

## Case Report

# Immunoproliferative Small Intestinal Disease: a Rare Disease with Common Presentation

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### Abstract:

*Immunoproliferative Small Intestinal Disease is a rare type of lymphoproliferative disorder that affects the small intestine. We present a case of a 50-year-old female patient who was diagnosed with IPSID after presenting with chronic diarrhoea, abdominal pain and weight loss. The patient underwent endoscopy and biopsy, which has confirmed the presence of atypical lymphocytes in the small intestine. The patient was treated with chemotherapy and responded well to treatment.*

**Keywords:** IPSID, Small intestine disease.

### Introduction:

Immunoproliferative small intestinal disease (IPSID) is a rare low-grade B-cell lymphoma arising from mucosa associated lymphoid tissue (MALT), representing approximately one-third of intestinal lymphoma. Histopathologically it is characterized by infiltration of small bowel wall with lymphocytes and plasma cells. The infiltrates produces an aberrant immunoglobulin (IgA), a truncated alpha heavy chain without the light chain component<sup>1,2</sup>. Lamina propria of these patients was infiltrated with plasma cells and lymphocytes with scattered malignant lymphocytes either within the infiltrate or throughout all mural layers. This disease became known as Mediterranean lymphoma<sup>3</sup>. Later a partial immunoglobulin heavy chain of the IgA class devoid of light chains was detected in serum and other body fluids of some patients with Mediterranean lymphoma<sup>4</sup>. It was soon determined that IgA heavy chain protein, called a-chain protein (a-CP), was secreted by plasma cells in the intestinal lamina propria<sup>5</sup> and Mediterranean lymphoma was renamed by some

investigators as a heavy chain disease<sup>6</sup>. There were subsequent reports describing a-CP in young adults with malabsorption syndromes who only had benign lymphoplasmacytic infiltration in small intestine without overt lymphoma<sup>7</sup>. Over the next several years, it was observed that some patients with 'benign' a heavy chain disease or Mediterranean lymphoma, progressed to diffuse small intestinal lymphoma<sup>8</sup>. In 1976, a panel of experts eventually concluded that a heavy chain disease and Mediterranean lymphoma represented spectrum of the same disease with benign, intermediate and overtly malignant stages and the disease was renamed Immunoproliferative Small Intestinal Disease (IPSID)<sup>9</sup>. Most of the cases of IPSID have been reported from North Africa<sup>10</sup>, Israel<sup>11</sup>, Middle East<sup>12</sup> and Mediterranean countries<sup>13</sup>. Few cases have also been reported from Central and South Africa<sup>14,15</sup>, East Asia<sup>16,17</sup> and South and Central America<sup>18,19</sup>. The patients usually come from low socioeconomic status, living in areas with poor sanitation and hygiene. Most are young in their second or third decades. The nearly equal male to female ratio.

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### Case report:

A 50-year-old women presented with the complaints of gradual onset of mild to moderate intensity colicky upper abdominal pain with no radiation, aggravated by taking meal and relieved to some extent by taking antispasmodic medication, associated with occasional vomiting, not induced, not mixed with blood, sometimes mixed with bile. She also had loose motion for 3 months, 3 to 4 times/day, watery to semisolid, moderate in amount, not mixed with blood or mucous, having nocturnal episodes, no relation with any particular food.

She had anorexia and significant weight loss. She had no H/O fever, cough, haemoptysis, breathlessness, and contact with known tuberculosis patient, per rectal bleeding, perianal discharge, oral ulcer, joint pain, redness of eyes or skin rash. She had H/O taking anti spasmotic medication and antibiotics several times with no improvement. On General examination patient was mildly anaemic. She had angular stomatitis, glossitis, average nutritional status. Her pulse was 74 beats/min, blood pressure was 120/70 mmHg & temperature was 98.4 F. She had bilateral pitting ankle oedema, but no peripheral lymphadenopathy. Abdominal examination and other systemic examination revealed nothing abnormality. Her investigations showed anaemia (Hb-10.3gm/dl), ESR-20mm at 1<sup>st</sup> hour, total WBC:8000/ mm<sup>3</sup>, neutrophil 75%, lymphocytes 21%, monocytes 2% and eosinophil 1%, platelet count 3,50,000 /mm<sup>3</sup>, CRP was negative, Stool R/E was normal, S. LDH was normal (302 U/L). She had hypoalbuminaemia (S. albumin 32 gm/L) & Iron deficiency anaemia. Her chest X-ray P/A view, Plain X-ray abdomen & abdominal ultrasonogram were normal, Mantoux Test was negative (06 mm). Endoscopy of UGIT showed erosions in antrum and duodenal bulb, mucosal nodularities in second part. Histopathology of biopsy from second part of duodenum showed chronic duodenitis with lymphoid hyperplasia. Immunohistochemistry concluded that the patient had IPSID with positive CD20 and positive atypical lymphoid cell. We consult with oncologist and they advised to start chemotherapy with CHOP (Cyclophosphamide, Hydroxydaunorubicin, Oncovin & Prednisolone) regimen. After 3 cycle of CHOP therapy her clinical condition improved without any complication.



**Figure 1:** Endoscopic image of second part of duodenum.

### Discussion:

Patients of IPSID usually present with chronic diarrhea, malabsorption syndrome, weight loss and abdominal pain of months to years duration. On examination, features of malnutrition like peripheral edema and clubbing and/or abdominal mass is often evident. Our patient had chronic abdominal pain, chronic diarrhoea, weight loss and features of malabsorption. Endoscopy of the upper gastrointestinal tract shows variable abnormalities including thickened mucosal folds, nodules, ulcers and mosaic pattern. Our patient had erosions at duodenal bulb & mucosal nodularities in second part. The small intestine was motionless due to submucosal infiltration, firm to touch and nondistensible<sup>20</sup>. Barium X-ray of the small intestine shows diffuse dilation of the duodenum, jejunum and proximal ileum. Mucosal folds are thickened with ragged edges resembling ‘postage stamp’<sup>21</sup>. Small bowel bacterial overgrowth and intestinal infestation with parasites, especially Giardia may be associated. Patients also have anemia and features of vitamin deficiencies. Serum IgG and IgM may be high or low<sup>21</sup>. Serum IgA usually is low or undetectable. Bence-Jones protein is characteristically absent. Circulating lymphocyte count and humoral and cell-mediated immune responses are often diminished<sup>22</sup>. a-CP can be detected in serum, urine, saliva or intestinal secretions by immunoelectrophoresis or by immunoselection, which is the most sensitive and specific method<sup>21,23</sup>. Traditionally, the pathology of IPSID has been defined in stages<sup>24</sup>. In the early stage, there is characteristic extensive infiltration of small intestinal lamina propria with plasma cells and/or lymphocytes. This infiltrate broadens villi and shortens and separates crypts. Similar changes may also be seen in mesenteric lymph nodes, colon and/or stomach. The intestinal epithelial cells may be columnar or cuboidal and remain intact. Mucosal ulceration may be present. Ulcers present even in the early stage of IPSID may represent a neoplastic process. The intermediate and late stages of IPSID are characterized by further broadening of villi, presence of fewer crypts and deeper mural extension of the immunoproliferation. There is infiltration of benign immunocytes by atypical lymphoid cells. Eventually, the patients develop overt lymphoma. All histological grades of lymphoma, namely low, intermediate and high, have been described in IPSID. In some patients, malignancy may be present only in deeper intestinal layers and in mesenteric lymph nodes, which makes laparotomy and full thickness biopsy of the small intestine necessary for accurate diagnosis and staging. In the later stages, liver, spleen, bone marrow and other extra abdominal sites may become involved. The

epidemiological association between *H. pylori* and primary gastric lymphoma is well established. It has also been seen that primary gastric lymphomas regress with eradication of *H. pylori* with antibiotics. This has led to the suggestion that MALTomas evolve from benign antigen driven B-cell responses and the malignant clone depends on antigen for survival for at least sometime. A similar pathogenesis may help explain why IPSID has a high prevalence among people living in areas with poor sanitation, because they have high prevalence of intestinal microbial infestation. It has thus, been suggested that IPSID probably represents a chronic immunoproliferative response to bacteria or parasites, which eventually becomes monoclonal. Therefore if diagnosed early, like *H. pylori* associated low-grade gastric lymphoma, IPSID may also regress after treatment with antibiotics. The treatment for early stage of IPSID is thus, with broad spectrum antibiotics with or without corticosteroids. This usually results in clinical and/or histological remissions. This is at times temporary, but sometimes durable<sup>25</sup>. Response rates vary between 33 and 71%. For non-responders and those with intermediate or late stage disease, total abdominal radiation with hepatic and renal shielding or, more frequently, combination chemotherapy can be used. With chemotherapy regimens used in treating non-Hodgkins lymphoma, like CHOP, CHOP-Bleo or m-BACOD, complete remission can be achieved in 64% patients. Some investigators recommend adding broad spectrum antibiotics like tetracycline to chemotherapy regimens<sup>26</sup>.

Early-stage IPSID responds to antibiotics (30%-70% complete remission). Most untreated IPSID patients progress to lymphoplasmacytic and immunoblastic lymphoma invading the intestinal wall and mesenteric lymph nodes, and may metastasize to a distant organ.

### Conclusion:

IPSID is a rare type of lymphoma that presents with chronic diarrhea, weight loss, and abdominal pain. Diagnosis relies on endoscopy and biopsy, and treatment involves antibiotics, chemotherapy or radiation therapy. Our patient responded well to chemotherapy and had an excellent prognosis. IPSID should always be considered in the differential diagnosis of individuals with chronic diarrhea and weight loss.

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