Prolonged Survival in a Nasopharyngeal Carcinoma Patient with Multiple Metastases: A Case Report and Review of the Literature

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Nasopharyngeal carcinoma is a common cancer in South East Asia. In the early stages, radiotherapy alone may achieve sustained control, but once metastasis occurs, it becomes an incurable disease with limited survival time. We report a case of nasopharyngeal carcinoma, initial stage T4N0M0, diagnosed in 1985 in a patient aged 36 years who received 70 Gy radiotherapy to the head and neck region. In 1988, relapse occurred with multiple lung metastases. The patient received many chemotherapy regimens with a very good response, including near complete remission with the first treatment regimen of cisplatin, 5-fluorouracil and leucovorin for lung metastases, and with the fifth chemotherapy regimen of ifosfamide as a single agent. After ifosfamide treatment, there was residual fibrotic change in the lung and complete disappearance, lasting for almost a year, of the liver and bone lesions. The patient eventually died in July 1995 due to progressive disease. Prolonged survival after mainly thoracic metastasis is possible in patients with nasopharyngeal carcinoma, especially if the tumor is chemo-responsive.

Key words: nasopharyngeal carcinoma – ifosfamide – metastases – survival

INTRODUCTION

Nasopharyngeal carcinoma (NPC) has an incidence of 5.36/100 000 persons/year and ranks as the 6th and 11th leading cause of cancer death in males and females respectively in Taiwan (1). Most cases of early-stage disease can be cured by local radiotherapy, with long-term survival (2,3). A survey reported in 1982/83 in Taiwan showed that the actuarial and relapse-free survivals of 966 patients at all stages were 82% and 49% at one year, 43% and 33% at 5 years and 36% and 22% at 10 years respectively, supporting Ho’s classification of 5 stages for survival analysis (4,5). Actuarial survival for stages I, II, III, IV according to Ho’s classification (6) has been reported to be 80.8%, 71.5%, 40.7% and 17.7% respectively at 5 years and 48.4%, 33.4%, 30% and 9.5% respectively at 10 years in Hong Kong, although stage V (any distant metastases) data were not reported (7).

In nasopharyngeal carcinoma patients diagnosed as having metastatic disease ab initio, the prognosis is poor, possibly reflecting the intrinsically aggressive behavior of the tumor (8). When metastatic disease develops after curative radiotherapy, bone is the most frequently involved site, followed by the lungs and liver. More than half of all patients have more than one metastatic site (9). Although the median survival of all patients with metastatic disease has been reported to be 8 months (9), [lung only, 11.8–12.5 months (5,9), bone only 6.5–8 months (5,9), liver, 3.8–5.4 months (5,9), skin and lymph node involvement below the clavicle, 20 months (5)], long-term survival is occasionally observed (5,8,9,10).

CASE REPORT

A 36-year-old male was diagnosed as having nasopharyngeal carcinoma in January 1985. The histology report was poorly differentiated epidermoid cell carcinoma (Fig. 1), clinical staging T4N0M0, stage IV according to Ho’s classification (6). CT scan of the nasopharynx and skull base showed a large right-sided abnormal soft tissue density in the nasopharynx, involving the right maxillary, ethmoid and sphenoid sinuses, with bony
Figure 1. Nasopharynx biopsy specimen showing sheets of hyperchromatic and pleomorphic tumor cells. Some inflammatory cell (chiefly neutrophil) infiltration is also evident.

destruction of the right pterygoid plate, roof of the nasal cavity and floor of the sphenoid sinus. Curative radiotherapy of 70 Gy was given and control of the primary lesion was good (11).

In August 1988 (3.5 years after initial diagnosis), lung metastases were found (Fig. 2) and bronchoscopic biopsy showed poorly differentiated carcinoma, compatible with NPC. Chemotherapy was suggested, but the patient refused. Subsequently, just over a year later, he returned with stable lung (Fig. 3) but new liver metastases, having received no specific cancer treatment. Continuous four-day infusion of cisplatin (20 mg/m²/day), 5-fluorouracil (2200 mg/m²/day) and leucovorin (120 mg/m²/day) every 4 weeks was given for four courses (12) and this resulted in almost complete disappearance of the lung lesions, although the patient discontinued the treatment.

In 1990, the lung lesions recurred, but the patient again refused treatment. From January 1991, PEFL (cisplatin, epirubicin, 5-fluorouracil, leucovorin) was given for four courses, with partial response of the lung metastases. In December 1991, multiple bone metastases developed. Carboplatin (300 mg/m²/day) and bleomycin (30 mg/m²/day) were given for one day every 3–4 weeks (15), for two courses, but this time there was rapidly progressive disease and therefore epirubicin (50 mg/m²/day) was added to the regimen (16), with minor effect.

The patient was now in a serious condition, with dyspnea at rest due to multiple lung metastases, pain from the bone metastases, and liver metastases. Starting in October 1992, single-agent ifosfamide (2.4 gm/m²) was administered for 3 days every 3 weeks (17), for a total of eight courses. In the first course, the patient received only 2 days of treatment before high fever developed with grade 4 leucopenia and infection, and subsequent cycles were reduced to 1.5 gm/m²/day. In January 1993, whole-body bone scan and abdominal sonography showed resolution of all the bone and liver lesions and a chest X-ray showed only residual fibrotic changes in the lungs (Fig. 4).

In January 1994, a CT scan showed multiple nodules over both lungs and the liver. The patient had poorly controlled non-insulin dependent diabetes mellitus, complicated by azotemia, and was not willing to receive any more therapy. He died in July 1995, just over 10 years after the initial diagnosis and 82 months after diagnosis of metastatic disease.

Figure 2. Chest radiograph taken in 1988, showing multiple metastatic lesions with several central cavitation foci over the bilateral lung fields, mostly in both lower lobes.

Figure 3. Chest radiograph disclosing multiple cavitary lesions over both lung fields in 1989. As compared with the previous films taken in 1988, no obvious change is evident without treatment.
DISCUSSION

Our patient survived 82 months from the time metastatic disease was first diagnosed and almost 10 years from the first presentation. This may have reflected the biologic behavior of his disease, having attained a 3.5-year disease-free interval after curative radiotherapy for T4 disease. Even after metastasis had occurred, the tumor was still highly responsive to treatment by many different chemotherapeutic agents, especially cisplatin/5-fluorouracil combination chemotherapy as well as single-agent ifosfamide.

Reports of long-term survival of patients with nasopharyngeal carcinoma after development of metastatic disease have been limited. In the largest serial report of 17 long-term survivors who survived more than two years after initial diagnosis of metastatic disease, analysis concluded that patients with only intrathoracic metastases, showing complete response to chemotherapy, and one patient with a completely resectable thyroid metastasis, were able to survive prolonged periods of more than 5 years (8). Comparable survival data have also been reported for three other patients with mainly thoracic metastases may still enjoy prolonged disease-free control if the tumor is chemosensitive.

Reports of long-term survival in an NPC patient have been published (17). Nasopharyngeal carcinoma patients with mainly thoracic metastases may still enjoy prolonged disease-free control if the tumor is chemosensitive. Excellent response has been attained with cisplatin-based chemotherapy in patients with recurrent or previously untreated advanced nasopharyngeal carcinoma. The response rates for combinations of cisplatin/5-fluorouracil/leucovorin, belomycin/epirubicin/cisplatin and ifosfamide/cisplatin for metastatic undifferentiated carcinoma of the nasopharynx have been around 60–90%, with complete response rates of 20–40% (11,13–16,18–19) and from the subset of complete responders there appears to be a subgroup of potentially long-term survivors. The typical profile of a long-term survivor with metastatic disease would be: initial diagnosis before the age of 40 years (7,8), long disease-free survival after initial radiotherapy prior to relapse, metastatic disease limited to the lung (with or without mediastinal lymph node involvement), without local recurrence, and complete response to aggressive multimodal therapy (8), the chemotherapy regimen being platinum based (8,11,18) and ifosfamide perhaps playing a potentially significant role.

Another unusual feature noted in our patient was the fact that metastatic disease remained stable and unchanged without any treatment for one year. Our patient underwent bronchoscopic biopsy at that time and the pathology was carcinoma, poorly differentiated type. Even after four previous chemotherapy combinations, the patient still attained near-complete remission with ifosfamide lasting 11 months. To date, there has been little information on single agent ifosfamide in NPC, although preliminary data have been reported (17). Nasopharyngeal carcinoma patients with mainly thoracic metastases may still enjoy prolonged disease-free control if the tumor is chemosensitive.

References


Figure 4. Fibrotic change over both lungs after 8 courses of ifosfamide.