SEROUS ATROPHY OF BONE MARROW: A RARE CAUSE OF PAEDIATRIC CYTOPENIA

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ABSTRACT

Serous atrophy of bone marrow also known as gelatinous transformation or serous fat atrophy is a rare finding. It is characterised by focal loss of hematopoietic elements, fat cell atrophy, and extracellular deposition of gelatinous substance with adjacent marrow hypoplasia. Pathogenesis of such atrophy is poorly understood and is considered to be a non specific finding, which can be associated with various haematological and non haematological conditions. It is mostly seen in adults with a few cases reported in the paediatric age group. We present a case of an 8 year old female patient with bilateral knee joint pains since one year. Blood counts and peripheral smear examination revealed bicytopenia (anemia and thrombocytopenia) along with a low normal total leucocyte count and a low reticulocyte count. Bone marrow aspirate consisted predominantly of sinusoidal blood and hence was inconclusive. Bone marrow biopsy from the iliac crest of right and left sides showed hypocellular marrow spaces with deposition of extracellular pink amorphous material suggestive of serous atrophy. Alcian blue at a pH of 2.5 was done to confirm the diagnosis and it stained the deposits blue. Therefore a diagnosis of hypoplastic bone marrow with associated serous atrophy was made. Bone marrow study is a vital tool in evaluation of cytopenias in pediatric age group as it helps to narrow down the list of differential diagnosis. In case of extracellular eosinophilic deposits with marrow hypoplasia, a differential of serous atrophy should be borne in mind.

KEYWORDS: Serous atrophy, pancytopenia, gelatinous transformation, alcian blue, mucopolysaccharides, bone marrow biopsy

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INTRODUCTION

Serous atrophy is an uncommon finding in the bone marrow, characterised by fat cell atrophy, gelatinous transformation of marrow spaces, and adjacent marrow hypoplasia. Histochemically the deposits are composed of hyaluronic acid and mucopolysaccharides\(^1\,^2\). It is a morphological diagnosis and can be confused with bone marrow necrosis, edema or amyloid deposits. Serous atrophy can be a telltale sign for the underlying disorder. It can form an important clue in approach to a patient with cytopenia, and the condition can be reversed if the entity is recognised early\(^1\,^3\). Here we report a case of serous atrophy in paediatric age group presenting as bicytopenia and diagnosed on bone marrow biopsy.

CASE REPORT

Following is a case of an 8 year old female who presented with bilateral knee joint pain and low grade fever since 1 year, with difficulty in sitting on the floor and squatting. Joint pain was aggravated on walking and other physical activities. There was no history of weight loss/ reduced appetite/ vomiting / abdominal pain or urinary complaints. Child’s development was appropriate for age, with height being 123.5cm (on 50\(^{th}\) centile) and weight being 17.8kg (on 3\(^{rd}\) centile). Primary immunisation of the child was complete. On physical examination patient was pale and afebrile. There was no organomegaly or lymphadenopathy. No icterus, cyanosis, edema or bony tenderness was noted. Patient was normotensive. The laboratory investigations revealed bicytopenia and peripheral blood smear showed normocytic normochromic anemia and thrombocytopenia. On differential count, Lymphocytes were 56% with reactive changes. Laboratory investigations are summed up in

<table>
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<tr>
<th>Laboratory data</th>
<th>Hematological, biochemical and serological data of the patient</th>
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<tbody>
<tr>
<td>Hb : 5.6g/dl</td>
<td>Serum ferritin : 131.6 ng/ml</td>
</tr>
<tr>
<td>RBC count : 2.11x10(^6)/µl</td>
<td>Serum Vit B12 : 347.2 pg/dl</td>
</tr>
<tr>
<td>Total leucocyte count : 5.6x10(^3)/µl</td>
<td>Serum ANA : Negative</td>
</tr>
<tr>
<td>Platelet count : 63x10(^3)/µl</td>
<td>Direct coomb's test : Negative</td>
</tr>
<tr>
<td>RDW : 23.3%</td>
<td>Serum C3 and C4 : normal</td>
</tr>
<tr>
<td>Reticulocyte count % : 0.4%</td>
<td>Antibodies to HIV1 and HIV2 : non reactive</td>
</tr>
</tbody>
</table>

Bone marrow aspirate was a dry tap (Figure 1) comprising predominantly of sinusoidal blood and was inconclusive. Bone marrow biopsy showed hypocellular marrow spaces with extracellular deposits of pink amorphous material and atrophied fat cells (Figure 2). Erythropoiesis, myelopoiesis and megakaryopoiesis were markedly suppressed. The amorphous deposits stained pale pink with periodic acid shiff (PAS) stain (Figure 3) and blue with alcian blue at a pH of 2.5 (Figure 4), ruling out possibility of amyloidosis, edema and necrosis. For this reason a diagnosis of serous atrophy or gelatinous transformation of bone marrow was made.

Figure 1
**Bone marrow aspirate smear, 10X,**
*Leishman stain: Dry tap*
Figure 2
Bone marrow biopsy, 10X, H&E: extracellular, eosinophilic amorphous to fibrillary deposits

Figure 3
Bone marrow biopsy, 10X, PAS: deposits are PAS positive

Figure 4
Bone marrow biopsy, 4X, Alcian blue: deposits are stained blue at a pH of 2.5
DISCUSSION

The documentation of serous atrophy of bone marrow in children has been limited to rare case reports. Bohm et al. attributed AIDS and febrile illness as the most common etiology for serous atrophy in age group of <40 years. Jain et al. attributed anorexia followed by protein energy malnutrition as the common cause of serous atrophy in paediatric age group, while Sen et al. in their review found infections and aplastic anemia to be the most common cause, followed by toxic bone marrow suppression. The most common presenting feature of serous atrophy in paediatric age group is anemia and a cachectic habitus on physical examination. Sen et al. suggested that serous atrophy can be a differential diagnosis while evaluating the causes of cytopenias other than megaloblastic anemia, aplastic anemia, myelophtisis anemia and meylo dysplastic syndromes. The exact pathogenesis of serous atrophy still remains unclear; it is postulated as a degenerative change occurring due to dietary deficiency leading to catabolism of the bone marrow fat. Accumulation of mucopolysaccharides fills and replaces the fat cells. This excessive accumulation inhibits the normal hematopoietic microenvironment leading to suppression of hematopoiesis which is reflected as peripheral blood cytopenias. Cytopenias improve once the underlying cause is treated. According to Singh et al., bone marrow was hypocellular in most of the cases. They documented increased capillary fronds in cases with infective etiology and inferred that an increase in lymphocytes, plasma cells, mast cells and stromal cells with less capillary proliferation and serous atrophy indicate an impending aplastic anemia. Morphological differential diagnosis of serous atrophy includes bone marrow necrosis, edema and amyloid deposits. Subtle morphological differences and special stains help in their differentiation.

<table>
<thead>
<tr>
<th>Etiology of serous atrophy</th>
<th>Malignancy</th>
<th>Leukemia post chemotherapy</th>
<th>Systemic lupus erythematosus</th>
<th>Chronic liver disease</th>
<th>Chronic renal failure</th>
<th>Severe hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia nervosa</td>
<td>Malnutrition</td>
<td>Acute febrile illness</td>
<td>AIDS</td>
<td>Alcoholism</td>
<td>Chronic heart failure</td>
<td>Cachexia secondary to chronic diseases like tuberculosis</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Morphological differential diagnosis of serous atrophy of bone marrow</th>
<th>Serous atrophy</th>
<th>Bone marrow necrosis</th>
<th>Bone marrow edema</th>
<th>Amyloidosis</th>
</tr>
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<tbody>
<tr>
<td>Character of deposits</td>
<td>Eosinophilic amorphous to fibrillary deposits</td>
<td>Granular morphology</td>
<td>Eosinophilic amorphous</td>
<td>Eosinophilic homogenous deposits</td>
</tr>
<tr>
<td>Fat cells</td>
<td>Fat cell atrophy</td>
<td>Destruction of marrow elements and surrounding bone</td>
<td>Fat cells are normal</td>
<td>Fat cells are normal</td>
</tr>
<tr>
<td>PAS</td>
<td>Stains the deposits pink</td>
<td>Negative</td>
<td>Weak pink stain</td>
<td>Stains the deposits pink</td>
</tr>
<tr>
<td>Alcian blue at pH 2.5</td>
<td>Stains the deposits blue</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Congo red</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Red with apple green birefringence under polarised light</td>
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</table>

Our case was a female child who presented with bicytopenia and showed serous atrophy of bone marrow along with hypoplastic marrow spaces. After ruling out malnutrition, chronic illness, autoimmune diseases by meticulous physical examination and laboratory investigations, it was concluded that serous atrophy associated with hypoplastic bone marrow can be attributed as a cause of cytopenia.

CONCLUSION

While evaluating a case of cytopenia, bone marrow examination gives vital information to bottle neck a wide range of etiologies. In the presence of extracellular accumulation of eosinophilic material along with fat cell atrophy and adjacent marrow hypoplasia, a diagnosis of serous atrophy should be borne in mind; it may suggest an underlying disease process warranting a meticulous diagnostic approach.

CONFLICT OF INTEREST

Conflict of interest declared none.
REFERENCES


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