Orbital involvement with desmoplastic melanoma*

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SUMMARY A 79-year-old woman developed an orbital mass five and a half years after excision of a cutaneous melanoma from the side of the nose. The initial orbital biopsy was interpreted histopathologically as a malignant fibrous histiocytoma, but special stains and electron microscopy showed it to be a desmoplastic malignant melanoma which had apparently spread to the orbit from the prior skin lesion by neurotropic mechanisms. The occurrence of a desmoplastic neurotropic melanoma in the orbit has not been previously recognised. The problems in the clinical and pathological diagnosis of this rare type of melanoma are discussed.

Orbital involvement with malignant melanoma most often occurs secondary to extrascleral extension of posterior uveal melanoma.¹ Primary orbital melanoma and metastatic cutaneous melanoma to the orbit are extremely rare.² Desmoplastic melanoma is a rare form of cutaneous melanoma which can extend from a superficial location into the deep reticular dermis by neurotropic mechanisms.^{3,4} We report a unique case of desmoplastic melanoma in which such a tumour extended from the nasal skin into the deep orbit, clinically simulating a primary orbital tumour.

Case report

A 79-year-old white woman was referred to the Oncology Service at Wills Eye Hospital in April 1985 because of a two-month history of proptosis, blepharoptosis, and blurred vision in the left eye. The patient gave a history of having had a 'basal cell carcinoma' removed from the left side of her nose in December 1979, followed by a repeat biopsy and a definitive wide surgical excision. She was subsequently involved in an automobile accident and suffered fractures of the left orbital floor and zygoma. In

August 1984 she had excision of scar tissue around the left eye and biopsy of a 'cyst' in the left upper eyelid, which was diagnosed at another hospital as a malignant fibrous histiocytoma.

A general physical examination gave essentially normal results, and complete examination of the right eye revealed no abnormalities. Examination of the left eye disclosed diffuse thickening of the periorcular skin and upper eyelid with 2 mm of proptosis and 4 mm of blepharoptosis (Fig. 1). There was mild

Fig. 1 Facial photograph of patient showing proptosis and blepharoptosis on the left side.

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Fig. 2A

Fig. 2 Computed tomography showing irregular but fairly well circumscribed left orbital mass (arrow) A: Axial view. B: Coronal view.

scarring on the left side of the nose where the 'basal cell carcinoma' was previously excised.

Computed tomography (CT) of the orbits showed a large irregular mass filling most of the left orbit superonasally and posteriorly (Figs. 2A, B). It appeared to extend to the orbital apex but showed no evidence of bone destruction.

In view of the patient's history and clinical findings the initial differential diagnosis included orbital recurrence of basal cell carcinoma, orbital recurrence of malignant fibrous histiocytoma, or possible granulomatous inflammation related to prior trauma. The

Fig. 2B

histopathological sections of the prior skin biopsies were requested.

It was elected to perform a biopsy of the orbital mass to determine which of the three diagnostic possibilities was correct. Therefore an incisional biopsy of the mass was performed by way of a superonasal brow incision and extraperiosteal approach. A wedge biopsy was taken from the anterior portion of a firm white orbital mass, and no attempt was made to excise it completely. Tissue submitted for routine frozen sections during surgery showed malignant spindle cells with considerable extracellular material. On frozen sections the specimen was interpreted as a malignant spindle cell tumour, most likely a malignant fibrous histiocytoma.

The permanent sections disclosed interlacing bundles of spindle cells with pleomorphic hyperchromatic nuclei, sometimes arranged in a storiform (closely packed in cartwheel) pattern, sometimes with a foamy-appearing cytoplasm (see discussion of pathology, below). The preliminary diagnosis was recurrent malignant fibrous histiocytoma of the left orbit. On the day after surgery a copy of the pathology report of the prior biopsy of the left eyebrow was received, and it also indicated a diagnosis of malignant fibrous histiocytoma.

On the following day we received word that the patient had been seen in consultation by the Pigmented Lesion Group at the University of Pennsylvania in December 1979. To our surprise the nasal skin lesion had been interpreted as lentigo maligna melanoma. Because the lesion had extended close to the surgical margins, a course of radiotherapy, giving 4920 rad over a 22-day period, had been administered. The revised diagnosis by the Pigmented Lesion Group was not indicated on our report from the other hospital, which still reflected the diagnosis of malignant fibrous histiocytoma.

In view of this new information the biopsy of the left upper eyelid and the orbital biopsy were reassessed. Both biopsies were finally diagnosed as a desmoplastic neurotropic melanoma (see following discussion on pathology). The patient was readmitted to the hospital and underwent an orbital exenteration with removal of the medial canthal area and upper eyelid. She is alive and well 14 months after our initial examination.

PATHOLOGY

A review of the initial shave biopsy of the original lesion from the left side of the nose demonstrated increased numbers of atypical melanocytes in the basal layers of the epidermis with evident desmoplasia in the dermis (Fig. 3). The areas of desmoplasia contained scattered atypical spindle shaped

Fig. 3 Photomicrograph of the original cutaneous lesion from the nose showing atypical melanocytes at the basal layer of the epidermis, consistent with the radial growth phase of lentigo maligna melanoma. Note the actinic elastosis in the superficial dermis. Haematoxylin-eosin.

melanocytes which exhibited perineural and endoneurial involvement in the subcutaneous connective tissues (Figs. 4 and 5). The diagnosis was lentigo maligna melanoma with a neurotropic desmoplastic reaction.

The orbital biopsy and the subsequent orbital exenteration specimen showed the tumour to be composed of fascicles and cords of atypical spindle cells with a marked desmoplastic reaction identical to that seen in the cutaneous tumour (Fig. 6A). In some areas the cells resembled fibroblasts, with rather uniform nuclei, while in other areas the nuclei showed considerable pleomorphism with a vesicular appearance and prominent nucleoli (Fig. 6B). Particularly near the margins of the specimen there was perineural and sometimes intraneural invasion by the spindle tumour cells. Fontana stains for

Fig. 5 More detail of dermal nerve from primary tumour, showing permeation of endoneurium and perineurium by cytologically atypical spindle cells (neurotropism) (arrows). Haematoxylin-eosin.

melanin were negative. The S-100 protein stain was positive in many of the tumour cells (Fig. 7).

The orbital lesion was processed for routine electron microscopy. The tumour was composed of spindle shaped fibroblast-like cells with abundant rough endoplasmic reticulum. Although some of the cells were void of melanosomes, a number of them contained spheroidal granular melanosomes, typical of poorly differentiated melanosomes seen in many melanomas (Fig. 8).

The final diagnosis was orbital metastasis of desmoplastic neurotropic melanoma arising from cutaneous lentigo maligna melanoma.

Discussion

Desmoplastic malignant melanoma is a rare variant of cutaneous spindle cell melanoma which was first

Fig. 4 Photomicrograph of subcutaneous tissues deep to skin lesion showing perineural invasion by atypical melanocytes and infiltration of subcutaneous fat by a spindle cell tumour with a fibrous stroma, characteristic of a desmoplastic and neurotropic melanoma. Haematoxylin-eosin.

Fig. 6A

Fig. 6 Photomicrograph of orbital mass showing haphazardly arranged malignant spindle cells with desmoplastic reaction. Haematoxylin-eosin. A: $\times 20$. B: $\times 125$.

described by Conley and associates in 1971.³⁴ In addition to their seven original cases about 25 other cases have been reported.⁵⁻¹⁷ Most reported cases have been in the head and neck region, with one case involving the eyelid.¹² The case reported here is apparently the first to have deep orbital involvement and to produce ipsilateral proptosis.

The typical evolution of a desmoplastic melanoma is now relatively clear. Most reported cases have been preceded by a lentiginous or (less often) by a superficial spreading melanoma in the face or neck region. The skin lesions often appeared innocuous clinically and were not usually interpreted microscopically as being highly malignant, because the desmoplastic and neurotropic components in the

Fig. 6B

Fig. 7 S-100 protein stain showing positive cytoplasmic staining in tumour cells (arrows).

deep reticular dermis were overlooked on microscopic examination.

Approximately six months to two years after excision of the initial lesion the patient characteristically develops a slowly enlarging, firm, subcutaneous mass deep to the site of the primary lesion. Biopsy of the recurrent (or persistent) lesion demonstrates bundles of atypical spindle cells with varying degrees of malignancy and marked desmoplasia. Neurotropic of the tumour is often observed.^{14 16 17} Melanin pigment often cannot be demonstrated in the deeper lesion, even with special stains and electron microscopy, though it is usually evident in the initial cutaneous lesion even by routine light microscopy. A few desmoplastic melanomas have been completely amelanotic, though they show intra-dermal patterns otherwise characteristic of melanoma.

The recurrent deeper lesion is often misdiagnosed histopathologically as fibrosarcoma, fibromatosis, scar tissue, or (as in our case) fibrous histiocytoma.⁴ In our case the Fontana-Masson stain for melanin was negative, but the use of immunoperoxidase stains and electron microscopy were helpful in establishing the diagnosis. Stains for S-100 protein were positive (Fig. 7), suggesting a tumour of neural crest origin, and electron microscopy showed spheroidal granular melanosomes in the cytoplasm of the tumour cells. These features, combined with the history of a prior cutaneous melanoma, strongly supported the diagnosis of melanoma, in spite of the fact that the diagnosis was less evident with routine light microscopy.

The mechanism of orbital spread in our case can be deduced from the histopathology and from a review of the literature on desmoplastic melanomas. Both in the original skin lesion and in the orbital recurrence

Fig. 8 Electron photomicrograph of the orbital tumour showing spheroidal granular melanosomes within cytoplasm of tumour cell (arrow). $\times 10\,000$.

there was marked perineural and intraneural involvement by tumour cells. It is recognised that the rare case of melanoma which shows neurotropism has a tendency toward desmoplasia (stimulation of fibrosis).¹³ It is most likely that the neurotropic tendency of our patient's tumour was responsible for spread of the tumour cells along peripheral nerves into the orbit, where they proliferated as a solid mass. This would be consistent with other reported cases, where the deeper nodule seemed to occur from neural spread of the melanoma to a deeper location. Review of the earlier biopsies in such circumstances may reveal tumour within nerves at the margin of the specimen, as was found in our case.

The most important considerations in the differential diagnosis of an eyelid mass with secondary orbital involvement are basal cell carcinoma and sebaceous gland carcinoma. The majority of such cases are basal cell carcinomas which have been neglected or inadequately excised. Sebaceous gland carcinomas also have a marked tendency to invade the orbit, particu-

larly the fossa of the lacrimal gland, where they can simulate a primary lacrimal gland tumour.¹⁸ Malignant melanomas of the eyelid are rare and generally do not secondarily invade the orbit. However, certain cases of lentiginous or superficial spreading melanomas have a tendency to neurotropism. When located in the eyelid area such neurotropic melanomas can easily invade the orbit and simulate a primary orbital tumour, as occurred in our case. In such cases biopsy of the orbital mass may disclose an amelanotic spindle cell tumour which is not at first glance similar to the original skin lesion.

The desmoplastic variety of melanoma should be considered in the differential diagnosis of a spindle cell tumour of the orbit, especially if there has been a prior history of excision of a melanocytic tumour of the eyelid. In such cases a review of the original biopsy combined with the use of special stains and electron microscopy may be helpful in establishing the correct diagnosis.

ADDENDUM

While preparing the manuscript we believed that this was the only case on record of orbital spread of desmoplastic neurotropic melanoma. However, a similar case was also presented at the 1985 Eastern Ophthalmic Pathology Society by Dr Mourad Khalil.¹⁹

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