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Short communication

A phase II study of vincristine in malignant mesothelioma – a negative report

Gunnar Mårtensson and Sverre Sörenson

Department of Pulmonary Medicine, Renströmska Hospital, University of Göteborg, Göteborg, Sweden

Summary. A total of 23 consecutive, previously untreated patients with radiographically evaluable, malignant pleural mesothelioma were treated in a phase II study with vincristine. Vincristine was given i.v. at a dose of 1.3 mg/m^2 once weekly for 4 weeks, then every 2 weeks. No response was observed. The result suggests that vincristine has little or no therapeutic value in the treatment of malignant mesothelioma.

Introduction

Malignant pleural mesothelioma is a rare tumour that usually presents as a pleural effusion [10]; an association with asbestos exposure is usually but not always present. The annual incidence of this tumour is 0.8/100,000 inhabitants in Sweden and is expected to increase (as in most industrialised countries) due to the extensive industrial use of asbestos after the second World War.

At present no curative treatment is available for malignant mesothelioma. Due to the previous rarity of the disease, most published, therapeutic studies include only small numbers of patients. Data presented in previous studies show that neither radiotherapy [4, 8, 14] nor surgery [1, 3, 7, 8] have anything but a temporary effect on the course of the disease. Regarding chemotherapy, most studies include only a few, usually previously treated patients, which makes the evaluation of new drugs less reliable. The greatest experience has been gained using doxorubicin; some studies have claimed that this drug is active against mesothelioma, with a response rate of up to 13% [9], whereas others have not reported any activity [12]. Activity against malignant mesothelioma has also been claimed for high-dose methotrexate [13], cisplatin [2] and carboplatin [2, 11].

Data on the activity of various single agents against mesothelioma are thus scarce, and no drugs have been reported to attain a remission rate of >25%. Further phase II studies of various antineoplastic drugs are thus needed to find drugs with significant activity. The aim of this study was to evaluate the antineoplastic effect of vincristine in a phase II study of previously untreated patients, as this drug has been included in combination chemotherapy programs with some activity against mesothelioma and, having mainly non-haematological toxicity, is thus suitable for combination chemotherapy.

Offprint requests to: Gunnar Mårtensson, Department of Pulmonary Medicine, Renströmska Hospital, P. O. Box 17301, S-402 64 Göteborg, Sweden

Patients and methods

Patients were admitted to the study between January 1982 and August 1986. Eligibility criteria included (a) a histopathological diagnosis of mesothelioma according to the WHO classification [16], (b) an age of <75 years, (c) radiographically measurable lesions on posteroanterior and/or lateral projections, (d) no previous antineoplastic treatment, and (e) acceptance by the patient. Microscopic examination was carried out by an experienced pulmonary pathologist, and chest radiographs were evaluated by two experienced observers.

All patients with pleural effusion were treated with pleurodesis using mepacrine at least 2 weeks prior to treatment with vincristine to prevent the interpretation of pleural fluid as pleural neoplasm at evaluation. Vincristine was given as an i.v. bolus injection at a dose of 1.3 mg/m^2 (maximum dose, 2 mg) weekly for 4 weeks and then every 2 weeks. Physical examinations, determinations of haematological status [erythrocyte sedimentation rate/h, haemoglobin, WBC count, platelet count, and determinations of liver transaminase and serum lactic dehydrogenase (LDH) levels] and plain chest radiographs (posteroanterior and lateral projections) were carried out prior to the initial treatment and then every 4 weeks. Evaluation of response was done according to WHO criteria [15]. Treatment was given until progressive diease or major side effects of the drug were noted.

Results

A total of 23 patients (4 women and 19 men) with a mean age of 62 years and a median age of 63 years (range, 41–75 years) were included in the study. Microscopic examination showed that 19 patients had the epithelial tumour type, 1 had the biphasic tumour type, and 3, the sarcomatoid tumour type of malignant mesothelioma. The diagnostic procedures carried out on the patients included thoracoscopy in 12 patients, transthoracic Tru-cut needle biopsy in 12, Abrams needle biopsy in 2, thoracotomy with open lung biopsy in 1, Daniel's biopsy in 1, and local excision in 1. The diagnosis was confirmed by autopsy in 10 patients and was verified by one biopsy procedure in

8 patients, by two biopsy procedures in 4, and by one biopsy procedure as well as a thoracotomy or autopsy in 11.

Treatment with vincristine was given for a period of 2–31 months, with a mean of 7 and a median of 4 months. During therapy, dose reduction and postponement of treatment were occasionally necessary due to moderate paresthesia in the fingers and toes of some patients. No severe toxicity was noted. The therapy was concluded due to progression of disease in all patients. None of the patients attained complete or partial remission of disease as determined by plain chest radiographs. The median survival from the onset of treatment was 7 months (range, between 2 and >69 months). Two patients with slowly progressive disease are alive 52 and 69 months after the onset of treatment.

Discussion

This phase II study revealed no antineoplastic activity for vincristine against malignant mesothelioma. Vincristine has previously been included in combination chemotherapy programs such as CYVADIC [5, 6] for mesothelioma, with occasionally verified activity that must have been due to drugs other than vincristine. The nature of this neoplasm, with tumour growth over large surfaces, indicates that future successful therapy would probably involve neither surgery nor irradiation. At present, further single-agent chemotherapy trials would seem to be the most appropriate approach in the search for a potentially curative treatment.

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