Acta Oncologica Vol. 35, No. 1, pp. 101–105, 1996

Case Reports

Case reports are accepted under this heading. These reports should be short and concise and contain a minimum of figures, tables and references.

HYPERTROPHIC PULMONARY OSTEOARTHROPATHY: IS THERE A ROLE FOR RADIOTHERAPY TO SYMPTOMATIC SITES? CASE REPORT AND LITERATURE REVIEW

Hypertrophic osteoarthropathy is a syndrome featuring clubbing of digits, chronic proliferative periostitis with subperiosteal new bone formation and arthritis of adjacent joints. There may be associated autonomic dysfunction (e.g. flushing, blanching, sweating) (1). It is classified as primary (idiopathic/hereditary) or secondary (to various thoracic, cardiovascular and gastrointestinal diseases). However, more than 90% of secondary cases are associated with intra-thoracic pathology (neoplasm, chronic sepsis) and so the syndrome is often called hypertrophic pulmonary osteoarthropathy (HPOA). In particular, approximately 10% of cases of pulmonary malignancy have some or all of the features (2). We report such a case where skeletal pain proved very resistant to medical measures and where palliative radiotherapy (RT) to the worst affected site was tried.

Case report. A 47-year-old smoker presented with clubbing and 5 weeks of headache and visual disturbance, head scan showing an enhancing right occipital lobe lesion. Subsequent chest x-ray, scan of the thorax and bronchoscopy confirmed a right upper lobe primary, biopsy-consistent with large cell undifferentiated carcinoma. He proceeded to craniotomy and excision of the brain lesion in January 1994, followed by whole-brain irradiation (36 Gy in 12 fractions over $2\frac{1}{2}$ weeks) in February 1994. Although asymptomatic and resectable at presentation, the lung primary rapidly progressed, and by the time of repeat scanning in March 1994, he had developed extensive mediastinal lymphadenopathy together with cough, dyspnoea and haemoptysis. This was managed by palliative chest irradiation (17 Gy in 2 fractions a week apart). By then, he was also complaining of severe pain in the legs, bone scan and plain x-rays consistent with HPOA involving the tibiae, femora, wrists and hands (Figs 1 and 2). The pain was poorly controlled despite aspirin, dexamethasone and later parenteral midazolam and morphine (to a dose of 180–360 mg per 24 h). It was associated with exquisite tenderness over the anterior legs and significantly impaired his mobility. Eventually, it was decided to try radiotherapy to the worse affected left leg, a single 8 Gy fraction mid-plane dose to the whole length of the tibia using opposed anterior and posterior fields. He rapidly deteriorated and was still complaining of pain in the left leg until the time of death $3\frac{1}{2}$ weeks later.

Discussion. The aetiology and pathogenesis of HPOA is unknown, but is presumed to be mediated by neuro-humoral factors elaborated by the underlying disease process (3). Cure of the primary tumour is the most effective treatment (2), but there have been reports of symptomatic relief by surgical procedures other than resection including vagotomy, hypophysectomy, sectioning of intercostal nerves, exploratory thoracotomy and division of the pulmonary artery without pneumonectomy (4). Medical measures including analgesics, steroidal and non-steroidal anti-inflammatory agents (5, 6), and chemotherapy (7–9) may also be effective.

The role of RT for HPOA is not clearly defined in literature, but case reports suggest doses as small as 20–25 Gy in two weeks to the primary tumour can produce improvement in joint pain (Table), typically within 2–4 weeks (4, 11). However, we could find no reports of RT delivered directly to bones/joints affected by HPOA. This is perhaps surprising in view of the fact that RT has been used extensively in the past for numerous other "inflammatory" musculo-skeletal conditions (e.g. ankylosing spondylitis, bursitis, synovitis, tendonitis, plantar fibromatosis etc) (14). The mechanism by which RT relieves pain in this setting, and indeed even in uncomplicated metastatic bone pain remains speculative, but is presumably due to inhibition of pain mediators (e.g.

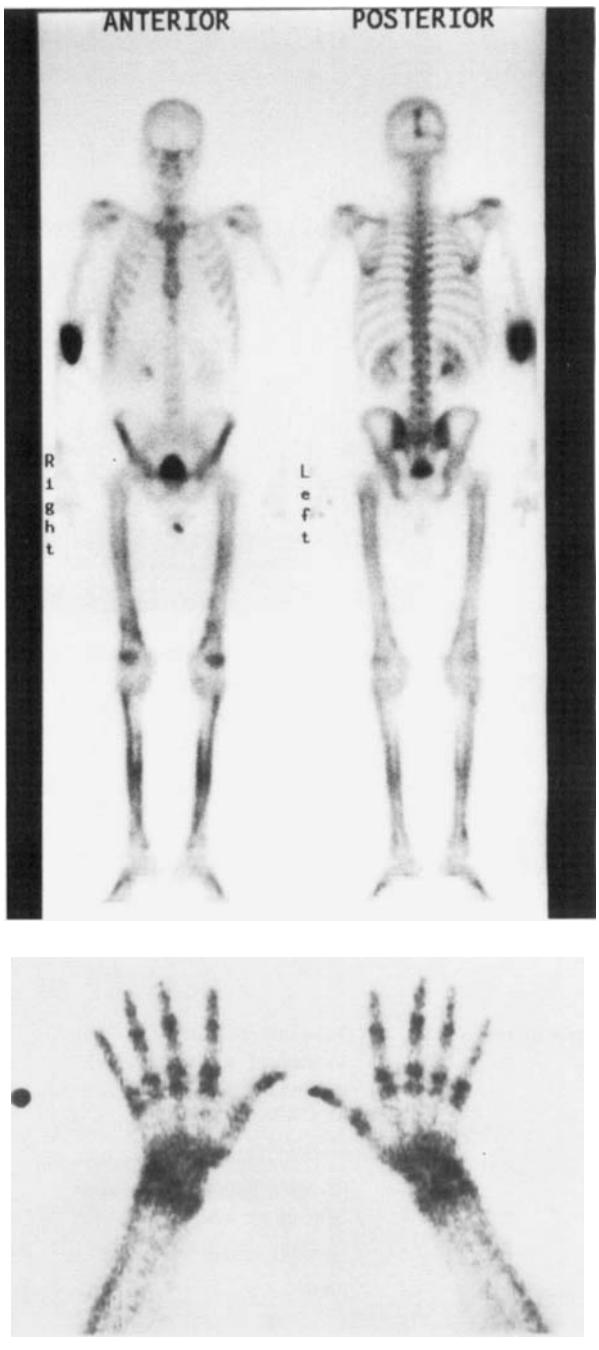

Fig. 1. Technetium bone scan showing characteristic involvement of a) tibiae, femora, and b) wrists and hands by hypertrophic pulmonary osteoarthropathy.

 ISSN 0284-186X

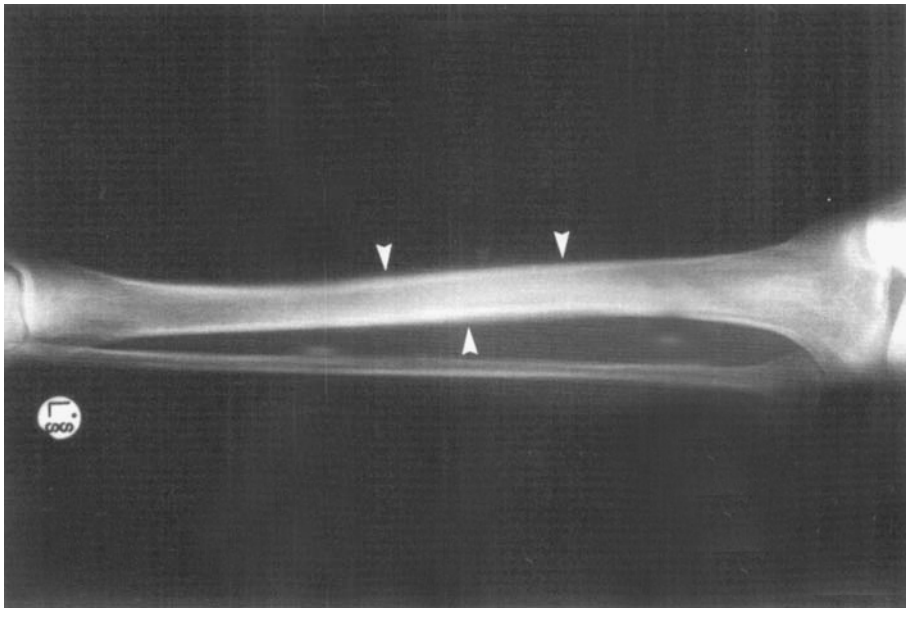

Fig. 2. Plain x-ray of symptomatic left leg demonstrating subperiosteal new bone formation along shaft of tibia (arrow heads), typical of hypertrophic pulmonary osteoarthropathy.

Table

Published results on radiotherapy to the primary tumour for hypertrophic pulmonary osteoarthropathy

Author	Primary tumour	Treatment	Outcome
Semple[10] (1955)	Lung—4 cases	Dose and fractionation not specified	Relief of joint symptoms: · complete (one patient) · partial (one patient) · nil (one patient) · not stated (one patient)
Papavasiliou[11] (1963)	Nasopharynx with subsequent intrathoracic (presumed) metastases on CXR-3 cases:	(1) 40 Gy*	(1) Complete relief of pain and swelling, improvement in XR abnormalities
	(1) left hilum		
	(2) right hilum/mediastinum, right upper lobe nodule	(2) 40 Gy in 4 weeks	(2) Complete resolution of pain, swelling and XR abnormalities
	(3) right hilum, right effusion	(3) 30 Gy*	(3) Resolution of XR changes
Steinfeld[4] (1974)	Lung	20 Gy in 2 weeks (pre-operative)	Considerable improvement in pain, resolution of clubbing prior to surgery
	Lung	25 Gy in 2 weeks	Marked improvement in pain
	Cervix	40 Gy in 4 weeks plus radium implant	Complete resolution of pain and clubbing, partial resolution of periosteal elevation
Rao[12] (1979)	Lung, metastasis in radius	55 Gy in 15 fractions over 3 weeks to the *radius* (lung primary not treated)	Relief in pain of HPOA, dramatic reduction in bone scan abnormalities
Carpeau[13] (1989)	Lung	3000R*	Complete clearance of pain and bone scan abnormalities despite progression of the primary

* fractionation not stated

prostaglandins, neurogenic peptides) (15). However, scientific evidence is lacking. The recent literature on *uncomplicated* bone pain suggests that a single 8 Gy fraction is as effective as fractionated treatment (15), 70–80% of patients obtaining pain relief within four weeks (16). In the present case of HPOA, a single 8 Gy fraction clearly failed to achieve analgesia in the effected leg within the remaining $3\frac{1}{2}$ weeks of the patient's life. This was despite clinical improvement in his chest symptoms following palliative lung irradiation, suggesting some response in the primary (although corroborative follow-up chest x-ray was not obtained in view of his rapid general decline). Interestingly, it has been observed that resolution of HPOA symptoms and bone scan abnormalities can occur both with chest RT and with systemic chemotherapy even in the absence of lung tumour response (9, 13). There has even been a report of similar improvement in HPOA systemically after irradiation of a concomitant solitary bone metastasis (in the radius) during which time there was progression of the untreated lung primary! (12). It is impossible to know whether the use of a higher radiation dose in the present case would have made any difference.

HPOA remains an enigmatic disease. Whilst RT to the lung can be effective in palliating the musculoskeletal symptoms, its role locally to affected sites is unproven.

ACKNOWLEDGEMENTS

Thanks to Dr Michael Ashby, radiation oncologist and former Director of Palliative Care, Royal Adelaide Hospital, for helpful discussions regarding the management of this patient and to Mrs Sandy Fitton for typing the manuscript.

DANIEL E. ROOS

Department of Radiation Oncology
Royal Adelaide Hospital
North Tce
Adelaide
South Australia

September 1995

Correspondence: Dr. Daniel E. Roos, Department of Radiation Oncology, Royal Adelaide Hospital, North Tce, Adelaide, South Australia 5000

REFERENCES

1. Hansen-Flaschen J, Nordberg J. Clubbing and hypertrophic osteoarthropathy. In: Braman SS, ed. Clinics in chest medicine: Pulmonary signs and symptoms. Philadelphia: WB Saunders Company, 1987: 287–98.
2. Charan NB, Carvalho P. Cardinal signs and symptoms in respiratory disease. In: Pierson DJ, Kacmarek RM, eds. Foundations of respiratory care. New York: Churchill Livingstone, 1992: 663–78.
3. Bunn PA, Ridgway EC. Paraneoplastic syndromes. In: DeVita VT, Hellman S, Rosenberg SA, eds. Cancer: Principles and practice of oncology. Philadelphia: J.B. Lippincott, 1993: 2026–71.
4. Steinfeld AD, Munzenrider JE. The response of hypertrophic pulmonary osteoarthropathy to radiotherapy. Radiology 1974; 113: 709–11.
5. Schumacher HR. Articular manifestations of hypertrophic pulmonary osteoarthropathy in bronchogenic carcinoma. Arthritis Rheum 1976; 19: 629–36.
6. Blackwell N, Bangham L, Hughes M, Melzack D, Trotman I. Treatment of resistant pain in hypertrophic pulmonary arthropathy with ketorolac. Thorax 1993; 48: 401.
7. Uchivama G, Ishizuka M, Sugiura N. Hypertrophic pulmonary osteoarthropathy inactivated by antitumour chemotherapy. Radiat Med 1985; 3: 25–8.
8. Davies RA, Darby M, Richards MA. Hypertrophic pulmonary osteoarthropathy in pulmonary metastatic disease. A case report and review of the literature. Clin Radiol 1991; 43: 268–71.
9. Dalgleish AG. Hypertrophic pulmonary osteoarthropathy: response to chemotherapy without documented tumour response. Aust NZ J Med 1983; 13: 513–6.
10. Semple T, McCluskie RA. Generalised hypertrophic osteoarthropathy in association with bronchial carcinoma. Br Med J 1955; 1: 754–9.
11. Papavasiliou CG. Pulmonary metastases from cancer of the nasopharynx associated with hypertrophic osteoarthropathy. Br J Radiol 1963; 36: 680–4.
12. Rao GM, Guruprakash GH, Poulose KP, Bhaskar G. Improvement in hypertrophic pulmonary osteoarthropathy after radiotherapy to metastasis. AJR 1979; 133: 944–6.
13. Campeau RJ, Rosales DR, Garcia OM, Correa OA. Resolution of hypertrophic pulmonary osteoarthropathy after radiotherapy in the absence of lung tumour response. Clin Nucl Med 1989; 14: 453–5.
14. Order SE, Donaldson SS. Radiation therapy of benign diseases. Berlin: Springer-Verlag, 1990.
15. Bates T. A review of local radiotherapy in the treatment of bone metastases and cord compression. Int J Radiation Oncol Biol Phys 1992; 23: 217–21.
16. Needham PR, Hoskin PJ. Radiotherapy for painful bone metastases. Palliative Medicine 1994; 8: 95–104.

BILATERAL OCCIPITAL LOBE INFARCTION PROBABLY DUE TO DISSEMINATED ZYGOMYCOSIS IN A PATIENT WITH LYMPHOMA

Zygomycosis is a rare life-threatening infection caused by a fungus of the Mucorales order (1, 2). These fungi destroy the elastic tissue of the vessel wall and proliferate in the lumen, inducing thrombosis, hemorrhage, infarction and necrosis. The infection may also metastasize to distant sites (3). Six clinical forms are recognized: rhinocerebral, pulmonary, cutaneous, gastrointestinal, cerebral and disseminated (4). The lungs are usually the initial site of the disseminated form (5), which is more frequent in patients with severe chemotherapy-related neutropenia (6–11), although it can also occur in treatments with steroids or deferoxamine (12).

We describe a patient with Burkitt's lymphoma who developed a bilateral occipital infarction in the course of disseminated zygomycosis.

Case report. A 33-year-old man was admitted to our hospital in July 1993 for evaluation of a 2-month history of upper abdominal pain. A week before admission a palpable mesogastric mass was observed. Fever (up to 30°C), weight loss (8 kg) and night sweats were additional symptoms. On physical examination the right palatine tonsil was hypertrophic; no peripheral lymph nodes were detected. The lungs and heart were normal but the abdomen was slightly distended, a bulky (12 cm main diameter) mesogastric mass was painful, the liver and spleen could not be felt. Genital, rectal and neurologic examinations were negative. The laboratory findings were: WBC count 8.3×10^9/l with a normal differential, Hb 12.3 g/l, platelets 360×10^9/l, ESR 117 mm, uric acid