A CLINICAL STUDY OF ADENOCARCINOMA OF UNKNOWN PRIMARY SITE IN HONG KONG

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ABSTRACT

Forty-two patients with adenocarcinoma of unknown primary (ACUP) presented to the Prince of Wales Hospital in Hong Kong from 1984 to 1985. They were studied for the site of symptomatic metastases at presentation, survival, and response to treatment. Bony (21) and lymph nodal (14) metastases were common. Survival was short with a median duration of 32 weeks and was not affected by sex, site of metastases at presentation, and development of new metastases. Response to combination chemotherapy with cisplatinum, adriamycin and cyclophosphamide (CAP) occurred in 4/31 (12.9%) patients with two complete responses and two partial responses and the responders survived significantly longer than non-responders with a median survival of 51 and 29 weeks respectively ($P < 0.05$). Twenty out of 36 (55.6%) treated with radiotherapy had a positive response including five complete responses and fifteen partial responses but there was no demonstrable improvement in survival for the responders.

Keywords: adenocarcinoma of unknown primary, clinical features, chemotherapy, radiotherapy.

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INTRODUCTION

Varying from 0.5% to 6.7% of the cancer population present with metastatic disease without obvious evidence of the primary tumours (1-6). In such instances, the primary is usually not found during life and even at post-mortem examination. As a syndrome it reflects a clinical state of advanced cancer having its metastases more symptomatic than its primary (7, 8). This paper describes the clinical features and treatment results of metastatic adenocarcinoma of unknown Primary (ACUP) seen in a major teaching hospital in Hong Kong serving 2.5 million people which represented approximately 45% of the total population.

METHODS

A retrospective analysis was conducted on all cancer patients presented to the Clinical Oncology Department, Prince of Wales Hospital from 1984 to 1985. The diagnostic criteria for ACUP was that all patients must have a histologic proof of metastatic adenocarcinoma without any evidence of primary tumour after a thorough history and physical examination, chest radiograph, stool for occult blood, α-fetoprotein and β-HCG assays, as well as blood for acid phosphatase in males and bilateral mammogram in females. Appropriate investigations included bronchoscopy, endoscopy and relevant radiological examinations such as Barium studies and ultrasonography when clinically indicated. Thirty-one patients with a Kamofsky performance status at or above 60 were treated with a combination chemotherapy (CAP) which consisted of cyclophosphamide 500 mg/m^2, adriamycin 50mg/m^2, and cisplatinum 50mg/m^2 given intravenously every 3 weeks. Cisplatinum was given by continuous infusion over 4 hours and pre- and post-treatment hydration. Twenty five of these 31 were further treated by radiotherapy. Eleven patients with poorer performance status were treated by radiotherapy alone.

For each course of radiotherapy, 30 Gy/10 fractions/2 weeks was given. Log rank test was applied for actuarial survival comparison and statistical significance was taken at 0.05.

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RESULTS

Out of a total of 1963 patients, 42 patients (2.14%) were diagnosed metastatic adenocarcinoma of unknown primary site.

Their age and sex distribution are shown in Fig. 1. The mean age for male and female patients was 58.1 and 57.6 respectively. The common sites of symptomatic metastases at presentation were bone and lymph nodes (Fig. 2).

Thirteen of the 21 bony metastases involved the dorsolumbar spine; others involved pelvis (3), femur (2), humerus (1), ulnar (1) and skull (1).

Ten of the 14 lymph node metastases involved the left supraclavicular group; the rest involved the right supraclavicular (2), the axillary (1) and the inguinal group (1).

The survival of the 42 patients with ACUP are shown in Fig. 3. Their median survival interval was 32.0 weeks (standard error = 2.83). There was no significant difference between the sexes. Development of new metastases during and/or after treatment and kind of metastases at presentation were not shown to be of prognostic significance. A total of 74 courses of CAP were given to 31 patients. Each patient received an average of 2.39 courses (range 1 – 7). Four out of 31 patients (12.9%) had a positive response to chemotherapy. This consisted of two complete responses of l mph nodal metastases, one partial response of lymph nodal metastases and one partial response of hepatic metastases. All responses occurred after the first or second course of chemotherapy. The 4 responders survived significantly longer than the 27 non-responders with a median survival of 51 weeks for the responders and 29 weeks for the non-responders ($P < 0.05$).

Twenty five of the 31 patients were further treated with radiotherapy after chemotherapy and eleven patients received radiotherapy without prior chemotherapy. A total of 40 courses of radiotherapy were given to thirty six pa-

tients; 20 patients (55.6%) had positive responses, with 5 (13.9%) complete response of lymph nodal metastases, 13 (36.1%) partial responses of brain metastases and 2 (5.56%) partial responses of bony metastases.

Prior chemotherapy or lack of response to chemotherapy were not shown to decrease the chance of response to radiotherapy. However, there was no survival benefit for the positive responders to radiotherapy.

Fig. 1 Age and sex distribution.

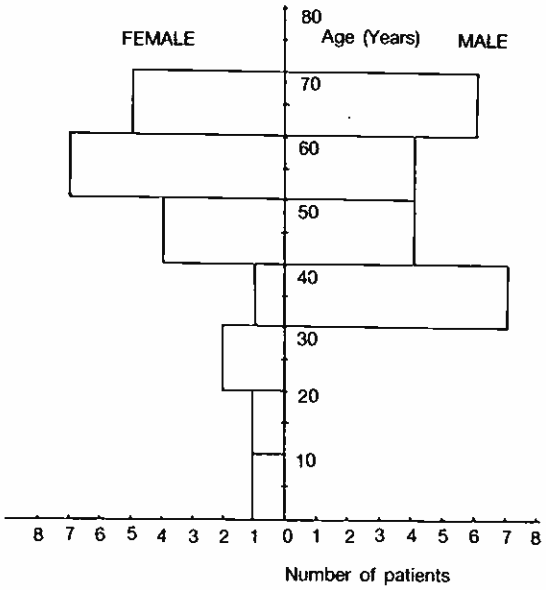


Fig. 2 Site distribution of symptomatic metastases at presentation.

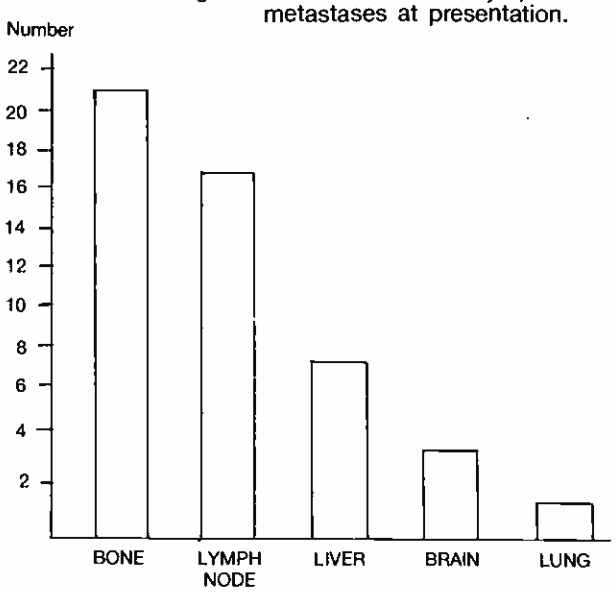
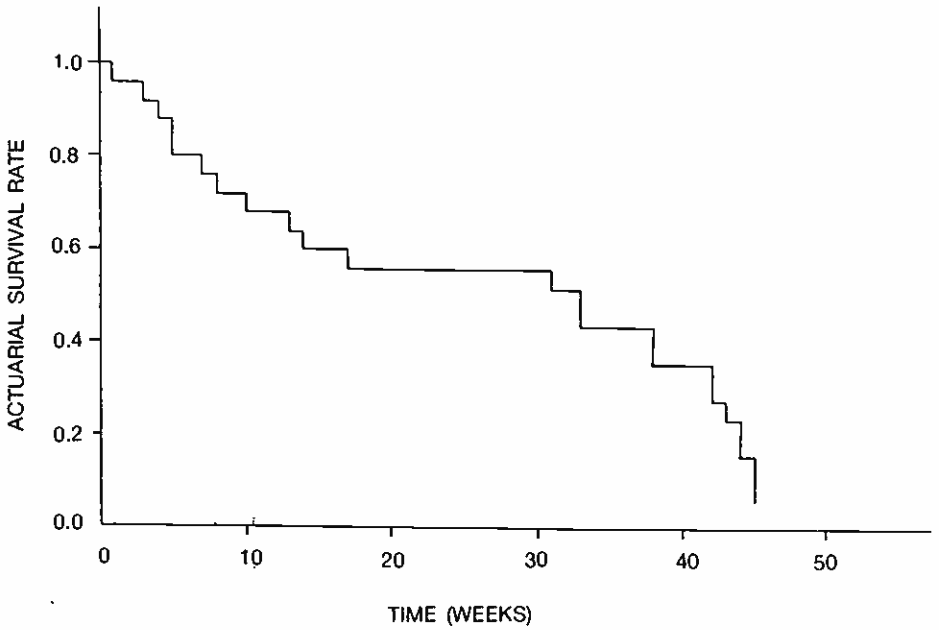


Fig. 3 Actuarial survival



DISCUSSION

Extensive investigation for ACUPs have been shown to be unfruitful, time-consuming, expensive, uncomfortable and frequently gives misleading information (5, 6, 9). Only 6/51 (12%) had their primaries discovered (10) after extensive investigation in one prospective study (10).

All our patients were diagnosed as ACUP after a thorough history, physical examination (including a pelvic and/or per-rectal examination), stool for occult blood, urinalysis, α-fetoprotein and β-HCG assays, chest x-ray, as well as blood for acid phosphatase in males and bilateral mammogram in females failed to reveal the primary tumour. All subsequent premortal investigations had failed to discover the primary disease after being so diagnosed as ACUP. Thus, we supported the view of the general lack of cost-effectiveness in routinely pursuing multiple investigations after a patient has been classified as ACUP by means of negative simple examinations.

The present distribution of sites of symptomatic metastases at presentation was different from others (7, 10). The main difference was in the low frequency of pulmonary metastases. This was probably due to the exclusion of our patients from the ACUP definition if

they had a solitary coin lesion and/or hilar masses on chest radiographs suggesting a bronchogenic primary.

In the present study, cisplatinum and adriamycin were used in combination because they had been demonstrated to be effective as a single agent in a wide spectrum of adenocarcinomas. Only 4/31 patients (12.9%) in the present study had a positive response. This reflects the overall low chemosensitivity of ACUP and the response rate is similar to other studies using different kinds of chemotherapy (10 – 13). However the responders survived longer than the non-responders.

There was an overall poor response to treatment in bony metastases. Of the 21 bony metastases, only 2 partial responses were noted after radiotherapy and none after chemotherapy.

The median survival of 32 weeks in the present study was notably longer than other reports (3, 6, 14). Sex of the patient, site of symptomatic metastases at presentation, and, development of new metastases had not been shown to be of prognostical significance.

We conclude that there is a constant need to explore for more effective chemotherapeutic agents to salvage this group of patients and radiotherapy remains useful in relieving many metastatic symptoms.

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