CASE REPORT

Crystal storing histiocytosis: a rare presentation of plasma cell myeloma

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Abstract Crystal storing histiocytosis (CSH) is a very rare association with plasma cell dyscrasias. It is presumed to be an intra-lysosomal accumulation of the secreted paraprotein aggregated into crystals and is associated with presence of variable numbers of histiocyte-like cells with phagocytosed crystalline inclusions in the bone marrow and other extramedullary sites. Herein we report a case of multiple myeloma associated with CSH with a rapidly downhill clinical course. There was diagnostic confusion at the outset with a histiocytic disorder which was clarified with the use of Immunohistochemistry along with serum protein electrophoresis and immunofixation.

Keywords Crystal storing histiocytosis · Plasma cell dyscrasias · Immunohistochemistry

Introduction

Crystal storing histiocytosis (CSH) is a very rare finding in the spectrum of plasma cell dyscrasias. It is presumed to be an intra-lysosomal accumulation of the secreted paraprotein or immunoglobulin chain which has a propensity to aggregate into crystals. It is almost always associated with kappa light chain type [1]. Crystal formation is associated with presence of variable numbers of histiocyte-like cells with phagocytosed crystalline inclusions in the bone marrow and other extramedullary sites [2]. The clinical course of patients with CSH is often downhill with death within months. Due to the rarity of this entity, these histiocytes may be mistaken for Gaucher and pseudo-Gaucher cells [2]. Herein we report a case of multiple myeloma associated with CSH with a rapidly downhill clinical course.

Case report

Clinical findings

A 54-year-old male presenting with loose motions for 2 years duration was evaluated in gastroenterology department for malabsorption where he was found to have low hemoglobin and high serum creatinine and subsequently referred to hematology for evaluation. He had developed cough of 2 months duration unaccompanied by fever, chest pain or shortness of breath. On examination, the patient had pallor, ascitis, hepatosplenomegaly (liver-7 cm and spleen-7 cm enlarged below costal margins) and right lower lobe consolidation with occasional coarse crepitations. On

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investigation, he had hemoglobin 78g/l, TLC $2.3 \times 10^9/l$ with 70% polymorphs and platelet count $20 \times 10^9/l$. His biochemical investigations showed hypercalcemia (Ca-12.1 mg %), hypokalemia (K-2.1 mg %) with raised blood urea (67 mg%) and serum creatinine (2.2 mg %). Radiologically, chest X-Ray showed right sided basal consolidation and effusion; skeletal survey did not show any lytic lesions. USG abdomen showed hepatosplenomegaly, ascitis and normal sized kidneys; Echocardiography showed EF-60% with dilated cardiac chambers. Serum electrophoresis showed the presence of an M band which was identified on immunofixation to be IgG Kappa. On quantification, IgG was 5860 mg%, IgA was 10 mg% and IgM was 27 mg%. Urine electrophoresis showed the presence of M protein. Serum β_2 microglobulin was markedly raised to 13668 $\mu g/l$.

Pathological findings

Peripheral smear showed rouleaux formation with the presence of occasional circulating plasma cells. The bone marrow was cellular and showed prominent numbers of histiocytic cells containing crystalline cytoplasmic inclusions (Fig. 1). Immature cells with plasmacytoid appearance comprising 45% of nucleated cells, also laden with similar cytoplasmic crystals were present (Fig. 2). The inclusions were negative for PAS and Perls stain for iron. The bone marrow biopsy was hypercellular and showed a diffuse replacement with crystal-laden histiocytic cells along with interspersed smaller plasmacytoid cells (Fig. 3). Immunohistochemistry with CD 68 showed strong, diffuse cytoplasmic staining of the crystal – laden histiocytic cells

Fig. 1 Bone marrow aspirate showing histiocytes (figure inset) and plasma cells with crystalline intracytoplasmic inclusions. (Jenner Giemsa staining x 1000)

(Fig. 4). Interspersed plasma cells were unstained. A literature search conducted revealed the rare entity called crystal storing histiocytosis associated with plasma cell dyscrasias. Immunostaining for CD 56, an NK cell marker which shows specificity for neoplastic plasma cells was performed. Nearly all the plasma cells showed membrane staining for CD 56 (Fig. 5). On the basis of presence of an M band and the above mentioned histopathological findings, a diagnosis of crystal storing histiocytosis with plasma cell dyscrasias (plasma cell myeloma) was therefore rendered.

Clinical course

The patient was admitted under hematology and treated with high dose dexamethasone and bortezomib. He

Fig. 2 Bone marrow aspirate showing numerous plasma cells and plasmablasts with crystalline intracytoplasmic inclusions. (Jenner Giemsa staining x 1000)

Fig. 3 Bone marrow biopsy showing diffuse infiltrate of plasma cells and histiocytes. (Hematoxylin and eosin staining x 400)

Fig. 4 Immunohistochemistry with CD 68 on bone marrow biopsy showing strong, diffuse cytoplasmic staining of the crystal-laden histiocytic cells (Immunoperoxidase for CD68 x 400)

Fig. 5 Immunohistochemistry with CD 56 on bone marrow biopsy showing membrane staining in the plasma cells. (Immunoperoxidase for CD56 x 400)

received broad spectrum antibiotics and antifungal agents. In spite of this, his right sided basal consolidation with effusion persisted. On the fifth day of therapy the patient developed jaundice (Bilirubin/C/UC-6.7/5.1/1.6 mg %) and increasing breathlessness. There was tense ascitis with raised liver enzyme levels of SGOT 1030IU, SGPT-644IU and AP-673IU. Subsequently the patient went into coma and succumbed to his illness with cause of death being intracranial hemorrhage and acute liver failure.

Discussion

Disorders associated with plasmacytosis have been associated with deposition of various materials in tissues and

with inclusions in the plasma cells. Crystalline inclusions in plasma cells are unique because of the rarity of this entity and the association with renal involvement in the form of renal tubular dysfunction leading to adult Fanconi syndrome and multi-organ dysfunction caused by proliferation and infiltration of tissues by histiocytes laden with crystalline inclusions. The inclusions have been shown to be made up of mutated kappa light chains [1]. The mutation leads to a block in the secretion of the kappa light chains and resultant accumulation within plasma cells. The prominent histiocytic cell proliferation which at times obscures the plasma cells leading to confusion with a storage disorder may be secondary to destruction of crystal laden plasma cells.

Most reported cases of crystal laden histiocytosis have been associated with plasma cell dyscrasias including MGUS. Fewer cases have been seen with benign plasmacytosis, as localized tumours in organs such as stomach and in association with multifocal fibrosclerosis [2, 3]. The majority of reported cases of plasma cell dyscrasia accompanied by crystal storing histiocytosis had kappa chain as the monoclonal light chain.

In our case the possibility of a histiocytic disorder was considered because the patient presented with hepatosplenomegaly, chronic diarrhoea and lack of osteolytic lesions. However he had hypercalcemia, presence of an M band and evidence of renal failure which raised the possibility of a plasma cell dyscrasia. Morphologically crystalline inclusions were present in cells which were clearly histiocytes and also in the immature plasmacytoid cells with eccentric nuclei, vesicular chromatin and basophilic cytoplasm. The nature of these cells were not clear at the outset. Immunostains for CD68 confirmed the histiocytic nature of the larger cells but left the smaller basophilic cells unstained. Hence CD56 an NK cell marker which is also reported to be marker of neoplastic plasma cells [4] was employed to clarify the nature of the smaller crystal laden cells. A positive membrane staining pattern was observed in the numerous basophilic cells confirming the neoplastic nature of the cells which, morphologically, were more like plasma cells than histiocytes.

The clinical implications of observing crystal containing histiocytes in a plasma cell dyscrasia is, first, the diagnostic confusion with a storage disorder. Secondly in most reported cases, persistent disease in spite of therapy and rapid disease progression leading to death has been observed, not the least because of infiltration of vital organs such as the lung, which was present in our case. The frequent association with renal involvement likely contributes to the morbidity and mortality. The diagnosis may be difficult in

cases where there is minimal plasma cell infiltration and levels of paraprotein are low by conventional tests [1, 2]. In such cases the presence of histiocytes containing crystalline inclusions should lead to the performance of more sensitive assays such as serum free light chains to pick up the underlying plasma cell dyscrasia.

Conclusions

A case of crystal storing histiocytosis associated with plasma cell dyscrasia (plasma cell myeloma) has been presented. This is a unique morphological entity with grave prognostic implications which may have diagnostic confusion with a storage disorder. Immunohistochemistry may be of immense help in resolving problematic cases.

References

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