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Case report

NEW INSIGHTS IN TO SYSTEMIC AMYLOIDOSIS: PRIMARY AMYLOIDOSIS ASSOCIATED WITH TUBERCULAR LYMPHADENITIS

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ABSTRACT

Tuberculosis is generally followed by secondary amyloidosis. The association of primary systemic amyloidosis with tuberculosis is very rare. There is only one case thus far reported in literature. We report such a rare case of primary amyloidosis with tuberculous lymphadenopathy. A 45 year old woman presented at the medicine department of all India institute of medical sciences , New Delhi with on & off erythematous rashes over both eyes for 1 year; low grade fever, fatigue and significant weight loss for 4 months, dysphagia for solid food since 1 month. Main finding on examination were pallor, macroglossia, bilateral periorbital erythematous rashes (racoon eyes), hepatomegaly & cardiomegaly. She had raised serum alkaline phosphatase level. Chest x-ray revealed cardiomegaly. USG abdomen revealed multiple retroperitoneal mesenteric lymph nodes and hepatomegaly. USG guided FNAC from mesenteric lymph node showed acid fast bacillus. Histological examination of liver biopsy showed amyloid deposition on congo red stain. Patient was treated with DOTS category I ATT with Bortezomib and Dexamethasone based weekly chemotherapy.

Keywords: Amyloidosis, Tubercular lymphdenopathy, Bortezomib

INTRODUCTION

The term amyloid was introduced in 1854 by the German physician scientist Rudolph Virchow (reviewed by Cohen, 1986).[1] Rudolf Virchow first described amyloidosis as an extracellular deposition of carbohydrate. What we know now is that there is an extracellular deposition of proteinaceous material which, when stained with Congo red gives apple green birefringence under polarized light. In 1838, Mathias Schleiden, a German botanist, coined the term 'amyloid' for the amylaceous constituents of plants. In 1854, Rudolf Virchow adopted the term to describe abnormal extra-cellular material that he encountered in the liver during autopsy.[2] Divry and associates[3] recognized that the amyloid deposits showed apple-green birefringence when specimens stained with Congo red were viewed under polarized light. This observation remains the sine qua non of the diagnosis of amyloidosis. We report a case of uncommon association of primary AL amyloidosis with a common disease.

CASE REPORT

A 45 year old woman presented with on & off erythematous rashes over both eyes for 1 year; low grade fever, fatigue and significant weight loss for 4 months, dysphagia for solid food since 1 month; intermittent spasmodic pain at umbilical region since 20days. Her BP was 100/70 mm/Hg, PR: 102/ min, RR:22/ min. She had pallor, macroglossia (figure1), petechial rashes over right arm & bilateral periorbital erythematous rashes (racoon eyes). On abdomen,

tenderness at right hypochondrium and enlarged firm tender liver (24 cm) were present. CVS examination revealed cardiomegaly only.

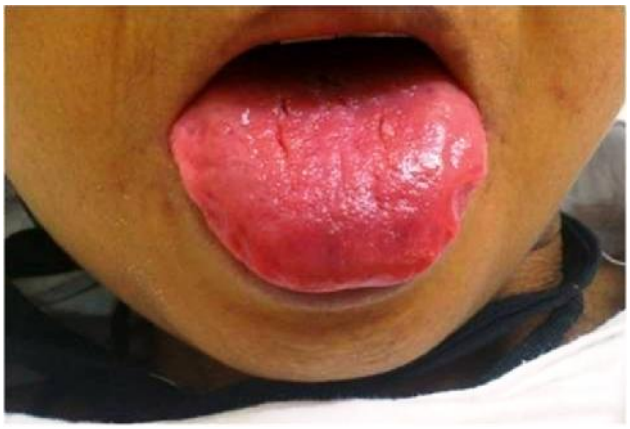

Fig 1: Showed macroglossia

Blood test showed Hb: 11.4g/dl, WBC: 14300/cu mm, Platelet: 561000/ul, ESR: 05mm/hr. She had isolated raised ALP: 840 IU/L) level. Urine routine microscopy and 24 hr. urinary protein were normal. Chest x-ray revealed cardiomegaly. Her ECG revealed low voltage QRS complex in the limb leads with poor progression of R wave in precordial leads. As a suspected case of infection - HIV, hepatitis viral markers, blood & urine gram stain culture done were negative. Though toxic granules containing neutrophils were present, no atypical malignant cells in the blood. Lactate dehydrogenase level was normal. Serum & urine protein electrophoresis showed no M band, but elevated lambda light chain level (λ=152. 53 mg/L) in serum free light chain assay. kappa & lambda light chain ratio was low (k:λ=0.06). Total protein & albumin – globulin ratio were normal.

USG abdomen revealed multiple retroperitoneal mesenteric lymph nodes, hepatomegaly, mild ascites and bilateral mild pleural effusion. Contrast enhanced computed tomography (CECT) of chest and abdomen confirmed the USG finding. USG guided Fine needle Aspiration Cytology (FNAC) from mesenteric lymph node showed Acid Fast Bacilli (AFB). Bone marrow biopsy showed 7% mature plasma cells, but it was negative for lymphoma deposits or amyloids. Abdominal fat pad biopsy was equivocal for amyloidosis. Subsequently liver biopsy was done and histopathologicaly revealed amyloid deposition (figure II). Immunohistochemistry of liver biopsy showed predominant lambda light chain deposition around blood vessels in the background of nonspecific lambda and kappa light chain deposition in the sinusoids.

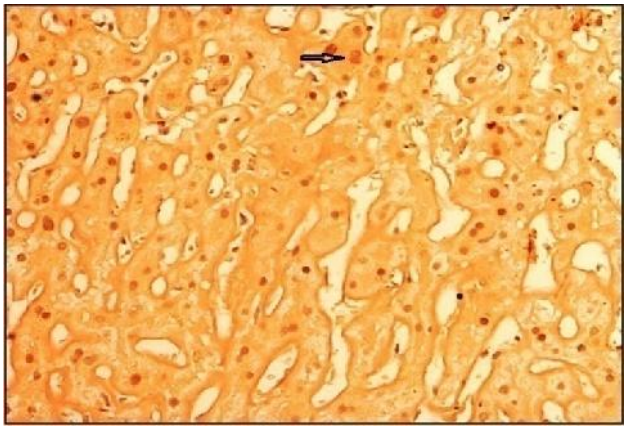

Fig 2: A Section of the liver stained with congo red reveals pink-red deposits of amyloid (arrow) along with sinusoids. (40x).

As the patient had progressive dysphagia, barium swallow was showed sluggish peristalsis with tertiary contraction in thoracic oesophagus but subsequent upper G.I. endoscopy was normal. Autonomic function tests revealed severe dysfunction, but the nerve conduction test was normal. Echocardiography showed bi-ventricular hypertrophy, bi-atrial enlargement, thickened IVS and posterior wall, granular sparkling of myocardium, severe left ventricular dysfunction (EF 27%) & mild pericardial effusion. Subsequent Holters study and BNP level were normal.

Based on the above, a final diagnosis of primary Amyloid Light-chain (AL) amyloidosis with abdominal Koch was made. For tuberculosis, category I anti tubercular treatment (ATT) and for amyloidosis, Bortezomib and Dexamethasone based weekly chemotherapy started. Though her symptoms improved temporarily in the form of decreased dizziness, fatigue, but after the third chemotherapy, she developed decompensated chronic heart failure (CHF) followed by diarrhoea. Appropriate treatment started & Bortezomib based chemotherapy withheld in the fear of drug induced diarrhoea. Later she started having direct hyperbilirubinemia with leucocytosis. ATT modified & broad spectrum antibiotics started as all the investigations to localize the infection were negative. Because of deranged LFT, Bortezomib chemotherapy stopped and Cyclophosphamide & Dexamethasone based weekly chemotherapy started. But the patient's condition deteriorated rapidly and she died of septic shock with aspiration pneumonia after 4 weeks.

DISCUSSION

Amyloidosis is a heterogeneous group of diseases associated with the common pathological process of extracellular protein deposition in various organs, leading to organ dysfunction and death.

Inspite of the fact that hepatic involvement in systemic amyloidosis is common histologically occurring in 60-100% of liver specimens[4] clinically apparent liver disease is infrequent. The patient had markedly elevated serum alkaline phosphatase which suggests an early phase of intrahepatic cholestasis. Jaundice is usually a terminal feature and most probably would have appeared if the patient had lived long enough. Intrahepatic cholestasis secondary to amyloidosis has been reported by several other workers.[5,6] Other parameters of liver function which reflect the integrity of the hepatic parenchymal cells, such as bilirubin level, serum albumin and prothrombin time were normal because hepatic amyloidosis is primarily an infiltrative disorder.

Tuberculosis is generally followed by secondary amyloidosis. The association of primary systemic amyloidosis with tuberculosis is very rare. Only one case thus far reported in literature.[7] Diagnosis of tuberculosis in presence of systemic amyloidosis can be challenging as Amyloid material in a lymph node can masquerade as caseous necrosis in cytology.[8] Our patient had AFB in the abdominal lymph nodes which regressed completely with ATT. The present case outlines the challenges in management of atypical cases where liver involvement with amyloid and use of potentially hepatotoxic drugs was required for the treatment of the patient.

There was no identifiable chronic inflammatory, infective or neoplastic disorder to account for amyloid deposition. Serum protein electrophoresis did not show abnormal band. There was no bence-jones protein in urine and bone marrow examination, did not show expansion of plasma cell. This suggests that the amyloidosis is most likely to be primary, but unrelated to any overt immunocyte dyscrasia.

Our patient had primary amyloidosis with Liver, Cardiac, ANS and GIT involvement with abdominal tuberculous lymphadenopathy. Bortezomib with dexamethasone is a proven therapy for primary amyloidosis.[9] Our patient was started on this treatment. Since she developed side effects, therapy was changed to cyclophosphamide. But she succumbed to her disease.

CONCLUSION

We conclude that tuberculosis is generally followed by secondary amyloidosis. The association of primary systemic amyloidosis with tuberculosis is very rare, but in this case we can also think that primary systemic amyloidosis can be associated with tuberculosis.

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Conflict of interest: The authors declare no conflict of interest.

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