

Aleukemic granulocytic sarcoma presenting at multiple sites: ovary, breast and soft tissue

Jitendra Singh Nigam, Vatsala Misra,
Varsha Kumar, Kachnar Varma

Department of Pathology, M.L.N. Medical
College, Allahabad, India

Abstract

An 18 year old female presented with the history of pain in abdomen, breast engorgement, swelling over both legs and breathlessness for three month. On clinical examination diagnosis of fibroadenoma breast was made. Ultrasonography of abdomen showed bilateral ovarian mass. Bilateral salpingo-oophrectomy was done and specimen was sent for histological examination. Two lobulated solid masses of tissues the larger one measuring 13×8×5 cm and smaller one measuring 10×7×5 cm in size received. Microscopic examination showed monomorphic population of discohesive, hyperchromatic small round cells had high N:C ratio, coarse chromatin, conspicuous nucleoli and scant to moderate amount of basophilic cytoplasm, lying in sheets and separated by fibrous strands and diffusely infiltrating the ovarian stroma. Fine needle aspiration from breast lump and leg swelling showed predominant population of blast cells. Myeloperoxidase was strongly positive and diagnosis of granulocytic sarcoma was confirmed.

Introduction

Granulocytic sarcomas are solid extramedullary tumors that can be composed predominantly of cells showing granulocytic differentiation (granulocytic sarcoma) or predominantly of cells showing monocytic differentiation (monocytic sarcoma).¹ It occurs in 2 to 14% of cases of acute myeloid leukemia (AML).² The tumors may occur as extramedullary masses without evidence of leukemia in blood or marrow, so-called nonleukemic granulocytic sarcomas, or in association with AML. The tumors originally were called chloromas because of the green color imparted by the high concentration of the enzyme myeloperoxidase present in myelogenous leukemic cells. Biopsy specimens are positive for chloracetate esterase, lysozyme, myeloperoxidase, and cluster of differentiation (CD) markers of myeloid cells.³ The tumors are usually localized; they often involve bone, periosteum, soft tissues, lymph nodes, or skin.

Common sites are the orbit and the paranasal sinuses, but other sites reported include the gastrointestinal tract, genitourinary tract, breast, cervix, salivary glands, mediastinum, pleura, peritoneum, and bile duct. Granulocytic sarcomas may occur at diagnosis of AML or may precede the diagnosis; they have also been seen in association with myelodysplastic syndromes or myeloproliferative disorders and usually predict transformation to acute leukaemia.² Patients with granulocytic sarcoma have a poor prognosis and the majority of patients without bone marrow infiltration at presentation die of leukemia within an average of 16.5 months after diagnosis.^{4,5} Granulocytic sarcoma of the breast is an unusual site of presentation occurring mainly in young women, with high incidence of bilaterality.^{4,8} The ovary contains tumor in approximately 25% of patients with non-Hodgkin's lymphoma at autopsy and in up to 50% of those with leukemia. However, with the exception of Burkitt lymphoma, ovarian involvement as the initial manifestation of lymphoma or leukemia is rare.⁹

Case Report

An eighteen year old female presented with the history of pain in abdomen, breast engorgement, swelling over both legs and breathlessness for three months. Clinical examination revealed bilateral breast masses. A clinical diagnosis of fibroadenoma breast was made. Bilateral ovarian mass were seen on ultrasonography of abdomen. Total leucocyte count was within normal limits. No blasts cells were identified in the peripheral blood smear. Bilateral salpingo-oophrectomy was done and specimen was sent for histological examination.

Gross

Two lobulated solid masses of tissues the larger one measuring 13×8×5 cm and smaller one measuring 10×7×5 cm in size received. Outer surface was encapsulated and cut surface of both the masses was tan grey with multiple small hemorrhagic and brownish areas (Figure 1A, B). Several pieces from different areas including center and outer surface were processed from both masses.

Microscopic examination

Sections processed showed monomorphic population of small round cells diffusely infiltrating the ovarian stroma. These cells were discohesive, lying in sheets and separated by fibrous strands of variable thickness. Cells were hyperchromatic, had high nuclear cytoplasmic ratio, coarse chromatin, conspicuous nucleoli and scant to moderate amount of basophilic

Correspondence: Jitendra Singh Nigam,
Department of Pathology, M.L.N. Medical College,
Allahabad, India. Tel. +91.941.262.8083.
E-mail: nigamjs@gmail.com

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cytoplasm. One-two mitotic figures per high power field were noted. One section showed large *corpus luteum* of ovary with central area of hemorrhage (Figures 1C-E and 2A,B).

Fine needle aspiration from breast lump and leg swelling were also done. Fine needle aspiration smears prepared showed predominant population of large round to oval cells with moderately high nuclear cytoplasmic ratio and moderate amount of pale blue cytoplasm. Nuclei were round to oval with two to four prominent nucleoli (blast cells). Few large monocytoid cells with prominent nucleoli were also seen (Figures 2C-E).

A diagnosis of small round cell tumor of ovary with differential diagnosis of Granulocytic sarcoma, Lymphoma, Small cell carcinoma and juvenile granulosa cell tumor was considered.

Immunohistochemistry for myeloperoxidase, LCA (CD45), CD 34, and placental alkaline phosphatase was done. It was strongly positive for myeloperoxidase. Rest three were negative (Figures 3A-D). A diagnosis of granulocytic sarcoma was confirmed.

A repeat peripheral blood smear examines but this time these smear showed normal total leukocyte count with occasional blast cells (Figure 2F). Patient was referred to oncology center for treatment. She did not report back to our center and lost to follow up.

Discussion

Ovarian involvement as the initial manifestation of lymphoma or leukemia is rare. Approximately half of the tumors are bilateral.⁹ Primary involvement of the ovary is exceedingly rare leading to under diagnosis of granulo-

cytic sarcoma.¹⁰ It can arise de novo and precede the development of acute nonlymphocytic leukemia, or be the sole manifestation of relapse.¹¹

In granulocytic sarcoma of the breast the patients mainly present with the breast engorgement and a painless mass without associated local symptoms.⁶

In granulocytic sarcoma ovary both diffuse and nodular growth patterns are encountered, but sclerosis can distort these patterns and result in compartmentalization of the neoplastic cells, as well as growth as nests and cords. The single-file arrangement of lymphoma and leukemic cells may simulate metastatic carcinoma, particularly one of breast origin. Granulocytic sarcoma on routine stains is often composed of cells with more finely dispersed nuclear chromatin and may have more abundant cytoplasm, which may be deeply eosinophilic. Confirmatory immunostaining may be crucial in making the diagnosis.⁹

In granulocytic sarcoma the growth pattern may simulate invasive lobular carcinoma or malignant lymphoma. The neoplastic cells forming broad sheets or cords invade into and around normal mammary parenchymal structures. Intra-epithelial extension of the leukemic infiltrate simulates in situ carcinoma. The diagnosis of granulocytic sarcoma may be suggested by cytoplasmic granules in maturing myeloid cells or by the presence of relatively numerous mature myeloid cells scattered throughout the lesion. Special stains are especially helpful to establish the diagnosis. The tumor cells do not contain mucin and they give a negative reaction for immunocytochemical epithelial markers such as cytokeratin and anti-endomyosial antibodies. The diagnosis of granulocytic sarcoma can be established by fine needle aspiration biopsy if immature myelocytic cells are recognized in the cytologic specimen.¹² The differential diagnosis includes non-Hodgkin lymphoma (predominantly mucosa-associated lymphoid tissue lymphoma and diffuse large B-cell lymphoma), small round cell tumors, granulosa cell tumor, undifferentiated carcinoma and in case of breast, lobular carcinoma also.¹² A complete panel of immunohistochemistry is helpful to recognize this entity with an isolated presentation. Granulocytic sarcoma is immunoreactive for myeloperoxidase, CD117 and CD68, CD43 is positive in most of the cases, and 75% are reactive for CD45. Lysozyme and CD68 PGM1 expression are evidence for monocytic differentiation.^{13,14} Multiple sites involvement in single patient was reported in literature.^{6,15-20} In the presented case multiple sites (both ovaries, both breasts, and leg swelling) were involved. Due to the rarity of isolated granulocytic sarcoma and different treatments, the clinical outcome and the prognosis in this group of patients is poor.

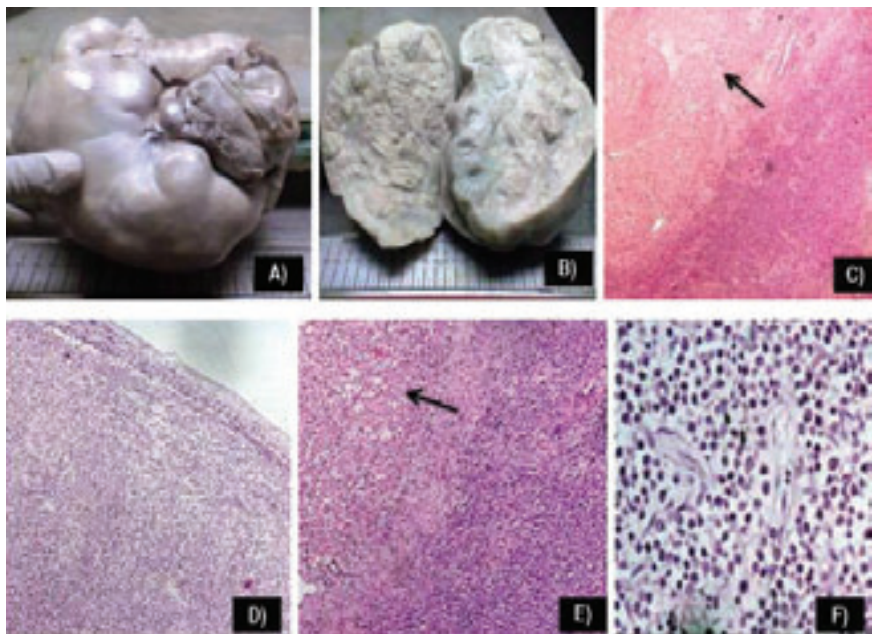


Figure 1. A) Gross: lobulated solid mass of ovary; B) cut surface of masses was tan grey with raised lobulated areas; C) monomorphic population of small round cells diffusely infiltrating the ovarian stroma with large corpus luteum of ovary, (arrow; Hematoxylin & Eosin 100 \times); D) monomorphic population of small round cells infiltrating the capsular (Hematoxylin & Eosin 100 \times); E) monomorphic population of small round cells diffusely infiltrating the ovarian stroma adjacent to leuteal cells (arrow, Hematoxylin & Eosin 100 \times); F) proliferating blood vessels and diffuse infiltration of hyperchromatic small round cells with high N:C ratio (Hematoxylin & Eosin 400 \times).

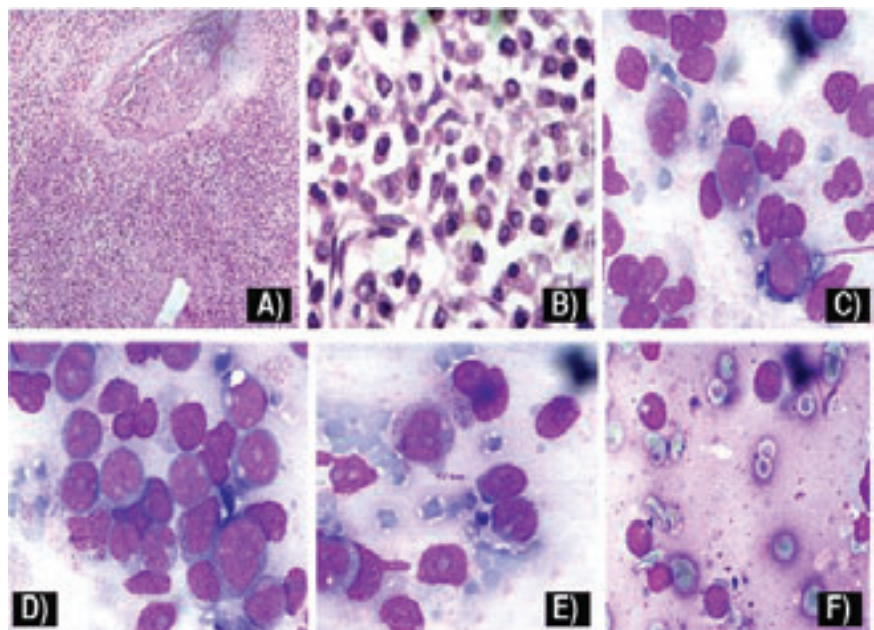


Figure 2. A) Large proliferating blood vessel surrounded by monomorphic population of small round cells (Hematoxylin & Eosin 100 \times); B) hyperchromatic small round cells had high N:C ratio, coarse chromatin and scant to moderate amount of basophilic cytoplasm (Hematoxylin & Eosin 100 \times); C) Fine needle aspiration (FNA) left breast: large round to oval cells with high nuclear cytoplasmic ratio and 2 to 4 nucleoli (Giemsa 1000 \times); D) FNA right breast: large round to oval cells with high nuclear cytoplasmic ratio and 2 to 4 nucleoli (Giemsa 1000 \times); E) FNA leg swelling: large round to oval cells with high nuclear cytoplasmic ratio and 2 to 4 nucleoli (Giemsa 1000 \times); F) peripheral blood smear: large round to oval cells with high nuclear cytoplasmic ratio and 2 to 4 nucleoli (Giemsa 1000 \times).

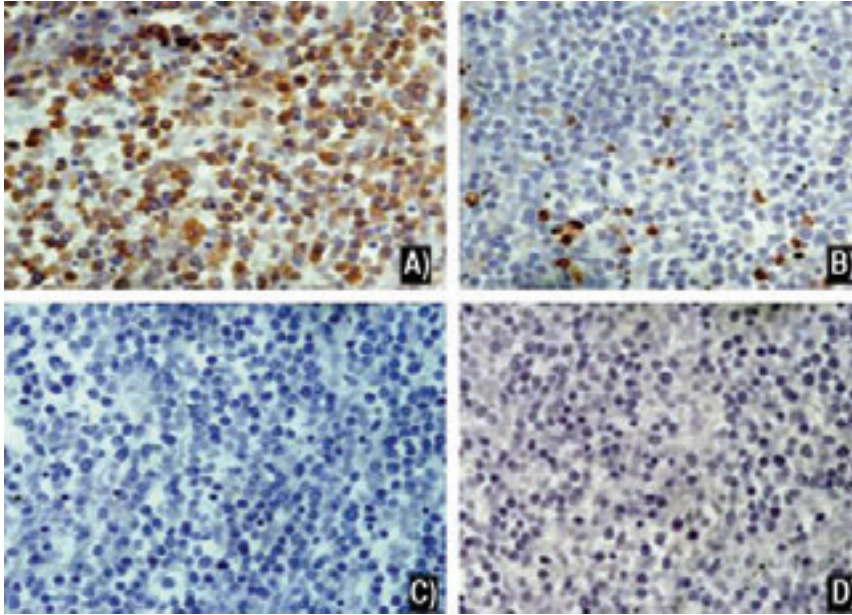


Figure 3. Immunohistochemistry: A) myeloperoxidase strongly positive in tumor cells (400×); B) LCA (CD45) was negative in tumor cells, infiltrating normal lymphocytes are positive (400×); C) placental alkaline phosphatase is negative in tumor cells (400×); D) vimentin is negative in tumor cells (400×).

Conclusions

Granulocytic sarcoma is uncommon in ovary and breast neoplasm and the clinical presentation without development of leukemia or myeloproliferative disorder is extremely rare. Immunohistochemistry and Ancillary studies are necessary to recognize this entity.

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