ABSTRACT
A case of immunoproliferative small intestinal disease (IPSID) was diagnosed and treated at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Although this rare disease entity has been reported from different countries, there are paucity of information about IPSID from Indian subcontinent. Careful assessment of patient and supportive laboratory investigations are required for its diagnosis. The patient is passing a comparatively good smooth course after getting medications.

Abbreviation: IPSID: Immunoproliferative small intestinal disease.

Keywords: IPSID, Bangladesh, Small intestine disease.


Source of support: Nil

Conflict of interest: None

INTRODUCTION
The first report of primary small intestinal lymphoma associated with malabsorption in young adults was published in the 1960s. 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. 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 and Mediterranean lymphoma was renamed by some investigators as a heavy chain disease. 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. Over the next several years, it was observed that some patients with ‘benign’ a heavy chain disease or Mediterranean lymphoma, as it was also called, progressed to diffuse small intestinal lymphoma. 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).

Most of the cases of IPSID have been reported from North Africa, Israel, Middle East and Mediterranean countries. Few cases have also been reported from Central and South Africa, East Asia and South and Central America. 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 is equal. Still, there is no reporting of this pathological condition from Bangladesh or Indian subcontinent.

CASE REPORT
The patient was a 16-year-old young girl who was normotensive and nondiabetic. She comes from middle-class socioeconomic background drinking boiled water, using sanitary latrine and staying in brick building. She was reasonably well 3 years back. Then she developed complaints of abdominal fullness, belching and indigestion, mainly after meals. She felt better in fasting state and preferred avoiding food. She also had complaints of alteration of bowel habit. She used to defecate once a day, but following onset of her symptoms, her bowel started moving 3 to 4 times per day. Consistency of stool was soft, moderate in amount, foul smelling, but contained no undigested food material, fresh or altered blood. She also experienced repeated episodes of watery diarrhea, once or twice a month persisting for 8 to 10 days. The symptom increased in severity gradually and in the last 1 year she was admitted in hospital twice for acute episodes of diarrhea. She became so sick that she stopped going to school for the last 9 months.

For the last 3 months, she experienced spontaneous as well as induced vomiting, 2 to 3 times a day, especially after meals. Vomitus contained partly digested as well as undigested food and was sometimes bilious. She also recorded significant weight loss.

The patient had no history of lump or pain in abdomen. She had no fever, swelling, nodule or rash anywhere in the body. There was no history of cough, chest pain or bleeding from any site. Her bladder habit was normal.

Her physical examination did not reveal any abnormality. Her investigations showed low hemoglobin 10.5 gm/dl, total...
count of WBC $13 \times 10^9/l$, neutrophil 76%, lymphocytes 20%, monocytes 2% and eosinophil 1%, platelet count $350 \times 10^9/l$, ESR 30 mm in 1st hour, target cells and neutrophil leukocytosis in peripheral blood film.

Liver profile of the patient showed serum bilirubin 15 µmol/l, serum alanine aminotransferase 37 u/l, serum aspartate aminotransferase 31 u/l, serum alkaline phosphatase 472 u/l and serum albumin 24 gm/l. She tested negative for anti-HIV-1 and HIV-2. Her IgG and IgM levels were border line elevated, but IgA was undetectable. The levels of serum creatinine was 0.7 mg/dl, serum calcium 8 mg/dl, serum inorganic phosphate 3.3 mg/dl, serum sodium 146 mmol/l, serum potassium 3.5 mmol/l, serum carbon dioxide 27 mmol/l, serum ferritin 19.83 µgm/l and serum total iron 52 µgm/dl. She had normal routine urine examination. Chest X-ray P/A view was normal, but multiple oval shaped hypoechoic areas were noted in abdominal ultrasonography in the peripancreatic region suggestive of peripancreatic lymphadenopathy.

Her endoscopy of upper gastrointestinal tract revealed an ulcer in the 2nd part. Biopsies were taken and histopathology showed dense infiltration of lymphocytes, plasma cells and few eosinophils in lamina propria extending up to submucosa. The villi were short and broad. The histopathologist concluded that the patient had IPSID (Figs 1 and 2). The patient was placed on long-term ciprofloxacin and at 3 weeks she has shown significant clinical improvement and a weight gain of 3 kg.

**DISCUSSION**

Patients with IPSID usually present with 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. Endoscopy of the upper gastrointestinal tract shows variable abnormalities including thickened mucosal folds, nodules, ulcers and mosaic pattern. The small intestine was motionless due to submucosal infiltration, firm to touch and nondistensible. 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’. 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. 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. a-CP can be detected in serum, urine, saliva or intestinal secretions by electrophoresis immunoelectrophoresis or by immunoselection, which is the most sensitive and specific method.

Traditionally, the pathology of IPSID has been defined in stages. 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 and usually
indicates advanced and possibly malignant lesion. 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 extrabdominal 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. Response rates vary between 33 and 71%. For nonresponders 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. Overall 5-year survival rates for patients with IPSID undergoing treatment have been about 67%.

**CONCLUSION**

Immunoproliferative small intestinal disease is a rare disease, but not unlikely to be encountered in our clinical practice. However, strong clinical suspicion is required to diagnose this condition, as otherwise many may proceed to irreversible disease and premature death. This is the first case report of IPSID from Bangladesh.

**REFERENCES**


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