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Preliminary Report on a Small Group of Patients with Advanced Hodgkins Disease

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INTRODUCTION

Hodgkins disease was first described as a clinical entity by Thomas Hodgkins in 1832[1]. It is relatively uncommon form of cancer. The total crude incidence in USA is 3.3 cases per 100,00 per year. Its incidence appears to be increasing, especially in young adults[2].

Radiation therapy was intially employed to treat Hodgkins disease. Response were dramatic but transient[3,4]. Although consistent subjective and objective responses were obtained, cure was a distant goal and extension of life debatable. Later, with the emergence of various chemotherapeutic drugs, after World War II Hodgkins disease, Non Hodgkins Lymphomas and leukiemias became the first diseases to respond to chemotherapy, Combination chemotherapy was intially employed by Lascher and Durani with promising result's[5] in Hodkings disease.

In 1969, Devita and his colleagues[6] put together an effective protocol (the MOPP regimen) consisting of vincristine, prednisone, procrbazine and nitrogen mustard. This altered the outlook for patients with advanced Hodgkins disease dramatically. Several other regimens were introduced later. However, the second most significant drug regimen to emerge was ABVD. This was introduced by Bonnadonna in 1973[7] and consisted of adriamycin, bleomycin, vinblastine, and dacarbazine. The new protocol was less leukemogenic than MOPP and since it did not overlap with MOPP, it could easily be used in MOPP resistant cases or in alternating cycles with MOPP. It is also very effective in advanced cases of Hodgkins III B and IV B.

The Oncology Department of Sheikh Zayed Hospital started a new protocol for patients with advanced disease which consisted of drugs which are active in Hodgkis, less leukemogenic, and easily available. This protocol was tried for several reasons. First, nitrogen mustard and procarbazine which are a part of MOPP regimen are not available in Pakistan. Second, the supply of decarbazine, an essential component of ABVD is erratic. The third reason is the 20% higher cost of ABVD compared to drugs used in our protocol. The purpose of this study was to evaluate the results of our regimen with the established MOPP and BVD regimens.

MATERIALS AND METHODS

The patients with advanced Hodgkins' disease of various age groups were selected for this study. Histological diagnosis was confirmed either by lymphnode biopsy of laparotomy. Surprisingly, all patients were diagnosed as mixed collularity Hodgkin's disease. They were staged according to the Ann Arbor staging classification prior to initial therapy. The staging procedure included history, physical examination., chest X-Rays, complete CBC, liver profile and renal profile. Abdominal and pelvic ultrasounds were done in all patients. CT scan was done in only three cases because of the excessive costs involved. Lymph angiograms were not performed due to non-availability of dye. Bone marrow aspirate and biopsy were done in all patients. Three patients presenting with pleural effusion had cytological examination of the fluid. Staging laparotomy was done in patient presenting with abdominal mass and intestinal obstruction.

The protocol was based on drugs active in Hodgkin's disease belonging to different classes and having no or minimal overlapping organ toxicities. Vincristine 1.4 mg/meter square day one and eight, adriamycin 45 mg/square metre day one, etiposide 110 mg/square metre for four days and prednisone 70 mg/square metre from day one to seven. Each cycle had a four week interval to allow host recovery. Patients were started on chemotherapy only on complete evaluation. Three patients had received previous therapy in the form of either radiation or drugs. Of these only one patient had received adequate therapy of six courses of MOPP. The other two patients had received neither proper treatement nor complete evaluation. All patients received full doses of chemotherapy according to the protocol. Treatment was delayed only if there was

severe infection or significant neutropenia of less thna 2000. All side effects were carefully monitored. All our patients except one received treatment on an ambulatory outpatient basis. The only exception was admitted to the hospital at his own behest and for his own convenience.

Follow up was based on monthly physical examination and laboratory evaluation.

RESULTS

The age of a patients ranged from 3 to 50 years with median age being 20 years. Five patients had Stage III B and the remaining five had Stage IV disease. All patients had B-symptoms, our criteria being fever, nightweats, and a weight loss of greater than ten present. Cervical lymph adenopathy was seen in eight out of ten patients. Eight out of ten patients presented with splenomegaly. Since abdominal lymphnodes were enlarged it was assumed that splenomegaly documented both clinically and on ultrasound was due to Hodgin's disease. Ultrasound examination peformed on all patients indicated enlarged lymphnodes for eight patients. The CT scan was positive for all the three cases for whom it was performed. Extra nodal disease was documented in five patients, three of which presented with lung infilitration and pleural effusion. The fourth patient had an unresectable pancreatic mass. Bone marrow involvement was seen in only one patient. After the first course there was marked regression of the tumor and after the third course complete regression was noted in seven patients. This was more marked in patients with parenchymal lung involvement. Three of the patients received radiation therapy to the bulky lesion which were supraclavicular. Table 1 shows the profile of the patients in the study.

Table 1: Patients profiles.

Sex	Age (years)	Stage	Response to treatment
M	10	III B	CR
M	50	IV B	CR
M	5	IV B	Relapsed
F	7	III B	CR (lost to F/U)
F	30	IV B	CR
M	32	III B	CR
F	12	III B	CR
M	18	III B	Relapsed
M	23	IV B	CR
F	20	IV B	Relapsed

CR = Complete remission: F/U = Follow-up.

The most significant side effects were nausea noticed on the first day in nearly all patients. Vomiting metochlorpromadie was given. Hair loss was distrressing and was seen in 100% of the cases. Constipation was seen in four patients and was related to vincristine. Only two patients required hospitalization and both came from very poor socioeconomic status. One patinet developed tuber-culosis probably due to immunosuppression and high dose steroids. Peripheral counts conducted on day one and fifteen revealed that it did not fall below 1500. No significant thrombo-cytopenia (less than 100,000) was noted.

DISCUSSION

Hodgkin's disease is a disease of young adults, mainly, with a biphasic distribution. IN the 1980's the prognostic outlook for Hodgkins diease is definitely more favourable than that in the previous decade. The main task is to learn to think in terms of optimal strategy and to achieve a high cure rate with moderate or minimal toxicity. This is especially true in the Third World countries where poverty, high incidence of infection, and poor compliance decreases the cure rate. The favourable outlook of Hodgkins disease has to be emphasized repeatedly to the patients. Treatment of Hodgkins disease has continously improved, particularly during the 1960s and 1970s. Today, about 70% to 80% of all patients can be offered a chance of cure. Although its fundamental nature, etiology and pathogenesis remains to be further elucidated, Hodgkins disease represents a remarkable example of how progress in clinical and laboratory research has been successfully translated into an effective management programme.

Table 2 shows various drugs which are active in Hodgkins disease and have been used in various protocols.

The development of MOPP in 1970 by DeVita showed that combination chemotherapy can produce a high and prolonged remission in advanced Hodgkins disease. This represented the first attempt to cure using effective drugs. The design and application of MOPP is representative and is based on the biological concepts of Skipper from the L1210 model of rodent leukemia. The concepts in making this drug combination were related to dose response effect, fractional tumor killing effects of drugs, and inverse relationship between cure of drugs and number of tumor cells at initiation of treatment. This has formed the basis of all combination chemotherapetuc regimens in cancer treatment.

Note

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