ann Dermatol* 2014; 26: 653-655.
- [5] Chamberlain MC, Tredway TL, Born D, Fink J. Teaching Neurolimages: sacral spine chloroma. *Neurology* 2013; 81: e87.
- [6] Aggarwal E, Mulay K, Honavar SG. Orbital extra-medullary granulocytic sarcoma: clinicopathologic correlation with immunohistochemical features. *Surv Ophthalmol* 2014; 59: 232-235.

- [7] Hoffman LM, Gore L, Maloney KW. Pulmonary presentation of relapsed acute myeloid leukemia. *J Pediatr Hematol Oncol* 2014; 36: 228-230.
- [8] Mehta J, Kane S. Primary granulocytic sarcoma of ovary—a rare presentation. *Leuk Lymphoma* 2004; 45: 845-847.
- [9] Morgan ER, Labotka RJ, Gonzalez-Crussi F, Wiederhold M, Sherman JO. Ovarian granulocytic sarcoma as the primary manifestation of acute infantile myelomonocytic leukemia. *Cancer* 1981; 48: 1819-1824.
- [10] Aguiar RC, Pozzi DH, Chamone DA. Granulocytic sarcoma of the ovary in a nonleukemic patient. *Haematologica* 1993; 78: 53-55.
- [11] Oliva E, Ferry JA, Young RH, Prat J, Srigley JR, Scully RE. Granulocytic sarcoma of the female genital tract: a clinicopathologic study of 11 cases. *Am J Surg Pathol* 1997; 21: 1156-1165.
- [12] Wang X, Liu H, Wu Z, Xu X, Chen X, Zhai Z, Sun Z. A case of acute promyelocytic leukemia presenting with a nonleukemic granulocytic sarcoma of the ovary, with subsequent development of acute myeloid leukemia associated with t (8;21). *Leuk Res* 2009; 33: 580-582.
- [13] Stefenelli T, Linkesch W, Radaszkiewicz T. [Myeloid sarcoma of the ovary]. *Wien Klin Wochenschr* 1991; 103: 717-718.
- [14] Sreejith G, Gangadharan VP, Elizabeth KA, Preetha S, Chithrathara K. Primary granulocytic sarcoma of the ovary. *Am J Clin Oncol* 2000; 23: 239-240.
- [15] Roy P, Biswas B, Sankari S, Manipadam MT, Jose R. Primary granulocytic sarcoma of ovary. *J Obstet Gynaecol India* 2012; 62 Suppl 1: 91-93.
- [16] Neiman RS, Barcos M, Berard C, Bonner H, Mann R, Rydell RE, Bennett JM. Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. *Cancer* 1981; 48: 1426-1437.