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IMMUNOPROLIFERATIVE SMALL INTESTINAL DISEASE (ALPHA HEAVY CHAIN DISEASE) : UNUSUAL PRESENTATION WITH ABDOMINAL MASS

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ABSTRACT

During the period of 1984-1995, nine young patients were admitted to Shiraz University Hospitals with a chief complaint of abdominal mass, weight loss and chronic diarrhea. Clinically, these cases were diagnosed as intestinal tuberculosis or lymphoma. Laparotomy revealed a huge mass involving the upper small intestine. Histologic sections showed diffuse infiltration of the intestinal wall with numerous mature and immature plasma cells. Serological tests showed increased levels of IgA. These cases were diagnosed and treated as immunoproliferative small intestinal disease (IPSID). Follow-up of these patients revealed that seven patients died 6-8 months after the operation and the other two patients were lost to follow-up.

Keywords: IPSID, Disease, Alpha heavy chain

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INTRODUCTION

Immunoproliferative small intestinal disease (IPSID) is also called Mediterranean lymphoma, because of its frequent occurrence in Mediterranean countries. It is also called alpha heavy chain disease, because of increased abnormal production of IgA[1,2,4,5,8-15,20] However, the World Health Organization has called this lesion IPSID because this disease is no longer limited to Mediterranean countries.[21] Moreover, it is reversible if treated in the premalignant stage.

Immunoproliferative small intestinal disease is a common cause of malabsorption syndrome among young patients in Iran. The male to female ratio is about 3:1. Usually these cases are characterized by diffuse thickening of the upper small intestine with numerous plasma cells. These cells are responsible for the abnormal production of IgA. Various laboratory tests are available for the demonstration of alpha or heavy chain protein in the urine and serum.[17,18] These patients can be treated successfully with prolonged antibiotic therapy (tetracycline) at the early stage of the disease. IPSID presenting with huge abdominal mass is unusual and only a few cases have been reported in the literature.[6,16] This paper describes the clinical and pathological findings of nine cases.

PATIENTS AND METHODS

During an eleven year period (1984-1995), nine

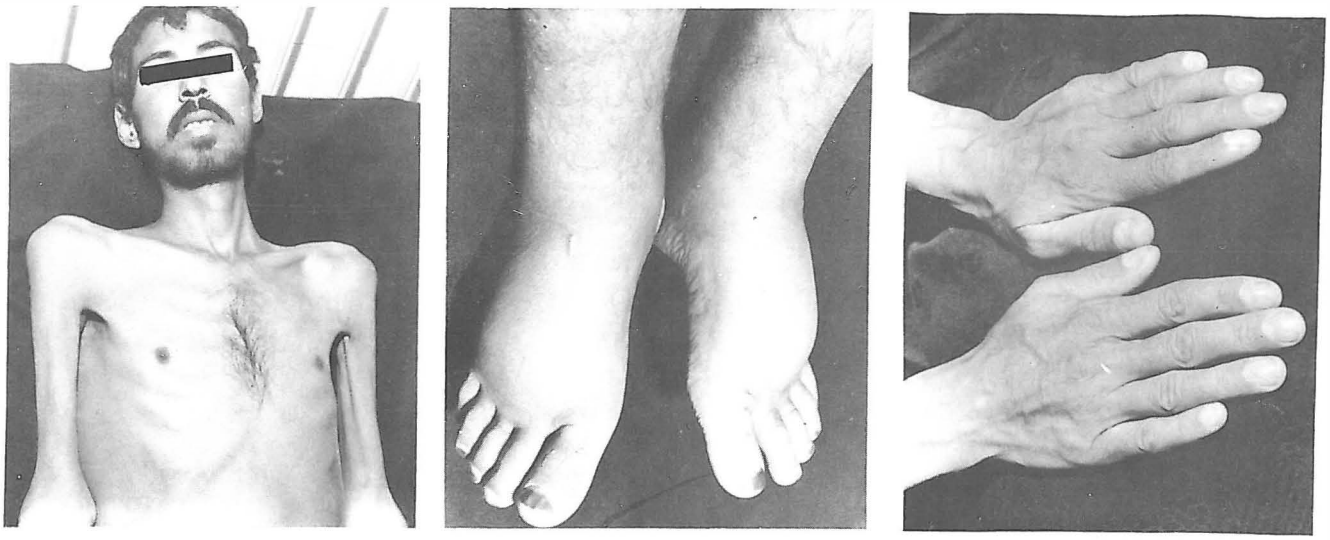

Fig. 1. (A, B, C). Shows cachexia, edema of feet, and clubbing of fingers.

patients were admitted to Shiraz University Hospitals (Faghihi, Nemazee and Beheshti) with the chief complaint of chronic diarrhea, weight loss and abdominal mass. All of them were from nearby villages of Shiraz, with low socio-economic status. Their ages ranged from 22 to 37 yrs, and eight were male and one was female.

Physical examination revealed cachexia, moderate clubbing of fingers, edema of the feet and abdominal mass (Fig. 1). No organomegaly or lymphadenopathy was noticed. Routine blood counts and bone marrow study revealed megaloblastic anemia and hemoglobin levels of 8-9 g/dL. The blood chemistry revealed normal findings, and serum protein electrophoresis revealed increased levels of IgA (Fig. 2).

RESULTS

During laparotomy a huge, gray-white, friable, fish-fleshy tumor was found in the upper small intestine. The sizes ranged between 15 to 20 cm (Fig. 3). Three cases also showed enlarged and matted lymph nodes. One case showed perforation. Histopathologic findings revealed diffuse infiltration of the wall of the intestine with numerous plasma cells at various stages of maturation. The villi were atrophied and broadened with frequent flattening of surface epithelium. The lamina propria and submucosa showed well-defined mature plasma cells. The muscular layer and serosal coat showed immature plasma cells with atypical bizarre multinucleated giant cells and numerous binucleated Reed-Sternberg like cells (Fig. 4). The special stain, methyl green pyronine, stained the plasma cells positively. Follow-up of the patients revealed that seven patients died within 6-8 months and two patients were lost to follow up.

DISCUSSION

The histogenesis of this tumor has been of some confusion. However recently, monoclonal immunoglobulin gene rearrangement studies suggest that IPSID is a neoplastic process *de novo*.[7,19] The main histologic feature in this disease is the diffuse infiltration of the upper small intestine and mesenteric lymph nodes by numerous plasma cells. These cells are responsible for the production of abnormally high levels of IgA. Depending upon the maturity of the plasma cells, IPSID is divided into three stages:[3]

Stage A: Well-defined mature plasma cells.

Stage B: Moderately-defined (OR) atypical plasma cells.

Stage C: Poorly-differentiated atypical bizarre plasma cells.

The depth of involvement of the wall of the intestine and mesenteric lymph nodes are not considered in the

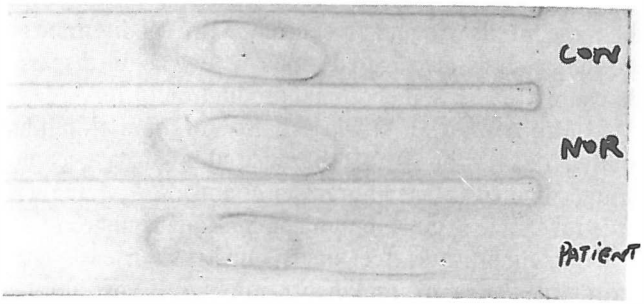

Fig. 2. Serum protein electrophoresis showing increased levels of IgA.

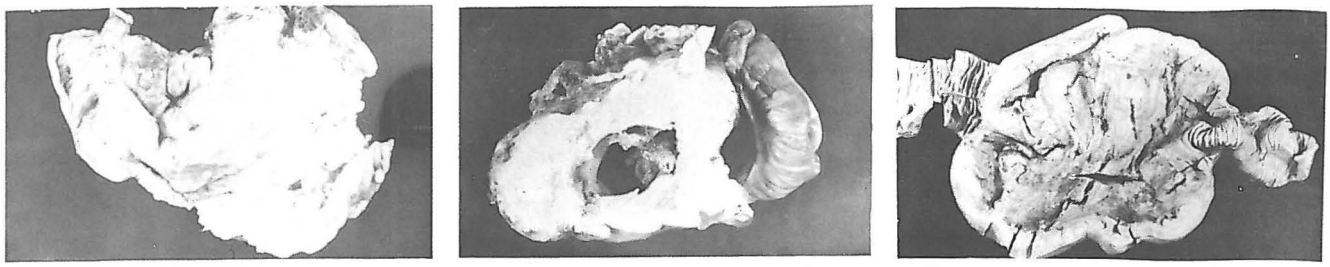

Fig. 3. (A,B,C). Gross picture of fish-fleshy gray white tumors of jejunum.

staging of IPSID. The abnormal production of IgA is noticed mainly in stages A and B, but IgA production is not common in stage C (immunoblastic sarcoma).

The treatment of IPSID is dependent upon the stage. If the stage is A and limited to lamina propria, medical treatment with tetracycline and metronidazole is advised. However, if the lesion is extensive and belongs to stage B or C, surgical resection of involved small intestine and mesentery is advised.

The main purpose of this paper is to report the unusual findings in these nine cases. Clinically these cases were diagnosed as tuberculosis because of clubbing, loss of weight and abdominal mass. Laparotomy revealed a huge fish-fleshy tumor involving the upper small intestine. This unusual finding of IPSID has been sporadically reported in the literature.[6,15] Non-IPSID lymphomas usually present with abdominal mass. Microscopic findings of these tumors are also very much confusing. The presence of numerous atypical, bizarre, multinucleated plasma cells, especially in the muscular layer, increased the possibility of Hodgkin's lymphoma and malignant histiocytosis. However because of the lack of significant eosinophils, absence of typical Reed-Sternberg cells and the lack of erythron or lymph phagocytic cells, the above-mentioned lesions were ruled out. The positive methyl green pyronine stain and the presence of numerous mature plasma cells in the lamina propria helped in correctly diagnosing these cases as IPSID. Another interesting finding was the presence of increased levels of IgA, which is a very unusual finding in stage C patients.

In conclusion, IPSID presenting with a huge abdominal mass is an unusual finding. Overall

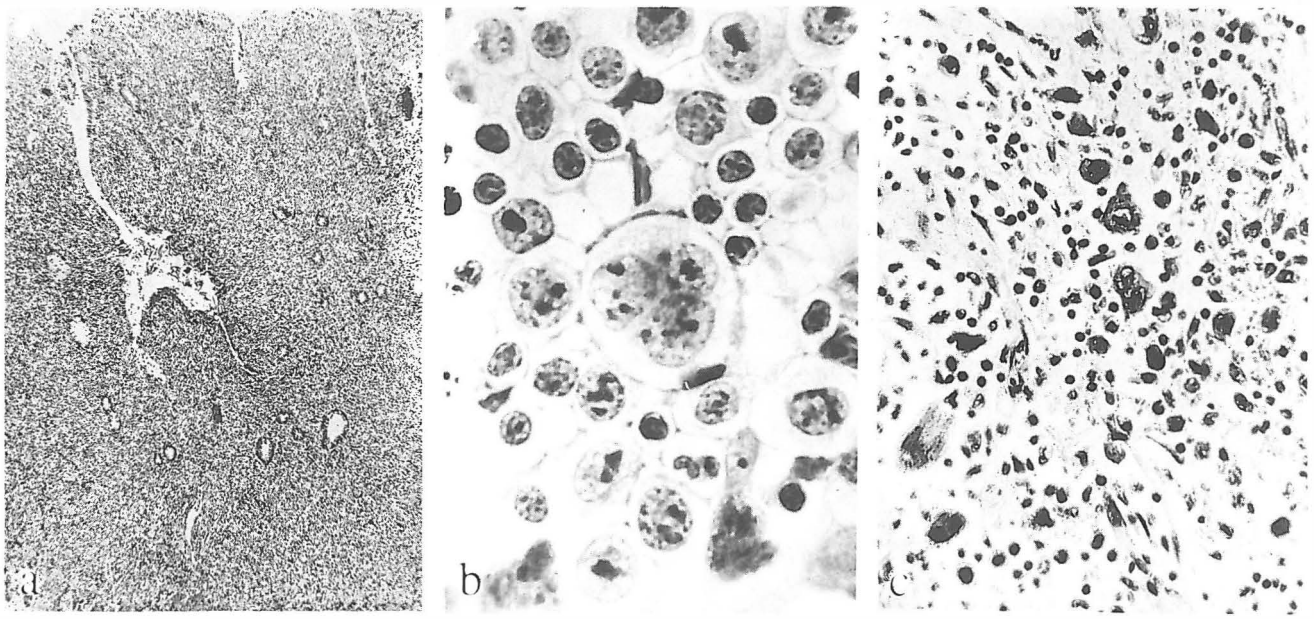

Fig. 4.

A: Low power view showing diffuse infiltration of wall of small intestine. (Hematoxylin-eosin, × 120).

B: High power view of lamina propria showing plasma cells at various stages of maturation. (Hematoxylin-eosin, × 900).

C: High power view of muscular layer showing bizarre, atypical and multinucleated cells. (Hematoxylin-eosin, × 800).

prognosis is not favorable. Microscopic findings are very much confused with Hodgkin's lymphoma and malignant histiocytosis.

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