IMMUNOPROLIFERATIVE SMALL INTESTINAL DISEASE - A CASE REPORT

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(Bang. Onc. J. 2009; 4 (2) : 90-92)

Introduction:

Malignant lymphomas of the small intestine are relatively common in certain geographic areas and they seem to be particularly so in developing countries, especially in the Middle East and North Africa[1].These lymphomas can be divided into 3 subtypes [2] Burkitt lymphoma, Western type of Non-Hodgkin lymphoma and the so called Mediterranean lymphoma. The term Mediterranean lymphoma is a misnomer. The disease mostly occurs in Mediterranean basin but not always[3]. It was also felt that the disease in its early stages does not appear to be truly malignant lymphoma. So in 1978, WHO recommended the term Immunoproliferative small intestinal disease (IPSID) for the syndrome associated with Mediterranean lymphoma[4]. Generally, IPSID is considered as a variant of mucosa-associated lymphoid tissue (MALT) lymphoma[5]. In recent WHO classification, IPSID is listed with heavy chain diseases as a special variant of extra nodal marginal zone B cell lymphoma (MALT) [6].

Immunoproliferative small intestinal disease (IPSID), also known as alpha chain disease, is a mucosa-associated lymphoid tissue (MALT) associated lymphoma characterized by infiltration of the bowel wall with a plasma cell population that secrets a monotypic, truncated immunoglobulin á heavy chain lacking an associated light chain[7,8,9]. It affects mainly young adults with almost equal sex incidence and involves predominantly the proximal small intestine and usually presents with diarrhea and abdominal pain[10].

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Case Report:

Md. Raihan, an 18 years old male hailing from Jatrabari, attended Radiotherapy Department Dhaka Medical College Hospital and 12.2.2006. He was apparently all right 3 months back. Then he developed loose motion. Initially the frequency of motion was 4 to 5 times a day but later it was less frequent but became chronic. He also developed anorexia and generalized weakness for same duration. He noticed weight loss. He lost about 10 kg of his body weight in last 3 months.

On Examination, he was mildly anaemic, nonicteric, normotensive, temperature was normal. There was no enlarged lymph node. Systemic examination revealed no abnormality.

Investigations showed a hemoglobin of 8 g/dl, WBC – 12000/dl, differential- Nutrophil 84%, Lymphocyte-14%, Platelets 320 x 10^9/dl . ESR was 80mm in 1st hour. Biochemical profile revealed normal renal & liver functions. Occult blood test of the stool was positive. Endoscopy of upper GIT revealed thickening of the mucosal folds of the duodenum. Colonoscopy showed rectal polyp. Barium follow through examination of small bowel revealed malabsorption syndrome. Histopathology of the duodenal tissue showed dense infiltration of plasma cells and lymphocytes in lamina propria suggestive of immunoproliferative small intestinal disease (IPSID). Imminoglobulin electrophoresis was suggestive of no abnormal accumulation of Ig molecule or free chain in the serum. Chest X ray was normal. Ultrasonogram of whole abdomen revealed no abnormality.

The patient was first treated with antibiotics-Tetracycline (250 mg 6 hourly) and metronidazole (400 mg 8 hourly) 8 hourly several

courses for 3 months with no response. Then he received 3 weekly 6 cycles of chemotherapy from 20-2-06 to 15-7-2006 as per schedule:

Inj Cyclophosphamide 600mg/m^2 IV D_1, Inj Doxorubicin 60mg/m^2 IV D_1 Inj Vincristin 1.4 mg /m^2 IV D_1 and Tab Prednisolone 60mg/m^2 orally daily $D_1 - D_5$.

Toxicity was minimal and was managed. Now the patient is on follow up for 3 year. He is asymptomatic now. He was lastly seen on 27-06-2009 and was asymptomatic on examination no abnormality was detected. Blood count chest x-ray P/A view ultrasonogram of the hole abdomen reports were normal.

Discussion:

IPSID is a unique mature B cell neoplasm regarding its epidemiology, clinical features, morphology and molecular pathogenesis[11]. It shares certain features with gastrointestinal MALT lymphoma, lymphoplasmacytic lymphoma as well as plasma cell neoplasms[12].

It affects mainly older children and young adults. The range is 10-35 years and the mean age is 25-30 years[12]. Our patient is 18 years old and he belongs to the common age group of IPSID.

IPSID commonly affects people of low socioeconomic status in developing countries [12]. This patient came from a lower middle class family.

Geographically, the majority of cases reported were from the Middle East, North and South Africa and Far East[13]. Sporadic cases have been reported from other countries, especially in immigrants from Middle East[14]. In Bangladesh IPSID is rarely found.

Clinically, intermittent diarrhoea and colicky abdominal pain are the most frequent symptoms[15-17].Other symptoms and signs are mainly related to malabsorption. Intestinal obstructions, abdominal masses and ascites are common in advanced stage[12].This patient presented with chronic diarrhoea, anorexia, weakness and weight loss. On examination he was mildly anaemic probably due to malabsorption. There was no other abnormality in general and systemic examination.

Although the clinical, laboratory and radiological findings are pathognomic, the final diagnosis is usually established by endoscopic biopsies and/ or laparotomy. Upper GI endoscopy shows abnormalities in the second, third and fourth part of the duodenum and upper jejunum. Thickening, erythema, nodularity of mucosal folds is noted[18]. In our patient, endoscopy of upper GIT revealed thickening of the mucosal folds of the duodenum.

The main pathological feature of IPSID is presence of dense mucosal infiltrate of "centrocyte like" and plasma cells involving long segments of small bowel mucosa, predominantly the proximal parts[2]. In this case, the histopathology revealed- sections of duodenal mucosa showing dense infiltration of plasma cells and lymphocytes in lamina propria suggestive of immunoproliferative small intestinal disease (IPSID).

The immunologic hallmark of IPSID is the presence of anomalous á heavy chain protein in the serum detected in 20% to 90% of patients [7,15,18,19]. Immunoglobulin electrophoresis of this patient was suggestive of no abnormal accumulation of Ig molecule or free chain in the serum.

Although spontaneous remissions occur in early stages, once establish the untreated disease progresses relentlessly causing severe malabsorption and malnutrition. Early treatment is recommended to control symptoms and prevent progression of disease[20]. For early stage patients first line antibiotics (Tetracycline & metronidazole) is recommended. Patients without marked improvement after 6 months or complete remission within 12 months should be given CHOP chemotherapy. Chemotherapy is also recommended along with antibiotics for patients presented with advanced disease[12]. This patient was treated with first line antibiotics tetracycline & metronidazole. As there was no marked improvement in 3 months, he was given 6 cycles of chemotherapy with CHOP schedule. Upto June 2006. Since then he is all right.

Conclusion:

IPSID is a rare disease in our country. In cases of chronic diarrhea and malabsorption we search for causes but often forget IPSID as a cause due to its less frequency. Thus the patients of IPSID are not diagnosed and treated. So, we should keep in mind that though rare it may occur and should investigate the patients with chronic diarrhoea and malabsorption properly to confirm and exclude IPSID.

References:

1. Azar HA. Cancer in Lebanon and the Near East. Cancer. 1962; 15: 66-78.
2. Al-Saleem T, Zardawi IM. Primary lymphomas of the small intestine in Iraq: a pathological study of 145 cases. Histopathology. 1979; 47: 221-226.
3. Bonadonna G. Malignant Lymphoma. Bonadonna G, de Lacuna GR. Handbook of Medical Oncology. 3rd ed. Masion STA, Milano. 1988; 799-836.
4. Bull D. Alpha- chain disease and related small intestinal lymphoma: a memorandum. Geneva, Switzerland: World Health Organization. 1976; 54: 615-624.
5. Isaacson PG. Gastrointestinal Lymphoma. Hum Pathol. 1994;25: 1020-1029.
6. Jaffe ES, Harris NL, Stein H, Vardiman JW. Tumors of Hematopoietic and Lymphoid Tissue. Lyon, France: IAARC; 2001.
7. Seligman M, Danon F, Hurez D, Mihaesco E, Preud'homme JL. Alpha- chain disease: a new immunoglobulin abnormality. Science1968; 162: 1396-1397.
8. Isaacson P, Wright DH. Malignant lymphoma of mucosa-associated lymphoid tissue: a distinctive type of B-cell lymphoma. Cancer 1983: 52: 1410-1416.
9. Isaacson PG, Dogan A, Price SK, Spencer J. Immunoproliferayive small intestinal disease: an immunohistochemical study. Am J Surg Pathol 1989; 13: 1023-1033
10. Ramot B, Shahin N, Bubis JJ. Malabsorption syndrome in lymphoma of small intestine: a study of 13 cases. Isr Med J. 1965; 47: 221-226.
11. Personnet J, Isaacson PG. Bacterial infection and MALT lymphoma. N Engl J Med. 2004; 350: 213-215.
12. Al-Saleem T, Al-Mondhiry H. Immunoproliferative small intestinal disease(IPSID): a model for mature B-cell neoplasms. Blood. 2005; 105: 2274-2280.
13. Fine KD, Stone MJ. Alpha- heavy chain disease, Mediterranean lymphoma and Immunoproliferayive small intestinal disease: a review of clinicopathological features, pathogenesis and differential diagnosis. Am J Gastoenterol.1999; 94: 1139-1152.
14. Al-Mondhiry H. Primary lymphomas of small intestine: east-west contrast. Am J Hematol.1986; 22: 89-105.
15. Gilinisky NH, Novis BH, Wright JP, Dent DM, King H, Marks IN. Immunoproliferative small intestinal disease: Clinical features and outcome in 30 cases. Medicine. 1987; 66: 438-446.
16. Rambaud JC.Small intestinal lymphomas and alpha-chain disease. Clin Gastroenterol. 1983; 12: 743-766.
17. Al-Bahrani ZR, Al-Mondhiry H, Bakir F, Al-Saleem T. Clinical and pathologic subtypes of primary intestinal lymphoma: experience with 132 patients over a 14-year period. Cancer. 1983; 52: 1666-1672.
18. Khojasten A. Immunopathology of small intestine. In: MarshMN, ed. ChiChester, UK: John Wiley, 1987: 121-150.
19. Doe WF. Alpha chain disease clinicopathological features and relationship to so-called Mediterranean lymphoma. Br J Cancer.1975; 31: 350-355.
20. Rambaud JC, Halphen M. Immunoproliferative small intestinal disease (IPSID): relationships with Alpha chain disease and Mediterranean lymphomas. Gastroenterol. Int. 1989; 2: 33-41.