Letters

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Spontaneous Growth Arrest of Lung Metastases of Osteosarcoma With a 28-Year Follow-up

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IN THE era before effective chemotherapy became available, most patients with osteosarcoma died of lung metastases, resulting in 5-year survival rates of approximately 20%. The only effective local procedure was amputation or exarticulation. Irradiation was considered ineffective for permanent local control. In the Netherlands, the principle of Cade [1] was adopted: after irradiation of the primary tumour to a dose of 6000–7000 rads, a waiting period of 4–6 months followed. If during this period lung metastases could not be demonstrated, the mutilation was considered worth the risk and ablative surgery was performed.

In February 1964, a 19-year-old female presented with an osteosarcoma of her left femur. According to Cade's principle, 6800 rads were applied with a telecobalt apparatus, using two opposing fields of 10 × 14 cm, with a daily dose of 200 rads. Shortly after completion of the irradiation, a chest radiograph showed multiple metastases in both lungs. She was treated with prednisone, 15 mg/day, until July 1964, when she proved to be pregnant. In February 1965, the patient gave birth to a healthy daughter. During pregnancy, the lung metastases had not increased in size or number. In April 1965, a lung biopsy was performed, which definitively confirmed the diagnosis of osteosarcoma secondaries. A watch-and-wait policy was instituted. In October 1991, the patient visited the hospital again, with some pain in her left knee. Her general condition was excellent. She had no pulmonary complaints. The function of the left leg was fairly good, with a flexion possibility of 90 degrees in the knee joint, and an almost normal walking pattern. There was some atrophy and fibrosis around the knee, and some lymph oedema of the lower leg. The radiographs of the femur and lungs showed no differences compared to those taken in 1965. In February 1993, this situation was unchanged. Revision of all slides from 1964 and 1965 by the Netherlands Committee on Bone Tumours reconfirmed the diagnosis: osteosarcoma with lung metastases. There are two remarkable and unexpected events in the course of the disease of our patient. Firstly, histologically confirmed lung metastases stopped growing 'spontaneously'; in 28 years their appearance and number did not change. In the time elapsed between the discovery of the metastases and the growth arrest, the patient used prednisone, 15 mg daily for 4 months, and subsequently experienced a pregnancy. It seems highly speculative to suppose that either of these two conditions was able to cause the growth arrest. Spontaneous maturation through differentiation of the neoplastic osteoblastic tissue is another possibility. The fact that oestrogen can act directly on clonal osteoblast-like osteosarcoma cells by a receptor-mediated mechanism, and thereby modulate the extracellular matrix and other proteins involved in the maintenance of skeletal mineralisation and remodelling [4], may provide a clue. Secondly, the radiotherapy produced definitive local control, without serious long-term side-effects. In the O2 and O3 trials of the EORTC [2,3], occasional permanent local control has been reported.

Our patient was not subjected to an amputation because of the appearance of lung metastases, according to Cade's principle. Until today she is happy with the miracle that followed.

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1. Cade S. Osteogenic sarcoma: a study based on 133 patients. *J R Coll Surg Edinburgh* 1955, **1**, 79–111.
2. Breur K, Cohen P, Schweisguth O, Hart AMM. Irradiation of the lungs as an adjuvant therapy in the treatment of osteosarcoma of the limbs. An E.O.R.T.C. randomised study. *Eur J Cancer* 1978, **14**, 461–471.
3. Burgers JMV, Glabbeke M van, Busson A, *et al.* Osteosarcoma of the limbs. Report of the EORTC-SIOP O3 trial 20781 investigating the value of adjuvant treatment with chemotherapy and/or prophylactic lung irradiation. *Cancer* 1988, **61**, 1024–1031.
4. Komm BS, Terpening CM, Benz DJ, *et al.* Estrogen binding, receptor mRNA, and biologic response in osteoblast-like osteosarcoma cells. *Science* 1988, **241**, 81–84.