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An Unusual Occurrence of Immunoproliferative Small Intestinal Disease in Elderly Patient Presenting with Chronic Diarrhea - A Rare Case Report

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ABSTRACT

Immunoproliferative small intestinal disease (IPSID) is a rare type of indolent B-cell lymphoma. It is a variant of extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue. It is commonly seen in older children and young adults in the age group of 10-35 years. It is more common in males with Male: Female ratio of 2.4:1. Duodenum and jejunum are the commonly involved areas in small intestine. Colicky abdominal pain and intermittent diarrhoea are the common symptoms. Here by, we report a rare case in a 74-year-old male patient presented with chief complaints of abdominal pain, diarrhea and weight loss for 3 months. CT scan findings revealed thickening of small intestinal wall and mesenteric lymphadenopathy. Upper gastrointestinal endoscopy findings revealed nodular and ulcerative mucosa in the duodenum. Histopathological examination revealed flattening of mucosa with villous atrophy, destruction of crypts and intraepithelial lymphocytic infiltrate is noted. Interstitium shows dense and diffuse collection of lymphoplasmacytic infiltrate. Immunohistochemistry was done and it showed CD20 positive lymphoid cells. Based on the above findings the case was reported as Immunoproliferative small intestinal disease. Clinicians should suspect IPSID in cases presenting with chronic diarrhea and abdominal pain refractory to treatment. Immunoproliferative small intestinal disease has indolent clinical course and it can be cured with antibiotics in early stages. Late stages have high mortality rate and has poor prognosis.

Keywords: IPSID, Alphachain disease, B cell lymphoma, duodenum, villous atrophy, lymphoplasmacytic infiltrate

INTRODUCTION

Immunoproliferative small intestinal disease (IPSID) is a rare type of indolent B-cell lymphoma. [1] It is a variant of extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue.[2] It was first described by Ramot in the year 1965.[3] This disease was first detected in Mediterranean countries and was previously called as Mediterranean lymphoma. Later, WHO coined the term IPSID in the year 1978, [2] because of the reason that, the disease is not looking like truly malignant in early stages. [4]

Although initially diagnosed in Mediterranean countries like Arab, non-European Jewish countries. Later, it was diagnosed in other countries like South, Central Africa and South East Asia. Recently in Europe and American continent, sporadic cases have also been documented. [2] IPSID is now occurring throughout the world because of reasons like poverty and

poor sanitation. [5] Chronic and recurrent gastrointestinal infections are the causes for predisposition to IPSID. [2]

IPSID is commonly seen in older children and young adults in the age group of 10-35 years.[4] It is more common in males with Male:Female ratio of 2.4:1.[2] Duodenum and jejunum are the commonly involved areas in small intestine.[6]

Histopathological features of IPSID are characterized by atrophy of villi with absent crypts. There is flattening of mucosa because of infiltration of lymphoplasmacytic cells in the lamina propria.[2] Immunohistochemistry shows CD20 positivity in lymphoid cells and CD138 positivity in plasma cells.[5]

Till now, worldwide very few cases of IPSID have been documented. Hereby, we report a rare case of IPSID diagnosed in a elderly 74 year old male presented with history of chronic diarrhea and abdominal pain.

CASE REPORT

A 74-year-old male presented to Medical Gastroenterology Department with chief complaints of abdominal pain, diarrhea and weight loss for 3 months. Haematological investigations revealed mild anemia, lymphocytosis and hypoalbuminemia. CT scan findings revealed thickening of small intestinal wall and mesenteric lymphadenopathy. Upper gastrointestinal endoscopy findings revealed nodular and ulcerative mucosa in the duodenum. Multiple biopsy bits were taken during endoscopy and was sent for histopathological examination to Pathology Department.

Grossly, five grey white soft tissue bits were received altogether measuring 8x8 mm. Histopathological examination revealed flattening of mucosa with villous atrophy and destruction of crypts. [FIGURE 1] Intraepithelial lymphocytic infiltrate is noted.[FIGURE 2] Interstitium shows dense and diffuse collection of lymphoplasmacytic infiltrate. Immunohistochemistry was done and it showed CD20 positive lymphoid cells.[FIGURE 3,4] Based on the above findings the case was reported as Immunoproliferative small intestinal disease.

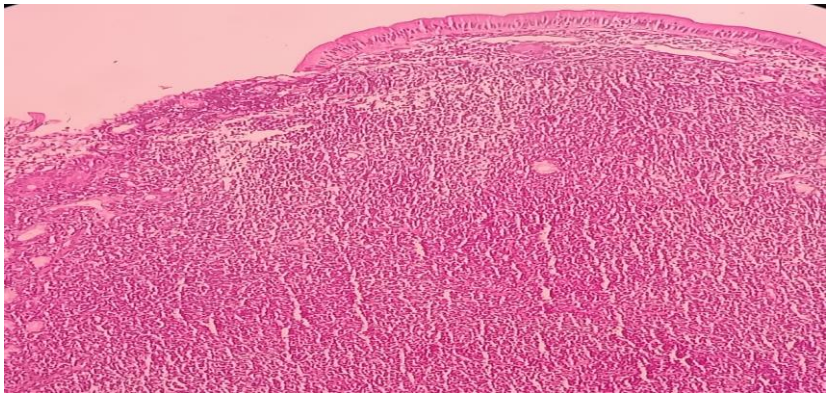

FIGURE 1- Microscopy showing villous atrophy,crypt destruction and lymphoplasmacytic infiltrate in laminapropria (H and E, X100)

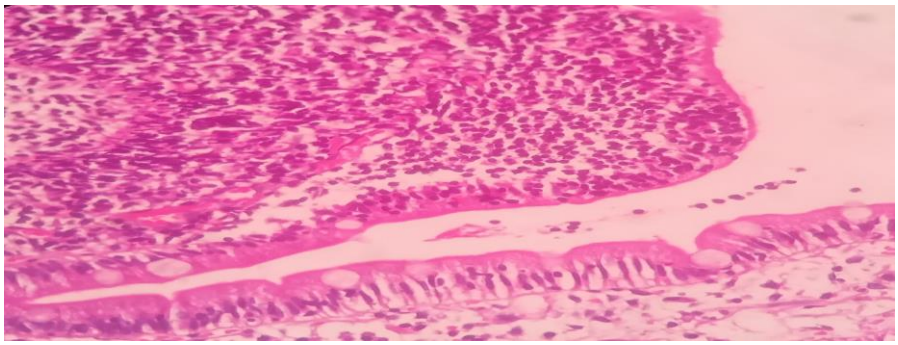

FIGURE 2- Microscopy showing intraepithelial lymphocytic infiltrate (H and E, X 400)

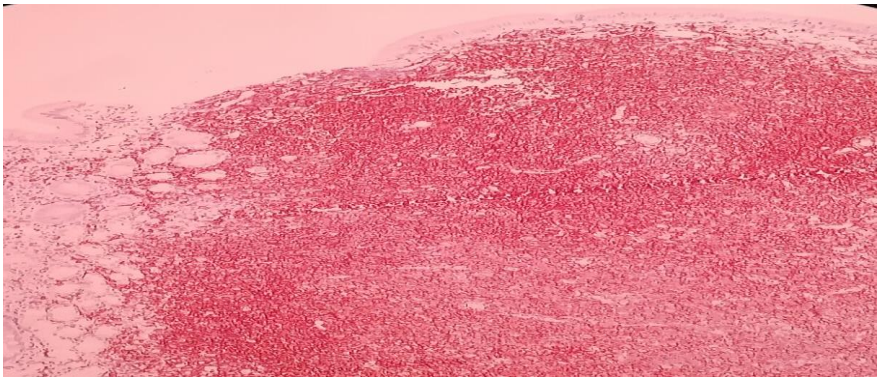

FIGURE 3- Microscopy showing CD 20 positive lymphocytes (IHC, X 100)

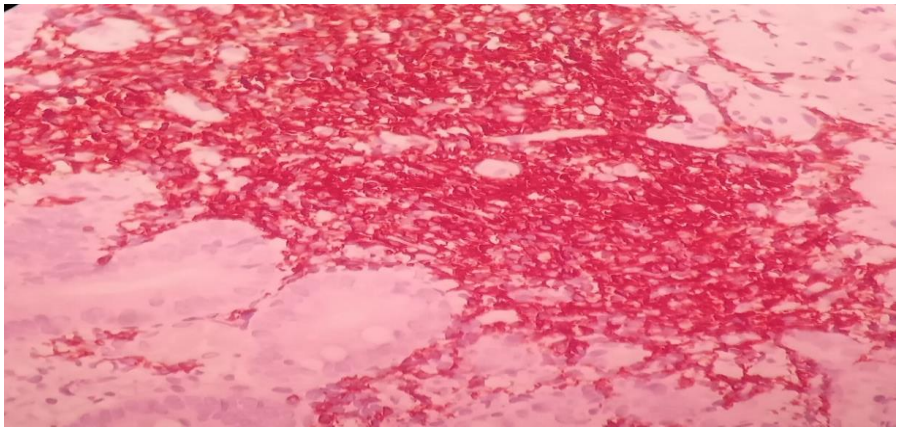

FIGURE 4 – Microscopy showing CD 20 positive lymphocytes in laminapropria (IHC, X400)

DISCUSSION

IPSID is a rare B-cell lymphoma having unique etiopathogenesis and molecular genetic abnormalities. [1,4] The characteristic feature of IPSID is the presence of abnormal IgA molecule in the patient's serum and body fluids. [5] Chronic antigenic stimulation of IgA secreting lymphoid tissue will occur because of recurrent and persistent intestinal infections. This IgA heavy chain acquires internal deletions, so that it cannot bind light chains leading to the expression of only defective heavy chains.[6] Because of lack of light chains and presence of only truncated alpha heavy chain protein, this disease was also known as "Alpha chain disease".[5]

The pathogenesis of IPSID is not clearly understood. Chronic antigenic stimulation by gastrointestinal infection like camphylobacter jejuni has been associated with IPSID. Genetic predisposition and association of HLA AW19, A9, B12 and B blood group has been documented. [4,5] Elevated alkaline phosphatase levels and defects in the cellular and humoral immunity is present in the affected individuals.[2]

Certain features in IPSID will resemble like other lymphoproliferative diseases like MALT lymphoma, Lymphoplasmacytic lymphoma and Plasma cell neoplasms.[4] Both IPSID and MALT lymphoma will arise because of antigenic stimulation of B-lymphocytes, there by leading to clonal proliferation and later malignant transformation. But t(11;18) which is seen in MALT lymphoma is absent in IPSID. Some of the molecular genetic abnormalities reported in IPSID include t(9;14); t(2;14), t(5;9), t(21;22)(q22;q11) $14q^{+}$ chromosome, PAX5 gene mutations and abnormal P32HC locus on chromosome 14 and light chain loci on chromosome 2 and 22.[2]

Depending on the cellular infiltrate, severity in small intestine and mesenteric lymph node involvement, Galian et al described the disease in three stages. [7,8] [TABLE 1]

TABLE 1: Histopathological staging system of IPSID

Stage	Small intestine	Lymphnode
Stage A (Benign)	Mature lymphoplasmacytic or plasmacytic infiltration of lamina propria and villi showing variable atrophy	Showing mature plasmacytic infiltrate. Nodal architecture is generally preserved.
Stage B (Intermediate)	Atypical lymphoplasmacytic/ plasmacytic infiltrate with presence of atypical immunoblast like cells extending into submucosa. villi showing subtotal or total atrophy	Showing atypical plasmacytic infiltrate with atypical immunoblast like cells. Nodal architecture is showing subtotal or total effacement.
Stage C (Malignant)	Malignant invasion through entire intestinal wall	Malignant effacement of entire lymphnode architecture

According to literature, IPSID commonly occurs in older children and young adults, [4,5] but in our case it occurred in very aged 74 year old patient, indicating that IPSID can occur in all age groups. Colicky abdominal pain and intermittent diarrhea are the common symptoms in IPSID.[9,10] Other symptoms are weight loss, steatorrhoea, nausea, vomiting, low grade fever, night sweats and malena. Malnutrition and electrolytic imbalances can also occur. Signs of malnutrition, abdominal distension, tenderness, peripheral edema and clubbing of fingers can be seen. Peripheral lymphadenopathy, hepatospleenomegaly and involvement of bone marrow is seen in advanced stages of IPSID.[2,5] Gastrointestinal complications which can occur are bleeding, perforation, intussusception, intestinal obstruction and infections. Extra intestinal complications are very rare which include nephropathy, osteoarthropathy and osteomalacia.[2]

Upper gastrointestinal endoscopy reveals changes in the small intestine and it can present as nodular, ulcerated and edematous changes in the mucosa.[1] In our case, the patient has nodular and ulcerative mucosa in the duodenum. CT scan findings which can be seen in IPSID are thickening of small intestinal wall, dilatations, strictures and mesenteric lymphadenopathy.[5]

The clinical presentation of IPSID is similar to other inflammatory and infectious gastrointestinal pathogenesis like celiac disease, tropical sprue, Whipple's disease, chronic intestinal infections and inflammatory bowel disease.[2] Hence, it is challenging, so detailed history along with histopathology, immunohistochemistry and serum protein electrophoresis are the confirmatory tests for the diagnosis of IPSID.

When compared to celiac disease, IPSID is less responsive to gluten free diet and stool culture is negative unlike other infections of intestine. Celiac disease has tissue transglutaminase antibodies in the serum. While, IPSID show abnormal serum IgA protein electrophoresis without corresponding light chains. Abdominal pain is usually not present in tropical sprue and reveals abnormal D-xylose test.[2]

Some, histopathological features are similar in both IPSID and celiac disease like surface epithelial damage, villous atrophy and lymphoplasmacytic infiltrate in the mucosa. But, IPSID has crypt atrophy, where as in celiac disease hyperplastic elongated crypts are present. [2,7] Progression to high grade lymphoma can occur in both celiac disease and IPSID. Celiac disease can progress to T-cell lymphoma, whereas IPSID generally progress to B-cell lymphoma. [2,6]

IPSID has indolent clinical course and it can be cured with antibiotics in early stages. However, it can progress to aggressive Diffuse large B-cell lymphoma if left untreated. [1,5] Late stages of IPSID (Galian stage C) have high mortality rate and has poor prognosis. [5]

Early stages of IPSID with no visible tumor is cured by antibiotics. In case of advanced disease with tumor, either with or without mesenteric lymph node involvement, chemotherapy is required. If bulky tumor is present, surgery and radiotherapy should be done before starting chemotherapy. [4,5]

CONCLUSION

IPSID is a rare type of indolent B-cell lymphoma. Clinicians should suspect IPSID in cases presenting with chronic diarrhea

and abdominal pain refractory to treatment. Clinical presentation of IPSID will mimic like that of other gastrointestinal conditions. So detailed history, histopathology, immunohistochemistry along with serum protein electrophoresis will help in definitive diagnosis. Early stages of IPSID have very good prognosis. Late stages of IPSID have poor prognosis and the patient needs regular follow up in view of transformation to Diffuse large B-cell lymphoma.

Declaration by Authors

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