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HEPATIC INVOLVEMENT IN SYSTEMIC AMYLOIDOSIS – A CASE REPORT.

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ABSTRACT

A 52 year old woman presented at the gastroenterology clinic of University of Nigeria Teaching Hospital Enugu with a 3-month history of pruritus, right upper abdominal pain, easy satiety and weight loss. She had been treated in a peripheral hospital 2 years earlier for epigastic pain. The main findings on physical examination were emaciation, scanty axillary hair, palmer erythema and hepatomegaly. Urine examination showed marked proteinuria. Serum alkaline phosphatase was markedly elevated. Histological examination of biopsy specimen of the liver showed marked hyaline-like amorphous perivascular and extravascular deposition, which proved to be amyloid with Congo red stain.

The patient later developed persistent vomiting and had one episode of haematemesis. Barium meal showed severe deformity and scarring of the duodenal bulb. Gastrojenostomy was carried out but the patient died 3 hours after surgery from severe haematemesis. We conclude that the patients had amyloid infiltration of the liver with probable involvement of the kidneys and upper gastrointestinal tract Amyloidosis should be suspected in any patient with unexplained hepatopathy and proteinuria

KEY WORDS: Amyloidosis, hepatic, cholestasis.

INTRODUCTION

Amyloid is a pathologic proteinaceous substance deposited between cells in various tissues and organs of the body in a wide variety of clinical settings. This deposition may be systemic, involving various organs of the body or localized as in the pancreas or brain.[1] In primary amyloidosis there is depositing of insoluble monoclonal immunoglobulin light chain fragments in various tissue whereas in secondary or reactive amyloidosis the abnormal deposit is usually a non-immunoglobulin protein synthesized by the liver in conditions of protracted breakdown of cells resulting from a wide variety of chronic inflammatory diseases such as tuberculosis, bronchiectasis, chronic osteomyelitis, rheumatoid arthritis and inflammatory bowel diseases. Although the liver may be involved in systemic amyloidosis, clinically evident hepatic dysfunction and liver chemistry abnormalities are often mild or absent.[2] In this report a 52 year old woman in whom hepatomegaly and markedly elevated serum alkaline phosphatase were due to amyloid deposition in the liver is presented.

CASE REPORT

Mrs. O.L, a 52 year old woman presented to the gastroenterology clinic of the University of Nigeria Teaching Hospital Enugu, Nigeria with a 3 month history of pruritus, right upper abdominal pain, easy satiety and weight loss. Past medical history revealed that she had epigastric pain 2 years earlier, which was treated empirically as peptic ulcer disease with good result. The main findings on physical examination were emaciation, scanty axillary hair, palmar erythema, and hepatomegaly 12cm measured below the right costal margin in the mid clavicular line with a span of 22 cm. The liver was hard and the surface smooth.

Initial investigations included abdominal ultrasonography which showed moderate hepatomegaly of normal echotexture, multiple gall bladder stones and enlarged pancreas. Liver function test showed markedly elevated serum alkaline phosphatase 509 iu/L (normal 25 – 92), prothrombin time was 14 seconds with a control of 13 seconds. Full blood count showed Hb of 13.6 gm/dl, WBC 5600/MM^3, (Neutrophil = 54%, lymphocyte = 46%) Platelets 250,000/mm^3, ESR 120 mm first hour (Westergren). Urine examination showed significant proteinuria (24 hour urine protein = 4.0 grams). She was negative for Hepatitis B surface antigen as well as antibodies to HIV 1 and 2. Chest X-ray and electrocardiogram did not show any abnormality. Total serum protein was 70 gm/L, Albumin was 32 gm/L and globulin was 38 g/L. Histological examination of needle biopsy specimen of the liver showed intact hepatic architecture with prominent amorphous hyaline deposits characteristically extracellular and extravascular, and areas of arteriolar wall infiltration by the hyaline material (Fig.1). Congo red stain showed the deposits as amyloid (Fig.2). Urine examination for Bence-Jones protein was negative. Serum protein electrophoresis did not

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show any abnormal band and bone marrow aspirate did not show any expanded plasma cell population.

The patient was placed on melphalan 10 mg daily and prednisolone 45mg daily. Four days into this treatment she developed epigastric pain and vomiting which became persistent with one episode of haematemesis. This was managed conservatively with intravenous fluids. When the vomiting subsided, barium meal radiography was performed and it showed severe deformity and scaring of the duodenal bulb. Laparotomy was then carried out and the findings were enlarged liver, chyllous ascites, distended gallbladder and distended stomach. Trunkal vagotomy and gastrojejunostomy were carried out but unfortunately the patient died 3 hours after surgery from massive haematemesis. There was no post mortem examination because the family refused to consent to it.

Fig. 1
High power view of diffuse amyloid deposition in the liver. Haematoxylin and Eosin X 200.

Fig. 2
High power view of diffuse amyloid deposition in the liver stained with Congo red. X200.

DISCUSSION

Inspite of the fact that hepatic involvement in systemic amyloidosis is common histologically occurring in 60-100% of liver specimens [2-4] clinically apparent liver disease is infrequent. Renal and cardiac involvement are often prominent in patients with primary amyloidosis while the kidney is most often involved in secondary amyloidosis.[5,6]

Amyloidosis was not considered clinically as a cause of the hepatopathy in the patient. For this reason liver biopsy was confidently embarked upon after routine coagulation screen. No other extra risk of haemorrhage was considered. If amyloidosis had been considered, alternative biopsy sites such as subcutaneous abdominal fat, rectum, skin or gingival might have been chosen. [7-8] Amyloidosis should therefore be suspected in any patient with significant proteinuria and evidence of chronic liver disease.

The patient had pruritus as well as a markedly elevated serum alkaline phosphatase. These suggest an early phase of intrahepatic cholestasis. Jaundice is usually a terminal feature[9] 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.[10-12] 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.

Other findings in the patient included enlarged pancreas (on ultrasonography) enlarged gallbladder and gallstones. The exact pathogenesis of these abnormalities is not clear but it is probable that these organs may have been involved in systemic amyloid deposition. A gallbladder whose wall is infiltrated by amyloid is predisposed to stone formation. Amyloidosis involving the gastrointestinal tract has been described by various authors and the characteristic manifestations include haemorrhage, obstruction and motility disturbances.[13-16]

The fatal reactionary haemorrhage that followed gastrojejunostomy in this patient is likely to be multifactorial. Amyloid deposition in the walls of blood vessels with consequent impairment of vasospasm probably played a major role.[14] In fact it has been suggested that whenever possible, other therapeutic options be employed in amyloidosis involving the gastrointestinal tract instead of surgery, for instance balloon dilation of ulcer-induced pyloric stenosis can be carried out in place of gastric drainage operation.[16] Also embolisation of vessels is recommended in gastrointestinal haemorrhage instead of surgery.[17] This patient had both pyloric stenosis and haemorrhage and surgery was the only readily available therapeutic option to deal with both complications. However, the outcome of surgery underscores the fact that it should be avoided in amyloidosis of the gut.

There was no identifiable chronic inflammatory, infective or neoplastic disorder to account for amyloid deposition in the patient. Serum protein electrophoresis did not show any abnormal band. There was also no Bence-Jones protein in urine and bone marrow examination did not show any expansion of plasma cell population. This suggests that the amyloidosis is most likely to be primary but unrelated to any overt immunocyte dyscrasia. Melphalan, which is an alkylating agent, is one so the few therapeutic options available for systemic amyloidosis even when there is no overt plasma cell dyscrasia. Delayed progression of such case, to overt multiple myeloma is a possible sequela[18] and probable would have occurred in this patient if she had lived long enough.

The prevalence of systemic amyloidosis in Nigeria is not known but it is definitely not a common clinical problem though chronic inflammatory conditions of infective origin such as tuberculosis, leprosy and leg ulcers abound in our environment. Reactive amyloidosis does not seem to be as common as these chronic infections. The reasons for this observation are not clear and studies are definitely needed in this subject.

This case also highlights some of the problems encountered in medical practice in developing countries. Gastroscopy would have been a better modality of investigation in this patient because it would have afforded the opportunity to take biopsies. The gastroscope was out of order at the time patient was managed. Also refusal to give consent for autopsy is a very frequent occurrence in tropical medical practice.

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