Case Report

Non-leukemic Granulocytic Sarcoma Presenting as Multiple Skin Nodules: A Rare Case Report

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ABSTRACT

Granulocytic sarcoma (GS) is a localized lesion comprising of immature granulocytes, monocytes, or both; involving extramedullary sites. GS is also known as myeloid sarcoma is a subtype of Acute myeloid leukaemia (AML) and related precursor neoplasms as per recent WHO classification of tumors of hematopoietic and lymphoid tissues. GS with no evidence of leukemia (non-leukemic GS) is a very rare. Here we report a 10 year old male child who presented with facial and back swelling which was subsequently diagnosed as non-leukemic GS by flow-cytometry examination on aspirated material. The patient was treated with chemotherapy as for regular AML, However succumbs after 2 course of chemotherapy due to febrile neutropenia.

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Introduction

Granulocytic Sarcoma (GS) is a localized tumor formed by immature myeloid cells or myeloblasts at an extra-medullary site.[1] According to WHO classification of tumors of hematopoietic and lymphoid tissues; this is a part of Acute myeloid leukaemia (AML) and related precursor neoplasms. It usually occurs in patients of AML as well as in patients with myeloproliferative neoplasms (MPN's). On rare occasions, GS may present without any other hematological malignancies and hence known as nonleukemic GS. The common sites of these nonleukemic GS are skin, central nervous system, lymph nodes, gastrointestinal tract, and gall bladder.[2] These usually present as diagnostic dilemmas because of absence of a prior diagnosis of leukemia and hence need be differentiated from other solid malignancies such as carcinomas, lymphomas etc. Here we describe a case of non-leukemic GS in a 10 year old male child who presented with facial and back swelling.

Case Report

A 10 year-old-male child was admitted to pediatric unit for complaints of fever and nodules over the left side of face and back for 1.5 months. On examination he had moderate pallor, cervical lymphadenopathy and bluish coloured subcutaneous nodules over face and back. The clinical possibilities of bacterial infection, acute leukemia and lymphoma were considered and the patient was investigated accordingly. Ultrasound abdomen revealed mild hepatomegaly with mild splenomegaly. Complete blood count showed hemoglobin of 6.9 gm/dl, platelet count of 213×10^9/L and total leucocyte count of 17.2×10^9/L with differential count of 65% neutrophils, 27% lymphocytes, 16% monocytes and 2% eosinophils. There were no leukemic cells in the peripheral smear. The blood cultures were sterile. Due to high degree of clinical suspicion of leukemia Vs lymphoma, a bone marrow examination and fine needle aspiration cytology (FNAC) were performed. The bone marrow was normocellular and showed adequate representation of all three hematopoietic lineages. There was no evidence of leukemia, myelodysplasia, myeloproliferative neoplasm and lymphoma involvement with in the bone marrow aspirate and biopsy [Fig-1]. On the other hand FNAC smears from the facial swelling were cellular and showed scattered immature mononuclear cells [Fig-2]. These cells were 2-3 times larger than the size of mature lymphocyte and had fine nuclear chromatin, conspicuous nucleoli and mild to moderate amount of amphophilic cytoplasm containing fine granules. The background showed few mature lymphocytes and polymorphs. FNAC smears from the left cervical lymph node also revealed atypical cells with similar morphology. Sample for flow-cytometry (FCM) was also taken at the same time from these subcutaneous nodules. The FCM examination revealed approximately 22.5% CD 45 positive events which showed presence of myeloid and monocytic markers (CD 45, HLA DR, CD 13, CD 117, CD 11c and CD14) and absence of all lymphoid markers (CD 3, CD 5, CD4, CD 8, CD 10, CD19, CD20, CD 22 and CD 79a) [Fig-3]. In view of absence of bone marrow involvement and presence of immature cells on FNAC along with presence of myeloid and monocytic markers on FCM, the

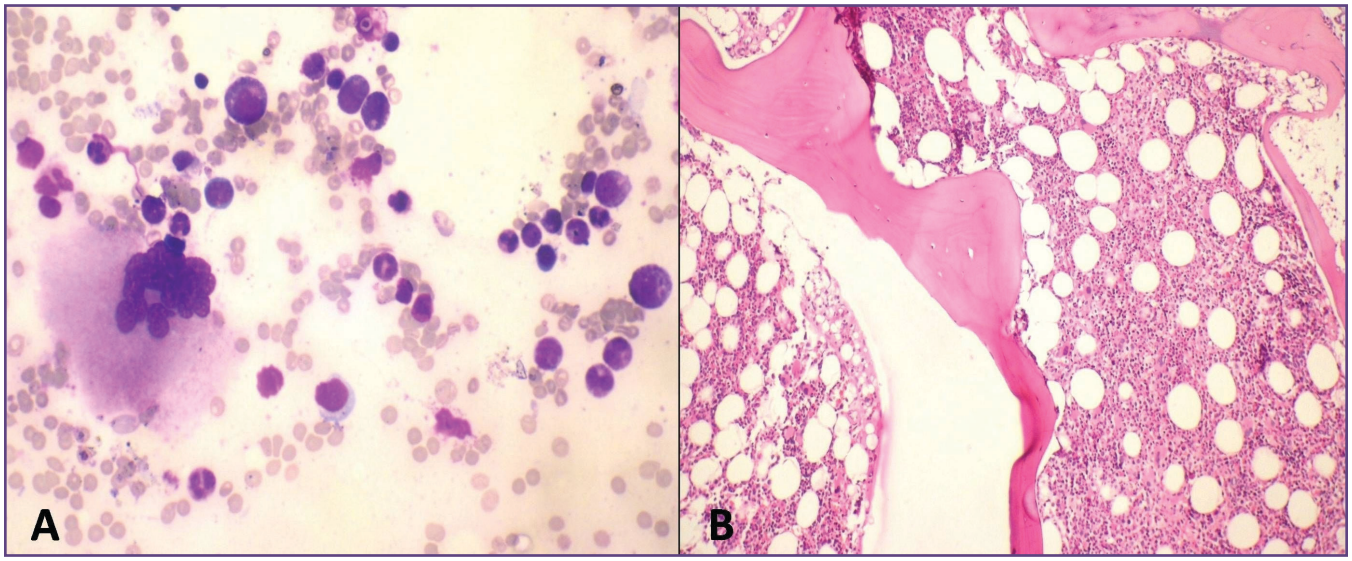

Fig. 1: [A] Bone marrow aspirate show presence of normal hematopoietic elements (MGG, 400X). [B] Bone marrow trephine biopsy also reveals normocellular marrow spaces (H&E, 400X). There is no evidence of involvement by leukemia.

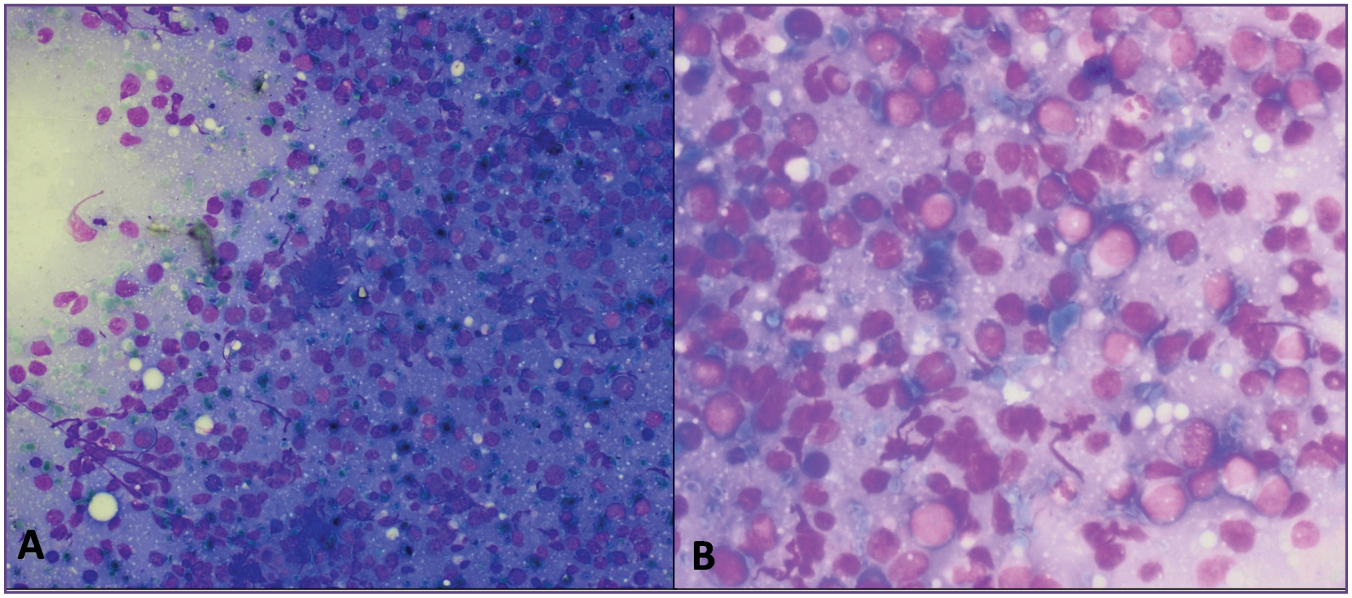

Fig. 2: [A] FNAC shows cellular smear with presence of singly scattered mononuclear cells (MGG, 200X). [B] High power view show that these cells have opened up nuclear chromatin, high nuclear cytoplasmic ratio and granular cytoplasm (MGG, 400X).

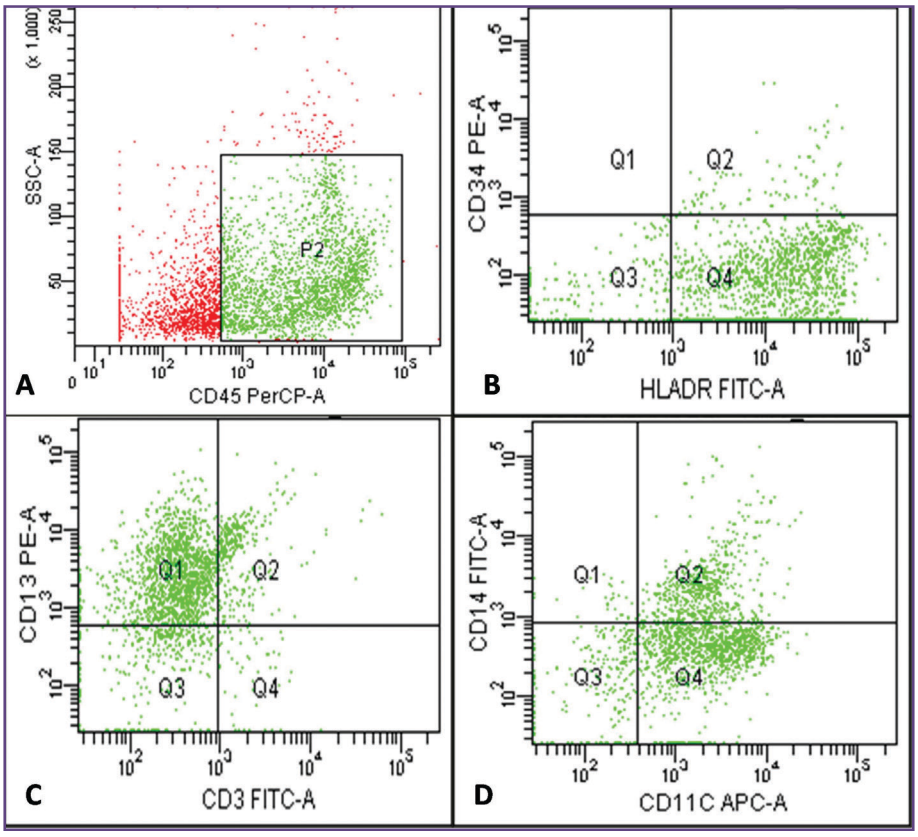

Fig. 3: [A] Panel of scatter plots showing the multicolor immunophenotyping from aspirated sample from facial swelling. The events are seen on side scatter (SSC) versus CD45 plot. The events in CD45 region are gated as P2 (22.5% of all events) and the same cells are analyzed in subsequent plots. [B] These cells show expression of HLA-DR and are negative for CD34. [C] These cells are positive for CD 13 and are negative for CD 3. [D] The same cell populations show expression of CD11c and CD14.

diagnosis of non-leukemic GS was considered. The patient was initiated on chemotherapy as for regular AML with UK-MRC-AML protocol (The first induction course included Cytosine Arabinoside, Daunorubicin and Etoposide) and the lesions clinically resolved following the first course of chemotherapy. Unfortunately the patient had died after 2 course of chemotherapy due to febrile neutropenia.

Discussion

GS is a rare extramedullary tumor that consists of immature granulocytic cells. This tumor was first described in 1811 and originally called as chloroma by King in 1853.[1- 3] Granulocytic sarcoma has been reported to occur in almost every anatomic location. These most common sites are the skin (13%–22%), central skeleton (9%–25%), and lymph nodes (15%–25%).[4]

GS is associated with 3% -8% of acute myeloid leukemia (AML) cases and rarely with MPN's. The exact incidence of nonleukemic GS is not well known. Benet C et al had found approximately 7.5% of the patients having leukemic skin infiltration without any underlying myeloid neoplasm, in a series of 173 patients with leukemia cutis.[5] Due to its rarity, non-leukemic GS is frequently misdiagnosed as other common malignancies. The differential diagnosis of non-leukemic GS is similar to that of GS which includes large cell NHL, lymphoblastic lymphoma, undifferentiated cancer, malignant melanoma, extra-medullary hematopoiesis and inflammation. [6] The critical point is to think about this entity and if there is a suspicion, the diagnosis must be confirmed by either immuno-histochemistry or FCM examination. In the index case FNAC of aspirated material also suggest the possibility of hematological malignancy however the exact diagnosis was confirmed by FCM on aspirated material from subcutaneous nodule.

Non-leukemic GS represents therapeutic dilemma as well because the optimal therapy for non-leukemic GS has not been determined. Several previous studies report that more than 80% of patients with nonleukemic GS who were treated by surgical excision or local radiation therapy eventually developed overt systemic leukemia within a few months. Some studies suggest that localized therapy alone would not be sufficient for the treatment of non-leukemic GS.[7-9] Yamauchi and Yasuda had reviewed 72 cases and concluded that the nonleukemic period after the diagnosis of GS was significantly longer in the patients who were treated with systemic chemotherapy, in comparison with the patients who did not received systemic chemotherapy. [2] The long-term prognosis of non-leukemic GS remains poor (as in our case) and the majority of these died within an average of 16.5 months after diagnosis.[10]

Conclusion

Nonleukemic GS is a very rare disease and have poor prognosis. This rare case of nonleukemic GS was diagnosed by FNAC and FCM of the aspirated material. In cases with a high index of suspicion, the applications of ancillary techniques are mandatory for confirmation of disease. Patients with nonleukemic GS should be treated with intensive systemic chemotherapy in the early course of the disease to decrease mortality.

Conflict of interest

The authors declare that they have no conflict of interest.

Source of support

Nil

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