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Case Series

Gaucher's disease is a common storage disorder but rare entity: Two case report

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ABSTRACT

Gaucher's disease is a rare, inherited autosomal recessive metabolic disorder due to deficiency of enzyme Glucocerebrosidase resulting in deposition of glucosylceramide. Deposition of glucosylceramide in different organs causes dysfunction and is responsible for specific systemic symptoms and signs. In the present cases, the first case was a 24-year-old female who presented with severe weakness with abdominal fullness due to massive splenomegaly. The unicity of the case was anti-nuclear antibody positivity. Although clinical signs and symptoms were classical in this case. The second case was a 20-year-old male who was already diagnosed case of Gaucher's disease but the only complaint was abdominal fullness due to massive splenomegaly. Special stains were play a tremendous role to highlighting Gaucher's cells.

1. Introduction

Gaucher's disease is the most common storage disorder but its overall incidence is very low. A countable number of cases are reported and best of our knowledge only one case with features of autoimmunity is reported in the literature. Diagnostic modalities include serum enzyme assay, radiology and microscopic examination. Bone marrow examination is important for diagnostic and prognostic purposes.

2. Case History

2.1. Case 1

The first case was a 24 year old female who presented in OPD with complaints of severe weakness since 5 years and abdominal fullness. On examination, massive splenomegaly and hepatomegaly were confirmed. Complete blood picture as follow: Hb: 9.6 g/dl, MCV: 86 fl, WBC: 6,700/cumm, Differential Count: Neutrophils: 32%, Lymphocytes:61%, Monocytes:07%, Eosinophils:00%, Basophils:00%, Platelets: 53,000/cumm. Viral markers for HBV, HCV and HIV were negative. Liver function test, thyroid function test, serum iron profile and serum vitamin B12 with folic acid levels were within normal range. A mild increase in serum protein was noted (9.2 gm/dl) due to a respective hike in globulin-5 gm/dl. CECT whole abdomen revealed gross splenomegaly and show diffuse heterogeneous attenuation of splenic parenchyma with multiple mesenteric lymph nodes. The sickling test by slide method was negative. Surprisingly Anti-nuclear antibody by indirect immunofluorescence method was positive with centrosome 2+ positivity.

Bone marrow biopsy and aspiration were performed. Bone marrow aspiration revealed trilineage hematopoiesis with abnormal scattered macrophages having abundant cytoplasm with crumpled tissue paper appearance and eccentric nucleus. Bone marrow biopsy had cortico-cancellous bone with 17 bony trabeculae showed more diagnostic features like diffuse infiltration of large cells

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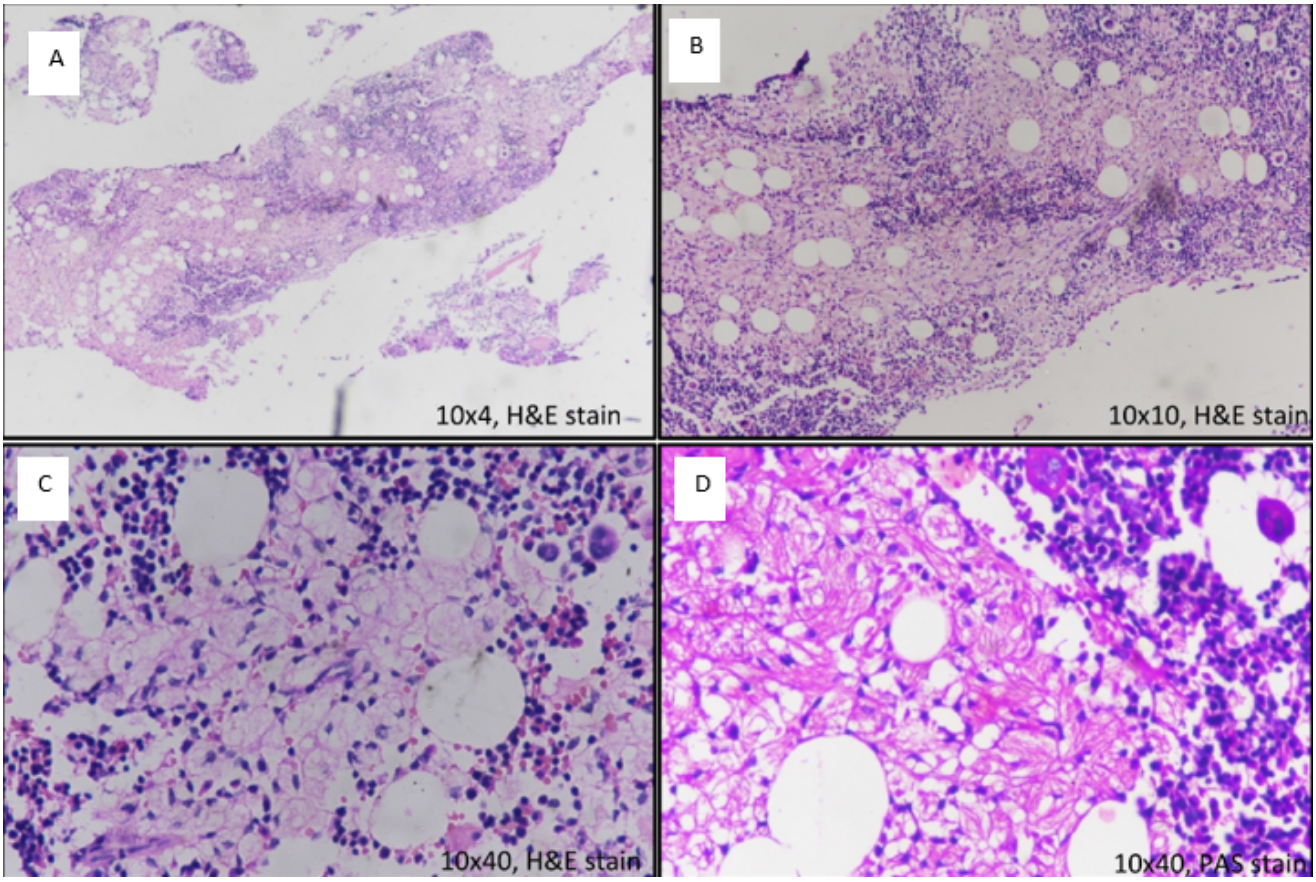

Fig. 1: Bone marrow biopsy had cortico-cancellous bone bony trabeculae showed diffuse infiltration of large cells arranged in sheets with abundant cytoplasm with crumpled tissue paper appearance and eccentric nucleus (**A;** 40x, **B;**100x, **C;**400x). These cells are Periodic acid Schiff (PAS) stain positive (**D;** 400x).

arranged in sheets with abundant cytoplasm with crumpled tissue paper appearance and eccentric nucleus. These cells are Periodic acid Schiff (PAS) and faint iron stain (Perl's Prussian blue) positive. Reticulin fibres were increased at the side of infiltration by these abnormal macrophages.

2.2. Case 2

The second case was a 20 year old male who had complained of only left side abdominal pain. Hemogram revealed Hb:14.0 g/dl; MCV:86.3 fl;WBC:5110 /cumm;DC: N68 %, L23 %, M05 %, E04 %, B00 %; Platelet:70,000/cumm. So normocytic normochromic anemia with thrombocytopenia was there in peripheral blood smear. The liver function test and renal function test was normal. Viral markers for HBV, HCV and HIV were negative. Examination revealed splenomegaly. CECT whole abdomen was revealed massive splenomegaly. Anti-nuclear antibody was negative in this case.

Splenectomy was performed and received for examination. Grossly spleen measures 25x16x15 cm, cut surface was congested. Histopathology examination of spleen displaying congested red pulp along with histiocytes showing finely granular cytoplasm.

3. Discussion

Philippe Gaucher described Gaucher's disease in 1882, and its familial nature was recognized by Brill et al. in 1904. In 1927, Oberling et al. discovered the neurologic component of Gaucher's disease, which is more common among the childhood forms.[1] Gaucher's disease is the most common lysosomal storage disorder although its incidence is very low at 1:100000 individuals.[1] Incidents are significantly higher in Ashkenazi Jews.[2] In the Indian population, the incidence is much lower as compared to in Israel. In the era of molecular pathology, specific genetic alterations are also identified which are involved in the pathogenesis of Gaucher's disease. Its includes N370S and L444P mutations.[3] L444P is more related to neurological symptoms.[3] Accumulation of glucosylceramide in different organs is the key to the etiopathogenesis of Gaucher's disease.

There are mainly 3 types described clinically for Gaucher's disease. Type I is the most common type and the incident is reported predominantly in adult individuals. The present case also follows the same trend. Type II and type III are seen predominantly in children. Neurological symptoms are most commonly associated with type II and type III. Hepatomegaly with bone pain with massive splenomegaly is the feature of type I Gaucher's disease. In presenting both cases also had hepatomegaly and massive splenomegaly. Skeletal abnormalities are the hallmark of type I disease. But in the present case, no skeletal abnormality was found. Binesh et al. reported a similar case.[4] Prognosis wise type I has a better prognosis. Two subtypes of type II are also reported recently 1) Gaucher disease, perinatal-lethal form 2) Gaucher disease, cardiovascular form. The perinatal-lethal form is associated with ichthyosiform or collodion skin abnormalities or with nonimmune hydrops fetalis. The cardiovascular form is characterized by calcification of the aortic and mitral valves, mild splenomegaly, corneal opacities, and supranuclear ophthalmoplegia.

Microscopically wrinkled paper like cytoplasmic macrophages was identified in the bone marrow imprint and biopsy of the first case which are classical Microscopic features of Gaucher's disease. However, pseudo-Gaucher's cells are also seen in Acute myeloid leukaemia, chronic myeloid leukaemia and chronic lymphocytic leukaemia. Diffuse infiltration of these macrophages was in concordance with cytopenia in the peripheral blood. Periodic Acid-Schiff (PAS) was performed which highlights the wrinkled cytoplasm of macrophages. In the second case, these histiocytes with only finely granular cytoplasm were evident.

Examination of bone marrow not only gives a diagnostic modality but also had its prognostic significance as Gaucher's disease has increased risk for haematological malignancy.[5] Parkinsonism's disease with Gaucher's disease was also reported but only one case was reported previously with Systemic lupus erythematosus.[2,6] In the first case, the divergent finding was ANA positivity. Teresa et al. reported a similar case before.[2] Teresa et al. reported that all diagnostic findings were present in their case related to SLE, but in the present case, only ANA positivity was noted without any systemic symptoms of SLE specifically renal impairment. Further studies are required to find out any proximity between these two condition. They also suggested trigging of autoimmunity due to excessive accumulation of abnormal lipid in the cells. Therefore, close follow-up is required.

Despite routine stains like Hematoxylin and Eosin (H&E), special stains highlight these Gaucher's cells very well. Periodic Acid-Schiff and Masson's trichrome stain are useful to highlight Gaucher's cells.

Due to overlapping clinical signs and symptoms with leukaemia and other systemic disorder, diagnosis of Gaucher's disease is always a diagnostic dilemma. A confirmatory diagnostic tool for Gaucher's disease is the demonstration of deficient Glucocerebrosidase status by biochemical examination.[7] Presenting both cases had low Glucocerebrosidase levels. Treatment modalities are generally palliative care and enzyme supplementation. Sometimes splenectomy is also performed to relieve the symptoms. It is recommended that before splenectomy bone marrow cellularity is checked for preventive measures.

4. Conclusion

B.M. examination with the presence of abnormal macrophages is the hallmark for the diagnosis of Gaucher's Disease histologically but other storage disorders and sometimes leukaemia mimics with overlapping signs and symptoms however; all suspects should be confirmed by demonstrating deficient acid β-glucosidase activity in isolated leukocytes. Although the diagnosis of Gaucher's disease is a combined approach towards the suspicion. Treatment is necessary as soon as the diagnosis is stabilized. Our aim to report these cases was to emphasize that Gaucher's disease is rare but close differential from leukaemia in individuals having unexplained splenomegaly, especially at a younger age. Also, ANA positivity is suggestive of the development of autoimmune disease due to abnormal lipid deposition in the cells.

5. Conflict of Interest

There are no conflicts of interest in this article.

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None.

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