Medical Journal of the
Islamic Republic of Iran

Volume 14
Number 3
Fall 1379
November 2000

NEOADJUVANT CHEMOTHERAPY WITH VINCRISTINE AND CISPLATIN FOLLOWED BY RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY FOR FIGO STAGE IB BULKY CERVICAL CANCER

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ABSTRACT

Twenty patients with bulky (>4 cm size) FIGO stage IB cervical cancer were treated with cisplatin 50 mg/m^2 and vincristine 1 mg/m^2, administered intravenously at 10-day intervals for a total of 3 courses before radical hysterectomy. A complete clinical response was noted in 1 patient (5%) and partial response in 5 (25%). Fourteen patients (70%) had stable disease. There was no grade 3 toxicity noted. Of the 20 patients who received chemotherapy (ChT), 3 patients had parametrial and para-aortic involvement; in these cases, the operation was aborted and radiation therapy given. The remaining 17 patients underwent radical hysterectomy and pelvic lymphadenectomy 10-15 days following ChT. Five of these patients (29.4%) had pelvic node metastases. Three patients had positive margins. These 8 patients received postoperative radiotherapy. Twenty-four months later 15 patients were alive (87%) and 2 had died.
MJIRI, Vol. 14, No. 3, 241-243, 2000.

INTRODUCTION

Both the size of the lesion and the depth of stromal invasion affect the survival of patients with stage IB cervical cancer. Delgado reported a 67% 5-year survival rate in surgically treated stage IB patients with a lesion diameter of 3 cm or greater compared to an 86% 5-year survival rate when lesion diameter was less than 3 cm.[1] Ballon noted a 5-year survival rate similar to their stage IIIB patients (43% versus 48%) when treated with radiation therapy alone.[2] Gauthier[3] noted if both lesion size was greater than 3 cm and cervical invasion was greater than 1.5 cm, the 5 year survival rate fell to 31% in surgically treated patients. In recurrent cervical cancer, the most effective single agent, cisplatin, has a reported objective response rate of 23%.[4] Response rates better when cisplatin-containing regimens are administered to previously untreated cervical cancer patients. Objective response rates of 67-100% and complete response rates of 15-46% have been recently reported.[5-8] The goal of this study was to evaluate clinical and surgical response and the toxicity of combined modality therapy in such patients.

MATERIALS AND METHODS

From November 1995 to September 1997 we conducted a study in 20 patients with bulky stage IB cervical cancer. All patients had either primary, previously untreated, histologically confirmed invasive squamous cell carcinoma (17 patients) or adenocarcinoma (3 patients). Bulky tumor was defined as a cervical lesion 4 cm or greater. Patients were not pregnant and had adequate bone marrow, renal and hepatic function. Prior to study entry, patients underwent clinical staging including pelvic examination, IVP, chest X-ray and routine serum chemistries. Cervical and tumor dimensions were determined by palpation, compass and ruler mea-

surement.

Patients received cisplatin, 50 mg/m² and vincristine 1 mg/m² intravenously every 10 days for three courses. Drugs were withheld if the white blood count was <3000/mm³ or platelets<100000/mm³. Patients were examined prior to each course of chemotherapy and immediately before laparotomy with cervical measurement of the tumor in 2 perpendicular dimensions. At the end of chemotherapy courses the operable (resectable) patients underwent type III radical hysterectomy and pelvic lymphadenectomy. Following surgery, patients were examined every three months. Adverse effects of chemotherapy were scored by the GOG criteria.[9]

Complete response was defined as disappearance of all measurable disease, partial response was defined as a 50% or greater reduction in the product of the transverse diameters of the lesion. Progressive disease was a 50% or greater increase and stable disease was any condition not meeting the preceding criteria.

RESULTS

Twenty patients were entered in the study. One had parametrial involvement after chemotherapy. Two had positive para-aortic nodes and the operations were aborted.

These 3 patients received standard radiotherapy. Median age was 46 years with a range of 23 to 68 years. Seventeen patients completed 3 courses of chemotherapy. There was no life-threatening or severe complication. Five patients showed partial response and one complete response. Fourteen patients had stable disease. Seventeen patients were eligible for surgery which was performed ten to twenty days following completion of chemotherapy. All patients received prophylactic antibiotics. We had no significant operative complications. One patient had elevated serum creatinine but recovered after two weeks. Three patients had adenocarcinoma and 17 had squamous cell carcinoma. There was five pelvic lymph node, two parametrial and one cervical margin involvement. Therefore eight patients received adjuvant radiotherapy following surgery.

Two patients had progressive disease and died at 12 and 15 months following initiation of therapy. The remaining eighteen patients were alive two years following study entry.

DISCUSSION

Compared to prior reported experiences with neoadjuvant chemotherapy in bulky stage IB cervical cancer,[5-8] our complete response is clearly lower. Bleomycin was not used in this study because of prior reports of significant pulmonary toxicity including one death[10] and a case of shock lung.[6] Tumor size decreased in all patients following chemotherapy. In one patient with complete pathologic response there was a visible lesion, but the pathology report was only dysplasia. Several studies have claimed a lower than expected rate of lymph node metastases in patients treated with neoadjuvant chemotherapy.[5-8]

Without a randomized prospective study, this claim is difficult to substantiate. The 29% rate of pelvic lymph node metastases supports this opinion. Maruyama[11] reported an 84% 5 year survival in 80 bulky stage IB cervical cancer patients treated at one institution with teletherapy and brachytherapy followed by hysterectomy. Delgado[1] reported a 67% 5 year survival in 152 similarly defined bulky stage IB disease cases treated with radical hysterectomy and pelvic lymphadenectomy. By comparison, our pilot study of a short program of neoadjuvant chemotherapy before radical surgery produced an 88% survival rate at 24 months. Only a prospective randomized study will answer the question whether this strategy improves survival.

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