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RADIOTHERAPY IN IMMUNOPROLIFERATIVE SMALL INTESTINAL DISEASE: A RETROSPECTIVE COMPARISON OF CHEMOTHERAPY PLUS RADIATION WITH CHEMOTHERAPY ALONE

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ABSTRACT

In order to evaluate the results of abdominal radiation plus chemotherapy in cases with stage II and III of immunoproliferative small intestinal disease in comparison to chemotherapy alone, fifty-one patients referred to Shiraz University of Medical Sciences' affiliated hospitals were studied between 1980 and 1994. Out of them 38 patients who had an abdominal mass were gathered into two groups retrospectively. Group A, including 21 patients, had received only chemotherapy after operation and tissue diagnosis. Group B, consisting of 17 patients, received radiation to the whole abdomen in addition to systemic chemotherapy.

Four patients (19%) in group A were alive with no evidence of disease after three years and in the other group (B) 7 patients (41%) who had received radiation in addition to systemic chemotherapy had survived in disease free status.

It therefore appears that radiation to the whole abdomen in small daily fraction doses and a total dose not greater than the optimal tolerance of the liver and other critical abdominal organs plus chemotherapy can be an effective adjuvant treatment in stage II and III disease.

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INTRODUCTION

Immunoproliferative small intestinal disease (IPSID) is a well known clinical entity in low socioeconomic populations in many developing countries. It is comprised of a variety of disorders commonly presenting with diarrhea, abdominal pain, weight loss and malabsorption. Patients have diffuse and extensive plasmacytic infiltration affecting the small bowel and mesenteric lymph nodes. The frequent finding of a paraprotein consisting of an incomplete alpha-chain devoid of light chains has coined the term alpha-chain disease.[1,2] IPSID was first reported in Mediterranean and Middle Eastern regions and was originally termed Mediterranean abdominal lymphoma.

PATIENTS AND METHODS

Fifty-one patients had referred to Shiraz University of Medical Sciences (SUMS) hospitals seeking medical help for long standing diarrhea, abdominal pain and weight loss between 1980-1994. They were young adults with age ranging from 16 to 30 years with a mean age of 21.5 years. Most of them were from low socioeconomic groups, from the city of Shiraz, its suburbs, and other cities all in southern Iran.

Their chief complaints were diarrhea, abdominal pain and weight loss for the past few years. Almost all of them had taken various treatments for chronic diarrhea with no benefit. A few cases had also been treated as tuberculosis.

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Table I. Comparison of patients with IPSID who were treated with chemotherapy alone vs. those who received chemotherapy+radiotherapy.

	Total cases	No. of cases who survived after 3 years with no evidence of disease (%)
Group A	21	4 (19%)
Group B	17	7 (41%)

A: Those who received chemotherapy.

B: Those who received chemotherapy+radiotherapy.

Finally, the diagnosis of all cases had been established by histopathological findings after laparotomy. Out of these 51 patients, 13 of them were not included into this study because they did not have a palpable abdominal mass; they were in an early stage.

RESULTS

Forty-three males and 8 females diagnosed as IPSID were evaluated. Physical examination revealed cachexia, clubbing of the fingers and edema of the feet. A palpable abdominal mass was present in 38 of them. Peripheral lymphadenopathy or organomegaly was not present in any patient. In paraclinical investigations peripheral blood and bone marrow study revealed megaloblastic anemia with increased plasma cells (10-15%). Hemoglobin ranged between 7-10 g/dL. White blood cell count was 6000-10000 and platelet count was within normal limits. Routine blood chemistry tests were also normal. Serologic tests of alpha chain had increased in 21 of them. Small bowel series showed a malabsorption pattern accompanied by mucosal fold thickening and nodularity and in most cases coexisting with multiple infiltrating or polypoid masses. In those for whom ultrasonography had been performed, abdominal mass, most probably enlarged lymph nodes, had been reported. Those with abdominal mass (38 of them in stages II or III) could be gathered in two groups, although all of them had undergone exploratory laparotomy in which debulking of the masses and resection of the involved portion of intestine had been performed. Group A: Twenty-one of them had received chemotherapy (Cyclophosphamide + Doxorubicin+ Vincristine + Prednisolone with or without Bleomycin) as the sole modality of treatment. They had received chemotherapy for 4-9 courses (11 of them had received 6 courses, each one 3 weeks apart). Group B: Seventeen of the patients had received radiation to the whole abdomen in addition to systemic chemotherapy.

Twelve of the patients after 6 courses of chemotherapy, four of them following 4 courses and one after 7 courses, received 2000-3000 cGy to the whole abdomen with two AP-PA open fields, 150 cGy per fraction and 5 fractions per week. All patients experienced GI disturbances; nausea, vomiting and diarrhea during radiation. One of them developed intestinal perforation necessitating surgical intervention.

After 3 years of follow-up, out of those who had taken chemotherapy alone (A), 4 (19%) patients were alive in disease-free status but among those who had also received radiation (B), 7 (41%) were alive with no evidence of disease.

The causes of death in both groups were: fulminant infections, profound electrolyte disturbances, uncontrolled tumor growth and complications of therapeutic procedures.

DISCUSSION

Immunoproliferative small intestinal disease previously had been called Mediterranean lymphoma. The term Mediterranean lymphoma was scientifically incorrect because the disease is not geographically confined to Mediterranean countries and does not necessarily start with lymphoma. Accordingly it was substituted by a more valid term which is IPSID or alpha-chain disease. Initially these cases were reported mainly from Mediterranean countries, but later they were reported from other countries too.[1,3-8]

IPSID is a distinct disease entity with characteristic clinical, pathologic and immunologic features. Clinically, patients with IPSID were young adults presenting with chronic diarrhea, weight loss, abdominal pain, clubbing of fingers and edema of the feet. Very rarely these patients presented with intestinal obstruction, bleeding and perforation. A history suggesting progressive malabsorption for a long time is very characteristic in these cases. One of the most important diagnostic criteria of IPSID was the synthesis and secretion of abnormal IgA immunoglobulin.[1,5-9]

Gross pathology is mainly confined to the proximal small intestine and is characterized by nodular thickening of mucosa, tumor formation and ulceration. Microscopically the findings were more distinctive and diagnostic. IPSID was always associated with a dense and compact plasma cell infiltration in the lamina propria, mucosa and submucosa. Depending on the maturity of plasma cells, IPSID can be

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classified into three groups: A) mature plasma cells, B) intermediate cells, C) immature plasma cells. The detailed clinical and histopathological findings of IPSID have been described in the literature.[7,10,11] In this study some of these cases were clinically diagnosed as giardiasis, tuberculosis or lymphoma before laparotomy.

Although long standing clinicopathologic remission following administration of tetracycline in patients in early stages has been frequently cited in the literature, [1,7,8,10,12] in more advanced stages other more aggressive choices such as systemic chemotherapy and/or abdominal radiotherapy should be elected.[13,14] The staging system is characterized by the presence of benign lymphoplasmocytic mucosal infiltration (LPI) and the absence of cytologic evidence of malignancy (stage 0), LPI and malignant lymphoma in either intestine (Ii) or mesenteric lymph nodes (In), but not both, LPI and malignant lymphoma in both intestine and mesenteric nodes (II), involvement of retroperitoneal and/or extraabdominal lymph nodes (III) (all our patients in the study were in stage II and III), and finally involvement of noncontiguous nonlymphatic tissue (IV).[6,7,11]

In conclusion, this and some other studies[1,14] demonstrate that total abdominal radiation can lead to frequent long standing disease-free status. However according to some reports, this approach can predispose some patients with bulky transmural lymphoma of the gut to catastrophic intestinal perforation,[6] but averting such a serious complication in this high risk group can be achieved by surgical resection of the bowel segment which is involved by a massive tumor and also giving a small daily fraction dose of radiation to avoid rapid regression of the mass.

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