Extrapulmonary small cell carcinoma of bone

Vinod Raina¹, Robert Milroy², Abdul Al-Dawoud³, David Dunlop¹ and Michael Soukop¹

Departments of ¹Medical Oncology, ²Respiratory Medicine and ³Pathology, Royal Infirmary, Glasgow G4 0SF, UK

Summary: Small cell carcinoma has been reported to arise in many extrathoracic sites. However, such tumours arising from bone have not been previously described. We report what we believe is the first reported case of extrapulmonary small cell carcinoma of bone. The tumour arose from the fifth dorsal vertebra in a 60 year old woman. The patient was treated with local radiotherapy and combination chemotherapy and remains in remission, 18 months after diagnosis. As such extrathoracic small cell tumours are rare, there seem to be no clear-cut guidelines for treating them, but combination chemotherapy is recommended.

Introduction

Extrapulmonary small cell carcinomas are described as tumours having the histological appearance of small cell carcinoma but with no evidence of thoracic malignancy (i.e. a normal chest X-ray, computerized tomographic (CT) scan of thorax and a negative bronchoscopy).¹ Such tumours have been described arising from a large number of organs but, as far as we are aware, there have been no reports of tumours arising from bone.^{1,2}

Case report

A 60 year old female with a long history of heavy smoking presented with a 4 week history of back pain. Routine examination and routine biochemical and haematological investigations were normal. X-rays of spine revealed a lytic lesion in D5 with wedging of the vertebra. Skeletal survey revealed no other lesions. Bone scan confirmed the lesion to be solitary. Needle biopsy of the lesion revealed an undifferentiated small cell carcinoma (Figure 1). The diagnosis was confirmed by positive staining with the epithelial marker CAM 5.2 and negative staining with common leucocyte antigen. X-ray of chest, CT scan of thorax, bronchoscopy with cytological examination of bronchial aspirate, and ultrasound of liver, were all normal. By definition, therefore, the patient fulfilled the criteria for diagnosis of extrapulmonary small cell carcinoma of bone.

The patient was treated with local irradiation (2,000 cGy in five fractions over 7 days) and then given a 4 cycle course of chemotherapy, comprising cyclophosphamide 1,000 mg/m² and doxorubicin 40 mg/m² intravenously day 1, VP16 100 mg/m² intravenously days 1 and 2, VP16 200 mg/m² orally day 3, methotrexate 50 mg/m² and vincristine 2 mg intravenously day 10, repeated at 21 day intervals. There was complete symptomatic improvement and the patient has remained disease-free since July 1989. Most recent X-ray of spine shows only wedging of D4 with no evidence of active tumour, and chest X-ray remains normal.

Discussion

Extrapulmonary small cell carcinoma is a rare condition. To date, small cell carcinoma has been reported arising from the paranasal sinuses, salivary glands, hypopharynx and larynx, trachea, thymus, oesophagus, small intestine, colon, rectum, pancreas, kidney, urinary bladder, prostate, cervix, uterus, breast, skin and common bile duct.^{1,2} To our knowledge, such a tumour arising in bone has not been previously reported.

The histogenesis of small cell carcinoma remains a subject of controversy. Small cell carcinomas are included within the amine precursor uptake and decarboxylation (APUD) system of Pearse.³ This model postulates a common ancestral cell derived from the neural crest, which then migrates to various epithelial tissues and sites within the body.⁴ The APUD system hypothesis explains the diversity of sites in which small cell carcinomas have been reported. On the other hand, the association

Figure 1 Fine needle aspirate of lytic bone metastasis. The characteristic features of small cell carcinoma, with densely staining nuclei and scanty cytoplasm are clearly seen.

of small cell carcinoma both in the lung and in extrapulmonary sites with carcinoma *in situ*, squamous carcinoma, mucin-producing adenocarcin-

oma and carcinoid tumours has prompted some authors to propose a totipotent stem cell origin for these tumours which has the ability to differentiate into both an epithelial and neuroendocrine lytic cell or small cell.^{5,6}

Remick *et al.* have suggested that the natural history of extrapulmonary small cell cancer in many cases resembles small cell cancer of the lung, and have suggested that similar staging procedures are appropriate.¹ Although our patient had limited disease, radiotherapy was supplemented by chemotherapy with the aim of cure. Good palliation and long-term remission can be achieved in a number of cases of extrapulmonary small cell cancer using this approach.^{7,8} However, until sufficient cases are documented and the natural history of such tumours is determined, treatment will continue to be empirical and individually based.⁹ Thus, although specific therapeutic approaches to extrapulmonary small cell carcinomas have not been defined, systemic combination chemotherapy is recommended.⁹

References

1. Remick, S.C., Hafez, G.R. & Carbone, P.P. Extrapulmonary small cell carcinoma. *Medicine (Baltimore)* 1987, **66**: 457–471.
2. Sabanathan, S., Hashmi, H., Nicholson, G. & Edwards, A.S. Primary oat cell carcinoma of the common bile duct. *J R Coll Surg Edinb* 1988, **33**: 285–286.
3. Pearse, A.G.E. & Takor, T.T. Neuroendocrine embryology and the APUD concept. *Clin Endocrinol (Oxf)* 1976, **5**: 229–244.
4. Weichert, R.F. The neural ectodermal origin of the peptide secreting endocrine glands. *Am J Med* 1970, **49**: 232–241.
5. Briggs, J.C. & Ibrahim, N.B.N. Oat cell carcinoma of oesophagus: a clinicopathological study of 23 cases. *Histopathology* 1983, **7**: 261–277.
6. Hernandez, F.J. & Reid, J.D. Mixed carcinoid and mucus secreting intestinal tumours. *Arch Pathol* 1969, **88**: 489–496.
7. Koss, L.G., Spiro, R.H. & Hajdu, S. Small cell (oat cell) carcinoma of the minor salivary gland origin. *Cancer* 1972, **30**: 737–741.
8. Silva, E.G., Butler, J.J., Mackay, B. & Goepfert, H. Neuroblastoma and neuroendocrine carcinomas of the nasal cavity. A proposed new classification. *Cancer* 1982, **50**: 2388–2405.
9. Remick, S.C. & Carbone, P.P. Extrapulmonary small cell cancer. In: Brain, M.C. & Carbone, P.P. (eds) *Current Therapy Haematology-Oncology 1987–1988*. B.C. Decker, Inc. and C.V. Mosby, Co., Toronto, in press.