Case report

SCLEROSING EXTRAMEDULLARY HEMATOPOIETIC TUMOR PRESENTING WITH GROSS ASCITES AND PERITONEAL NODULES: A DIAGNOSTIC CHALLENGE ON CYTOLOGY

ABSTRACT

Introduction: Sclerosing extramedullary hematopoietic tumor (SEMHT) is an uncommon lesion seen in association with chronic myeloproliferative disorders especially idiopathic myelofibrosis. We present a case of SEMHT in an elderly female, presenting with ascites. **Case presentation:** A 50-year old female, apparently asymptomatic one month back, presented with abdominal distension, loss of appetite and early satiety. Ultrasound abdomen revealed altered liver architecture with ascites. Ascitic fluid analysis was suspicious of malignancy. CECT abdomen showed multiple thickened nodules in omentum and peritoneum. CA125 levels were elevated and clinical diagnosis of metastatic peritoneal nodules with ovarian primary was made. However, biopsy of these lesions was suggestive of a mesenchymal neoplasm. In view of peripheral leucoerythroblastic picture, bone marrow examination was done which showed primary myelofibrosis. Retrospective review of clinical history revealed that she underwent splenectomy four years back for unknown cause. The peritoneal nodules were finally reported as SEMHT in a case of primary myelofibrosis, status post splenectomy. **Discussion:** Idiopathic myelofibrosis is characterized by leukoerythroblastic picture, marrow fibrosis, hepatosplenomegaly with evidence of extramedullary hematopoiesis (EMH) in spleen in most of the cases. In patients with splenectomy, EMH at other sites especially peritoneum and omentum should always be suspected, as in our case. **Conclusion:** SEMHT, though rare should be always suspected in known cases of myeloproliferative disorders especially myelofibrosis.

KEYWORDS: Extramedullary hematopoiesis, myelofibrosis, cytology

INTRODUCTION:

Sclerosing extramedullary hematopoietic tumor (SEMHT) is an uncommon lesion seen in association with chronic myeloproliferative disorders (CMPDs) especially chronic idiopathic myelofibrosis. SEMHT is most common in elderly with a predilection for mesentery and retroperitoneum[1-2]. We report the case of a 50 year old female who presented with ascites and peritoneal nodules on imaging. Though difficult and challenging, SEMHT can be diagnosed on cytopathology especially in proper clinical context as in this case.

CASE PRESENTATION: A 50-year old female, postmenopausal, P1L1, presented with abdominal distension of one month duration with history of loss of appetite and early satiety. It was insidious in onset and gradually progressive in one month duration. There was history of pedal edema since two days. There were no other systemic symptoms. Past history revealed anemia four years back, for which she received three blood transfusions. She has no comorbidities. On examination, she was severely cachexic, afebrile, had pallor, and there was no icterus/ cyanosis/ clubbing/lymphadenopathy. There was gross distension of abdomen with an ill-defined mass extending from bilateral costal margins to below the umbilicus. Vitals were stable and examination of other systems was normal. Ultrasound abdomen revealed altered liver architecture with massive ascites. Serum CA-125 levels were elevated (426 IU/ml). In view of raised CA-125 levels, a clinical diagnosis of peritoneal metastasis probably from ovarian primary was made. Ascitic fluid analysis and peritoneal nodule biopsy were done. Ascitic fluid cytology showed very few singly scattered large cells with central to eccentrically placed pleomorphic, hyperchromatic nuclei with moderate to abundant bluish cytoplasm against a background of lymphocytes and hemorrhage. In view very occasional scattered cells, it was reported as suspicious of malignancy (shown in Fig.1).

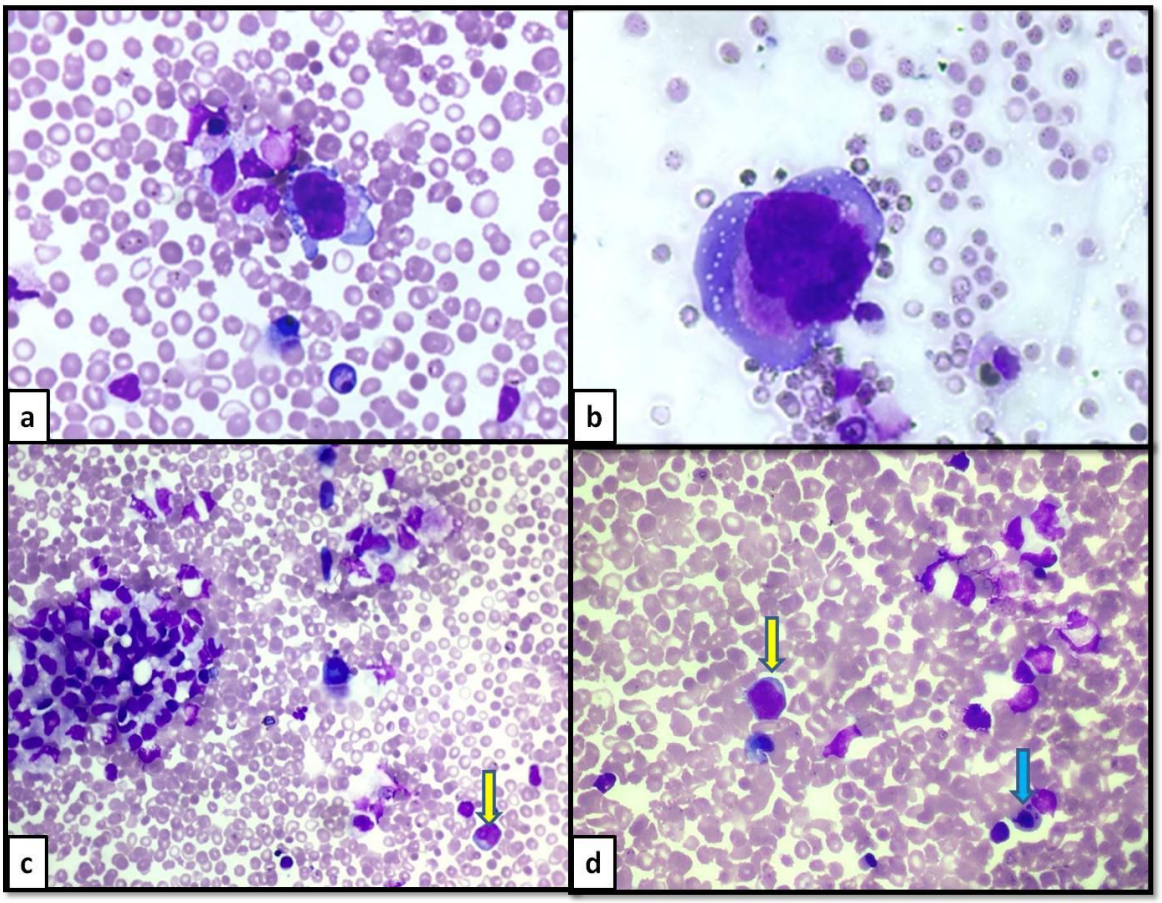

Fig. 1. Ascitic fluid cytology. a,b. singly scattered large cells with round to lobulated nuclei and moderate to abundant blue granular cytoplasm (megakaryocytes mistaken for malignant cells) c.Cluster of mesothelial cells and macrophages; d.yellow arrow –immature myeloid precursors, blue arrow-nucleated red cells;(MGG) (a,b,d- X400;c-X100).

Cell block of the fluid was done followed by ancillary testing and the large cells were negative for pan cytokeratin. Peritoneal nodule biopsy showed hypocellular collagenous tissue with spindled cells, elongated nuclei suggestive of mesenchymal neoplasm. The cells were positive for smooth muscle actin, beta catenin, and negative for Pan cytokeratin (CK), CK7 and CK 20 (shown in Fig.2).

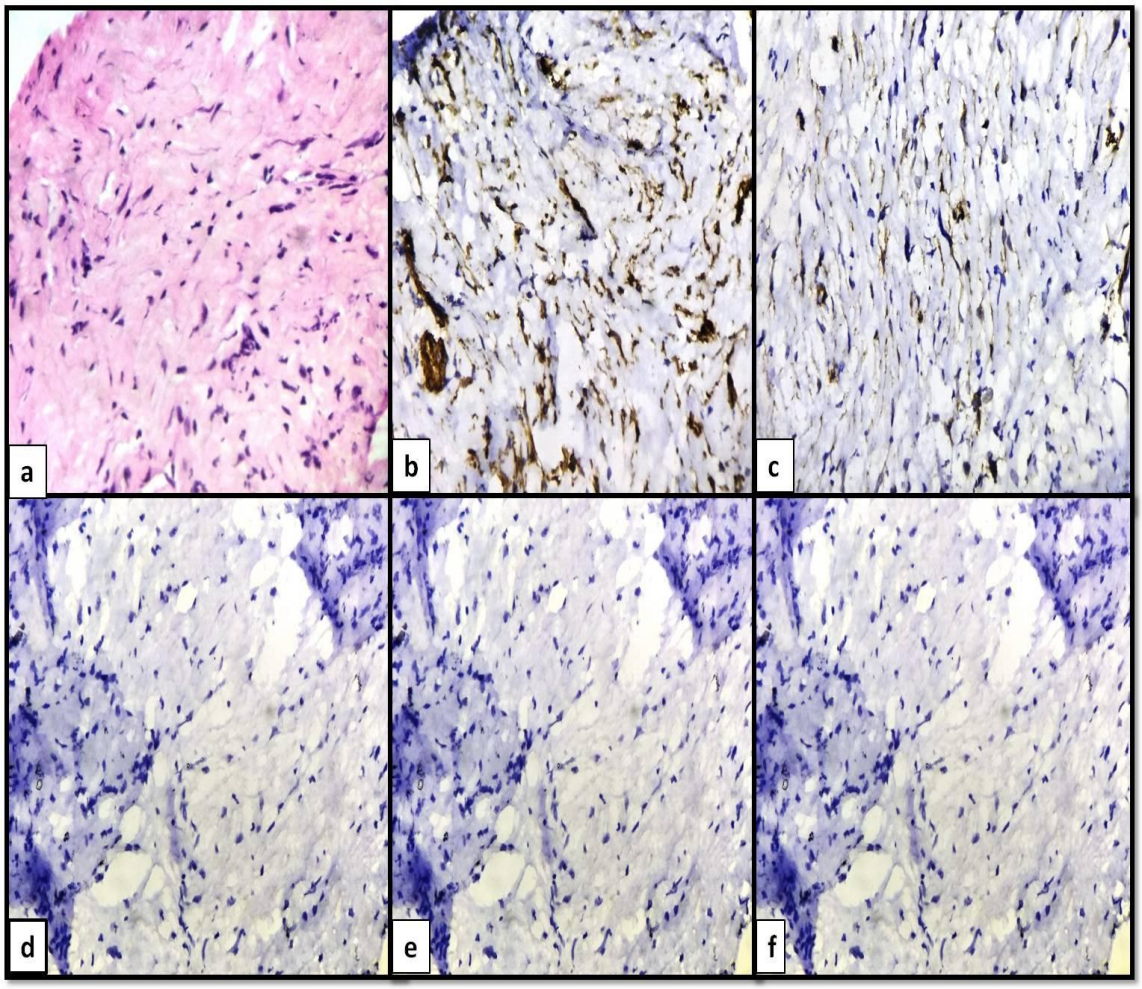

Fig. 2. a. Peritonal biopsy showed hypocellular collagenous tissue with spindled cells and elongated nuclei suggestive of mesenchymal neoplasm (H&E x400); b-f. IHC positive for b. SMA, c. Beta catenin; and negative for d. Pan CK, e. CK7, f. CK 20. (X400)

In view of inconclusive morphological diagnosis, further imaging was done. CECT abdomen revealed gross ascites, minimally enhancing omental and peritoneal nodules and soft tissue density deposits in left kidney pelvis with hydronephrosis. (shown in Fig.3). Portal cavernoma with non-visualization of splenic vein and spleen was also noted. Diffuse skeletal lesions with areas of lysis and sclerosis were seen. Uterus and bilateral ovaries were normal ruling out ovarian neoplasm. Differentials on imaging were lymphoma versus peritoneal carcinomatosis.

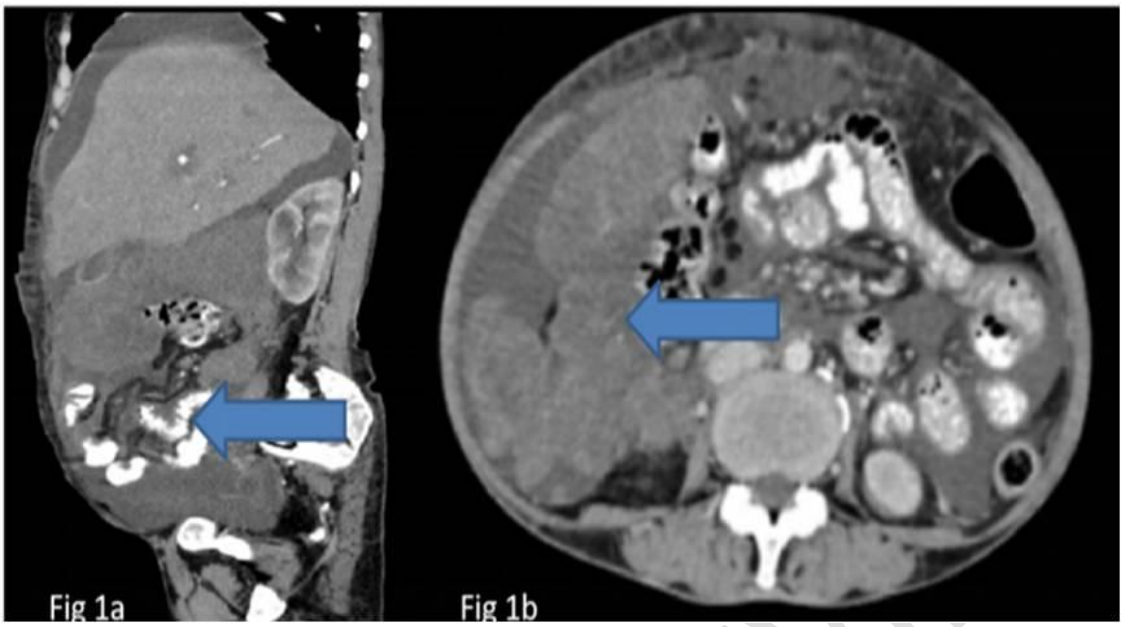

Fig. 3. Sagital (1a) and axial (1b) sections of CECT abdomen respectively shows a large heterogenously enhancing intraperitoneal soft tissue mass (blue arrow) in right paracolic gutter.

Complete blood counts (as depicted in Table 1) with peripheral blood smear examination was done which revealed leucoerythroblastic picture and bone marrow study was advised.

Table1: Complete blood counts of the patient with reference ranges

Test parameter	**Result**	**Laboratory Range**
Hemoglobin	4.9 gm/dL	11.5–15 gm/dL
PCV	18.9 %	35–45%
RBC	2.2 X 10^6/µL	4–5.50 × 10^6/µL
MCV	86.0 fL	80–100 fL
MCH	22.3 pg	27–32 pg
MCHC	25.9 gm/dL	32–36 gm/dL

TLC	51.2× 10^3/µL	4–9 × 10^3/µL
Platelet	1600× 10^3/µL	150–450 × 10^3/µL

Bone marrow aspirate was aparticulate and biopsy showed extensive osteomyelosclerosis and myelofibrosis with irregularly thickened bony trabeculae and osteoblastic rimming. Cellularity was less than five percent with extensive areas of fibrosis and focal paratrabecular megakaryocytes. Reticulin stain showed grade three condensation. Massons trichrome stain highlighted the collagen/fibrosis. (shown in Fig.4)

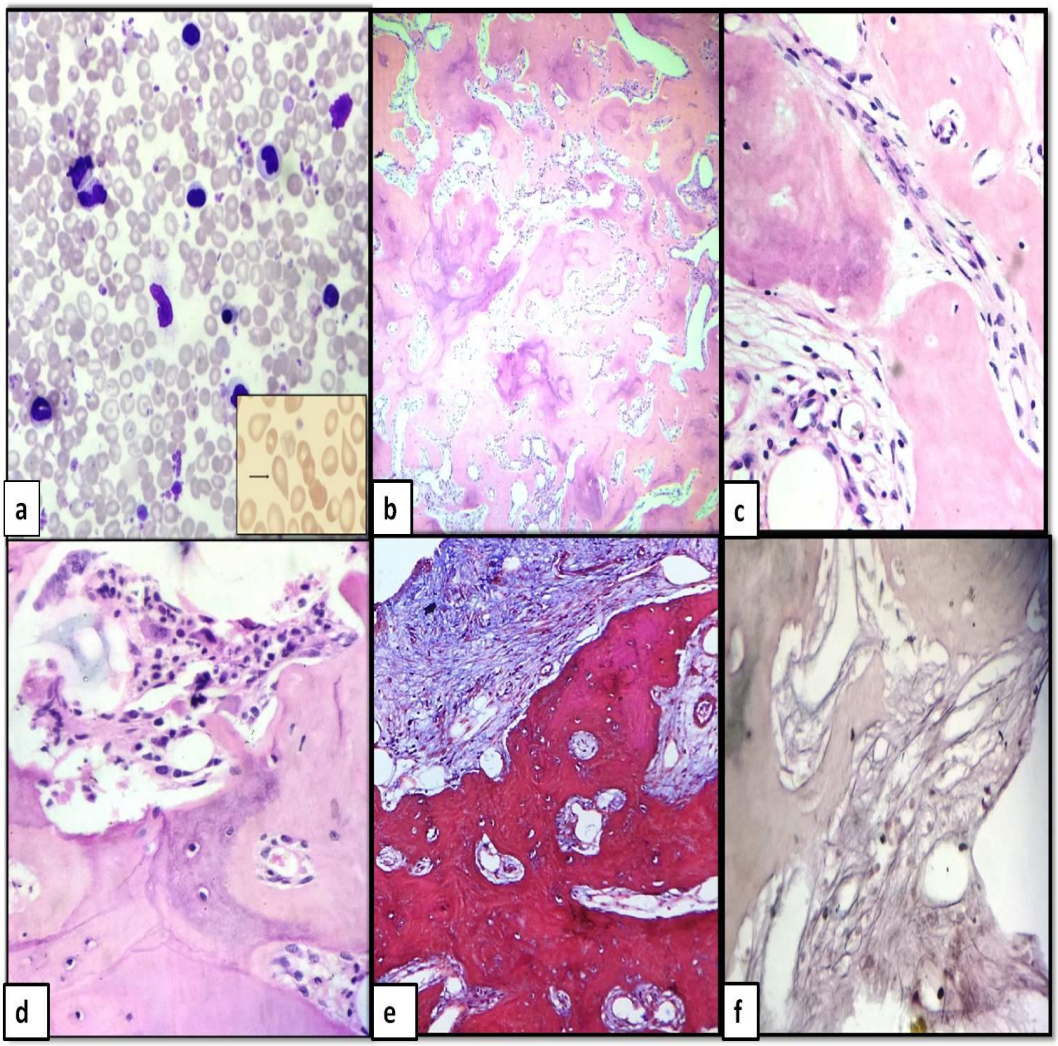

Fig. 4. a. Peripheral blood - leucoerythroblastic picture (inset-teardrop cell) (Giemsa X400); b-d. Bone marrow biopsy with extensive osteomyelosclerosis and myelofibrosis (H&E

x400); e. Massons trichrome stain positive collagen/fibrosis (X400); and f. Reticulin stain-grade 3 condensation (X400).

Further review of past clinical history revealed that she underwent splenectomy four years back for unknown reasons. Ascitic fluid cytopathology slides were reviewed and the large cells were redesignated as megakaryocytes in a background cell population of few immature erythroid and myeloid precursors. (Fig.2) A final diagnosis of SEMHT in a case of primary myelofibrosis, status post splenectomy was made and analysis for JAK2 V617F mutation was suggested. However, patient was only on supportive care and her conditioned worsened due to severe cachexia and she expired before the mutation analysis was done.

DISCUSSION:

SEMHT is an uncommon lesion associated with CMPDs [1]. SEMHT usually presents as multiple nodules characterized by sclerotic stroma with thick collagen bundles, trilineage extramedullary hematopoiesis and large atypical megakaryocytes with “ink blot-like” nuclei and eosinophilic cytoplasm. The presence of JAK2 V617F mutation may suggest the clonal nature of the lesion [2]. Immunohistochemistry using glycophorin A, myeloperoxidase and factor VIII antigen can highlight erythroid, myeloid series and megakaryocytes respectively. [3,4]

Our case presented with ascites and peritoneal nodules and the clinical differential diagnosis included were tuberculous peritonitis, metastases, idiopathic retroperitoneal fibrosis, mesothelioma, gastrointestinal stromal tumors and lymphoma. [5, 6]

Diagnosis of SEMHT on cytology is very difficult in unsuspected cases, especially (i) when the clinical history is misleading as in our case with a high tumor marker (CA-125) levels, (ii) rarity of the lesion (and thus pathologist with reduced familiarity with the lesion) (iii) absence of information regarding the predisposing hematological conditions and (iv) distinct microscopic appearance on cytology as well as the biopsy. On fluid cytology, points that favor SEMHT over other malignancies were depicted in Table 2 below.

Table 2: Differences between SEMHT and other visceral malignancies on fluid cytology

Cytology feature on fluid cytology	SEMHT	Visceral malignancy
Cellularity	Low	Moderate to high
Cell arrangement	Discrete, singly scattered cells	Clusters, 3-dimensional balls, glands ± isolated cells
Cell size	Large cells (≥30μ)	Variable (from 15≥40μ)
Nucleus	Round to multilobated nucleus	Round to irregular
Nucleolus	Inconspicuous	Prominent
Background cells	Immature granulocytes and nucleated red blood cells	Mature red blood cells and white blood cells

The differential diagnosis of peritoneal nodule on microscopy included were sclerosing liposarcoma, malignant fibrous histiocytoma/pleomorphic sarcoma, sarcomatoid/anaplastic carcinoma and Hodgkin lymphoma [1,2]. The dense fibromyxoid to sclerotic stroma especially in the tiny core biopsies mislead the diagnosis towards a spindle cell neoplasm. However, extensive myelofibrosis on marrow redirected our case to the diagnosis of SEMHT with extramedullary hematopoiesis in peritoneum and the large abnormal cells in ascitic fluid cytology were redesignated as megakaryocytes.

Extramedullary hematopoiesis (EMH) is defined as the presence and growth of immature hematopoietic cells in locations other than marrow as a consequence of a low production of hematopoietic cells in the bone marrow from various causes [7]. EMH is very common in patients with CMPDs, especially primary myelofibrosis [4], and more commonly affects the liver, spleen and lymph nodes. Other rare locations include peritoneum, mesentery, retroperitoneum, kidneys, adrenal glands, pelvis, uterus, breast, heart, thymus, lung, pleura, dura mater, paraspinal region, gastrointestinal tract, skin and soft tissue [1, 2, 8, 9, 10]. SEMHT is reported in various locations which include liver, spleen, lesser omentum and mesentery, retroperitoneum, kidney, adrenal

gland, lacrimal gland, pelvis, skin, thyroid gland, lung, breast, heart and lymph node [11, 12, 13]. In all the reported cases, the lesion was not suspected initially due to its rarity and the diagnosis was made on histopathology with ancillary tests like immunohistochemistry.

SEMHT itself is a marker of advanced disease [9] and has a variable [7] prognosis and depends on the underlying disease. The disease could be stable for a long duration or may have a reduced survival rate possibly related to advanced disease. Review of literature shows that advanced age, anemia, leukocytosis, thrombocytopenia and skin involvement [12] are the unfavorable prognostic factors.

To the best of our knowledge this is the first case where, cytological features of SEHMT were discussed and also the case where marrow morphology has redirected the case towards accurate diagnosis in spite of a deficient clinical history.

CONCLUSION:

SEHMT is a rare entity, and the present case contributes to the expansion of current knowledge on cytological diagnosis of SEHMT. Pathologist should be aware of this rare lesion in the differential diagnosis of tumors with anaplastic morphology. Proper clinical history and accurate morphological diagnosis can reduce the delay in diagnosis in such cases.

STATEMENTS:

The statement of Ethics and consent: Written informed consent for publication was obtained from patient's relative. Patient(s) identity was never disclosed in the entire study. The study was not submitted to the institutional Ethics committee for approval, as it is a retrospective observational study and included data retrieved from archives.

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