Metachronous sarcomas in a patient with bilateral retinoblastomas

A case report

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Summary

This is the first reported case of two metachronous sarcomas developing in a patient after treatment of bilateral retinoblastomas. The histogenesis of the tumours is not clear.

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There are few published case reports of multiple malignant tumours in children.[1] When more than one tumour type occurs in an individual it may reflect an inherent predisposition to neoplasia or, alternatively, it may be related to therapy.

When radiation therapy and/or chemotherapy are administered for the palliation of malignant disease, death usually occurs before the late complications of these therapeutic modalities become manifest. In children, however, therapy may be curative and hence treatment-related neoplasia may occur. Patients who have received radiotherapy for retinoblastoma have been known to develop rhabdomyosarcomas,[2,3] osteogenic sarcomas,[4] malignant mesenchymoma,[5] malignant epithelial tumours,[6] fibrosarcomas,[7] involving the orbit and/or adjacent structures, and leukaemia[8] 4 - 20 years after the initial therapy.

A child with bilateral retinoblastomas, who subsequently developed an embryonal rhabdomyosarcoma and an osteogenic sarcoma, is described.

Case report

A 14-year-old black girl first presented to hospital in 1972 at the age of 11 months with bilateral retinoblastomas. She was an only child and there was no family history of this condition. She underwent enucleation of the right eye and received 4 500 cGy of cobalt-60 to the right orbit and left eye.

Histological examination of the right eye confirmed the presence of a small round-cell tumour (Fig. 1). There was scleral and optic nerve invasion. Flexner-Wintersteiner rosette formation, mitotic activity, and extensive tumour necrosis were seen. Rhabdomyoblastic differentiation was not noted and the diagnosis of retinoblastoma was made.

In June 1980, at the age of 8 years, the child presented to hospital with a large soft-tissue swelling below the right orbit. A biopsy specimen was removed from this swelling, which was later excised. The orbit was irradiated. Sections of the tissue removed showed histological features of malignant sarcoma. A distinct lobular pattern, formed by dense fibrous tissue bands dividing the tumour into small nodules, was noted. The tumour was composed of spindle-shaped cells lying in a myxoid stroma (Fig. 2). These cells had eccentric nuclei and abundant eosinophilic cytoplasm. Definite strap cells or cross-striations were not noted. Pleomorphism was a prominent feature and mitotic figures were numerous. Immunohistochemistry showed positive cytoplasmic staining for myoglobin and desmin and the diagnosis of rhabdomyosarcoma was made.

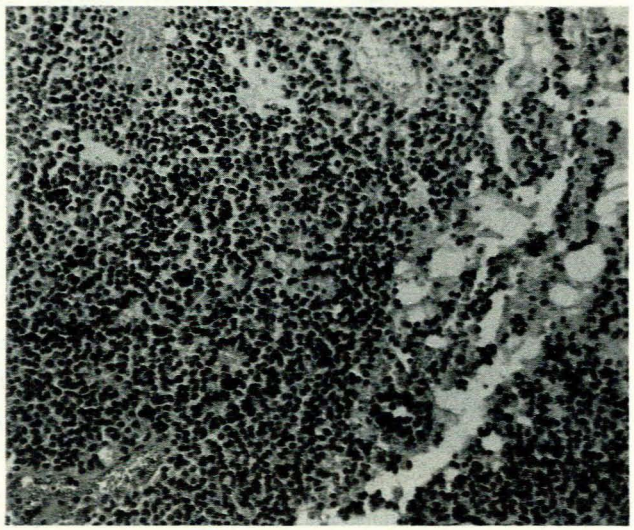

Fig. 1. Retinoblastoma of the right eye with well-formed rosettes (H and E x 200).

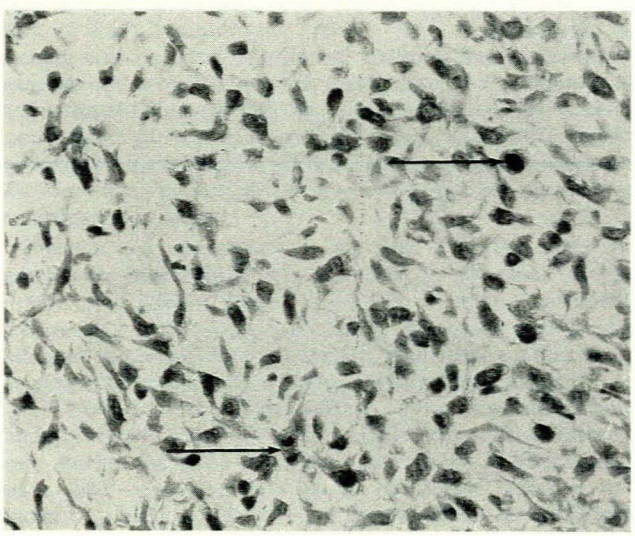

Fig. 2. Tumour showing rhabdomyoblasts lying in a myxoid stroma. Numerous mitotic figures are present (arrow) **(H and E x 400).**

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The child was asymptomatic until her re-admission to hospital in August 1986 complaining of a painful swelling over the right maxilla. Radiography showed bony erosion by a tumour containing abundant calcium. The lesion was biopsied and showed features of osteogenic sarcoma. Cellular pleomorphism was marked, numerous tumour giant cells were present, mitotic figures were abundant and extensive extracellular osteoid was seen (Fig. 3).

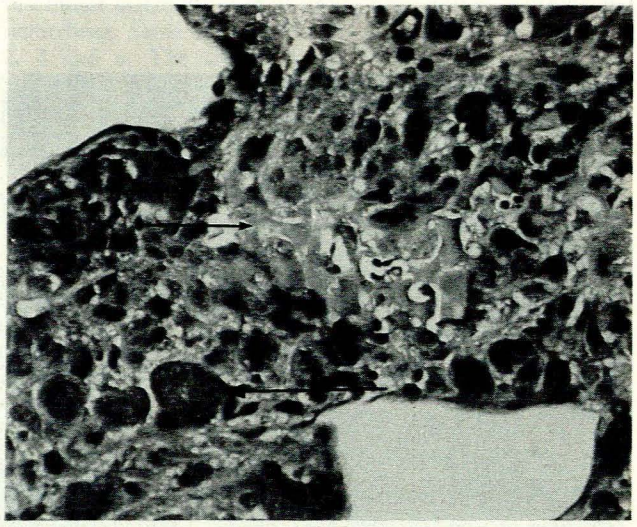

Fig. 3. Osteogenic sarcoma showing abundant extracellular osteoid (short arrow). **Numerous multinuclear osteoclastic giant cells are present** (long arrow) **(H and E x 400).**

Discussion

This is the first reported case of two malignant sarcomas developing in a patient after the treatment of bilateral retinoblastomas. In previous studies[1,9] all patients developing sarcoma after therapy for retinoblastoma were dead within 12 months of diagnosis. The patient under discussion has survived and remains well 6 years after the diagnosis of rhabdomyosarcoma and 13 years after the initial diagnosis of retinoblastoma. The metachronous tumours are therefore behaving in an unusually indolent manner.

Irradiation-induced orbital rhabdomyosarcomas and orbital osteogenic sarcomas have been well described.[10] Furthermore, patients with bilateral retinoblastomas often demonstrate 13q deletion and, according to the two-hit theory proposed by Knudson,[11] are predisposed to the development of malignant tumours, including rhabdomyosarcoma and osteogenic sarcoma outside the field of irradiation. The patient described here had a normal chromosome complement at a cytogenetic level.

Rhabdomyoblastic differentiation may be found in many neuro-ectodermal neoplasms, particularly malignant schwannomas, ganglioneuromas and medulloblastomas.[12] These tumours are referred to as malignant triton tumours. It is possible that the later development of a rhabdomyosarcoma may, in fact, represent mesenchymal differentiation in a recurrence.

The case described poses a question about the exact histogenesis of these three tumours. Is this an illustration of therapy-induced dual neoplasia or is this a single tumour exhibiting different phenotypic properties or are these multiple tumours arising in a patient genetically predisposed to neoplasia?

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