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Immunoproliferative Small Intestine Disease (IPSID): A Case Report

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Abstract

Immunoproliferative Small Intestinal Disease (IPSID) is the syndrome associated with Mediterranean lymphoma (a rare form of non-Hodgkin's lymphoma). Many of the patients diagnosed with secretory IPSID have variable level of abnormal immunoglobulins in serum or other bodily fluids, identified as truncated alpha heavy chain globulins. Most cases are characterized by a loss of ability to synthesize light chains. As such, IPSID has been classified as a heavy chain disorder B-cell lymphoma. We present here the case of a 12-year-old boy admitted in our department for edema, abdominal pain and Failure to Thrive (FTT), in whom we suspected the diagnosis of IPSID.

Key Words: Case report, IPSID, Immunoproliferative small intestinal disease.

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Introduction

Immunoproliferative small intestinal disease (IPSID) is a special variant of, extranodal marginal zone B-cell lymphoma, which affects the small intestine. In early to mid 1960s it was referred to as 'Mediterranean lymphomas', during the late 1960s the term a-heavy chain disease was also used for patients with similar clinico-pathological presentations. Later it was realized that both Mediterranean lymphomas and a-heavy chain disease represented a spectrum of the same disease which presented in different stages i.e., benign (A), intermediate (B) and overtly malignant (C) and the disease was named IPSID (1)

Case report

A 12-year-old male presented with weight loss, diarrhea, abdominal pain, and acral edema from 6 months ago. He was the first-born of his parents, with a birth weight of 3.5 kg. At presentation, weight and height were below the 5th percentile normal for his age. During the past 6 months, he was hospitalized several times for diarrhea and edema. His appendix had been removed 4 months before, after complaining of abdominal pain. Physical examination showed hand and foot clubbing, pallor, symmetric acral pitting edema, and abdominal distention without organomegaly. Initial evaluation revealed normal renal and liver function tests, and normal Purified Protein Derivative (PPD) tuberculosis skin test, serum antibodies to Tissue Transglutaminase (TTG) were normal and Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) , Hepatitis C Virus (HCV), Protozoan Toxoplasma gondii (TOXO), Epstein–Barr virus (EBV), Cytomegalovirus (CMV); were negative. Urin Analysis (U/A), Urin Culture (U/C) were normal. Stool exam has moderate White Blood Cells (WBC) but no Red Blood Cell (RBC). Thyroid Function Test (TFTs) was normal. Hemoglobin (Hb) was 9g/dl, Albumin was 2 mg/dl, Total Protein (TPr) was 3.5 mg/dl, Calcium 6.5 mg/dl, phosphorus (P) 3.2 mg/dl, Magnesium (Mg) 1 mg/dl, sodium 128 mg/dl, potassium 3 mg/dl. Immunologic test were normal, Ig electrophoresis results were normal (Table. 1). Abdominal ultrasonography, echocardiography, upper Gastrointestinal (GI) series, Bone Marrow Aspiration (BMA) were normal. Abdominal Computed Tomography (CT) with oral and Intravenous (IV) contrast showed diffuse mural thickening of the small intestine in the middle jejunum with mesenteric lymphadenopathy. Colonoscopy was normal, but endoscopy showed diffused erythema in duodenum with no ulceration (biopsy: moderate villous blunting and lymphoplasmacytic infiltration in lamina propria). The Rapid Urease Test (RUT) for Helicobacter pylori was normal. Flow cytometry results were normal. Protein electrophoresis revealed an increase in alpha-2 globulin to 22.5 g/dl (normal range, 9 to 14 g/dl). After initial treatment with albumin, high protein dietary intake, metronidazole and tetracycline, our patient's clinical status was improved and he gained over 1 kg in weight and after 4 months follow up he has not any problem and he was free symptom.

Discussion

IPSID (also known as Mediterranean lymphoma) is considered to be a subtype of extranodal marginal zone B-Cell cell lymphoma. IPSID occurs in the proximal small intestine in children (1- 3). The clinical presentation of IPSID usually involves malabsorption syndrome, weight loss and chronic abdominal pain, diarrhea, clubbing, hepatosplenomegaly, lymphadenopathy. Laboratory findings of IPSID show elevation of alpha heavy chain protein, low serum immunoglobulins and albumin, high alkaline phosphatase, sugar and fat malabsorption, hypocalcemia and

hypomagnesaemia, mild to moderate anemia, parasitic (especially giardiasis) infestations (2-5). Endoscopy of the upper gastrointestinal tract shows thickened mucosal folds, nodules, ulcers and mosaic pattern. In early stages of IPSID the pathology exam is characteristic, with plasma cell and lymphocytic infiltration of small intestinal lamina propria. This infiltrate broadens villi and shortens and separates crypts. Progression of the disease is associated with further broadening of villi, presence of fewer crypts and deeper mural extension of the immunoproliferation and infiltration of atypical lymphoid cells. . Eventually, the patients develops overt lymphoma (5). The diagnosis requires multiple duodenal and jejunal mucosal biopsies showing dense mucosal infiltrates, consisting of enterocyte-like and plasma cells. Progression to higher grade large cell lymphoplasmacytic and immunoblastic lymphoma is characterized by increased plasmocytic atypical infiltrate with formation of aggregates, and later on sheets of dystrophic plasma cell and immunoblasts invading the submucosa and muscularis propria (6, 7). Alpha Heavy Chain (AHC) paraprotein is present in most cases (6-8). The differential diagnosis includes chronic enteric infection, celiac disease, and other types of lymphoma (6). IPSID also needs to be distinguished from bowel infections with Helicobacter pylori (H. pylori) or Campylobacter jejuni. The majority of reported cases have originated from Mediterranean countries, although sporadic cases of IPSID have also been reported from other parts of Europe, South America, and the United States. Common demographic characteristics of IPSID are a lower socioeconomic status, poor personal hygiene, predominance of male sex, and a peak age between the first and third decades (8). Patients in the early phase of IPSID can be treated with antibiotics, including tetracycline. However, most patients will progress and need combination chemotherapy (6-9). Early phase of IPSID can completely remit with antibiotic therapy. However, medium- and long-term follow-up is needed, as transformation to Diffuse Large B Cell Lymphoma (DLBCL) may occur (10, 11). Our patient was successfully treated with antibiotic therapy and there was no need for chemotherapy at this point, but prolonged follow-up is warranted in order to identify progressive disease.

Table 1: Evaluation of patient tests

WBC(White blood cells)	13.5 (1000/ml)
HB(Hemoglobin)	9 (g/dl)
MCV (Mean corpuscular volume)	70 (fl)
PLT (Platelet)	120 (1000/ml)
PBS (Peripheral blood smear)	NL
ESR(erythrocyte sedimentation rate)	70 (mm/h)
CRP (C-reactive protein)	3+
WRIGHT	NEG
WIDAL	NEG
PPD	NEG
HBV (Hepatitis B virus)	NEG
HCV (Hepatitis C virus)	NEG
HIV (Human immunodeficiency virus)	NEG
EBV (Epstein–Barr virus)	NEG
CMV (Cytomegalovirus)	NEG
TOXO (Protozoan Toxoplasma gondii)	NEG
Clostridium difficil	NEG
U/A(Urin analysis) , U/C(Urin culture)	NEG
S/E (Stool exam) WBC RBC Fatdrop, Droplet, Elastas1 S/C (Stool culture) Redused substance	20-30 5-6 NL GIARDIASIS NEG
Immunoglobulin electrophoresis	NL
NBT (Nitroblue-tetrazolium test)	NL
TG (Triglycerides) CHOLESTROL Uric acid Fasting blood sugar	100(mg/dl) 80(mg/dl) 4(mg/dl) 70(mg/dl)
TTG(Anti-tissue Transglutaminase Antibody)	NL
Sweat test	NL
CA(Calcium) P(Phosphour) MG(Magnesium)	6.5(mg/dl) 3.2(mg/dl) 1(mg/dl)
ALB(Albumin)	2(mg/dl)
BUN(Blood urea) CR(Creatinine)	10(mg/dl) 0.5(mg/dl)
ALK(Alkaline phosphatase)	1600U/L
CPK (Creatine phosphokinase) LDH (Lactate dehydrogenase)	NL NL

Conflict of interests: None.

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