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CORRESPONDENCE

Post-chemotherapy maturation of a pineoblastoma

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Pineoblastoma is defined as a highly malignant embryonal tumour of the pineal gland [3]. As conveyed by the adjective embryonal, it is a small blue cell tumour resembling a PNET [2, 3]. It is found at one end of a morphological spectrum, at the other end of which lies the pineocytoma. In between, amidst poorly and better differentiated tumours, are parenchymal pineal tumours of intermediate differentiation, consisting of a variety of transitional types [2, 3]. Seldom are the latter composed of both poorly and well differentiated tissues. Tumours of intermediate differentiation and pineocytomas are rare in the first decade, while pineoblastomas occur in the first and second decades, though rarely in infants. We describe a case of infantile pineoblastoma showing diffuse neuronal maturation after treatment.

An 8-month-old male developed symptoms related to increased intracranial pressure. Neuroimaging revealed a pineal tumour with hydrocephalus, without craniospinal seeding (Fig. 1a–c). CSF cytology was negative. Third ventriculostomy was performed owing to the hydrocephalus; after a few days, several biopsies from distinct parts of the tumour were obtained. Histologically, the tumour was composed of small cells with round to oval nuclei and scant, slightly basophilic cytoplasms, embedded in a myxoid matrix (Fig. 2a, c). The nuclei varied moderately in size, with only slightly irregular contours and small eosinophilic nucleoli. A few Homer-Wright rosettes were seen. Neither calcifications nor necrosis were encountered. Mitotic index was 7/10 HPF; labelling index was 30% (Fig. 2g). Tumour cells expressed chromogranin A (Fig. 2e), synaptophysin, and focally NeuN. GFAP was negative. INI1 expression was retained. The patient underwent intensive induction chemotherapy, followed by high-dose chemotherapy with peripheral blood stem cell reinfusion. Neuroimaging demonstrated reduction of tumour volume (Fig. 1d–f). Thereafter, a two-step subtotal resection was performed. This time, the histology showed a hypocellular tumour composed of a mixture of small round cells with neurocytic appearance and larger, often bi-nucleated, ganglion cells (Fig. 2b–d). No mitoses were present; labelling index, 1% (Fig. 2h). The tumour cells expressed neurofilament protein (Fig. 2f), synaptophysin, and NeuN. Chromogranin A and GFAP were negative. Fractional conformal radiotherapy on the tumour bed concluded the treatment. The only sequela was mild converging strabismus with diplopia. Remission status was ongoing 9 months after the end of therapy.

In this case a difference between the first biopsies and those performed after therapy appears clearly. At first surgery, the lesion fulfilled the criteria of an embryonal small cell tumour with a neuronal phenotype consistent, on the basis of location, with a pineoblastoma. The latest biopsies disclosed a neuronal tumour composed of a mixture of ganglion and neurocytic cells (the final diagnosis was low-grade neuronal tumour).

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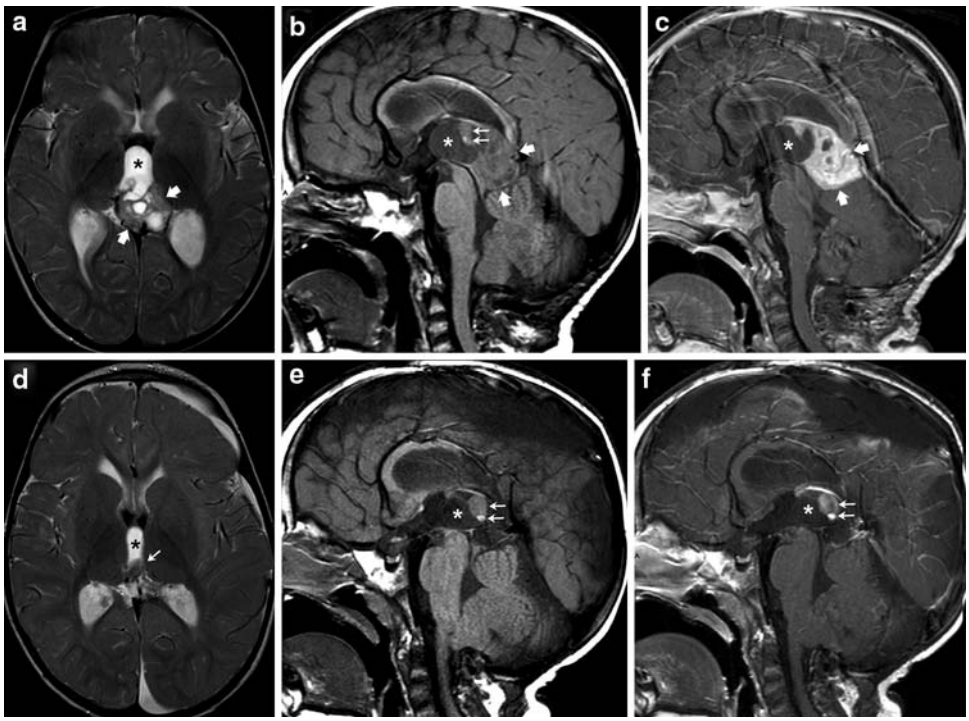

Fig. 1 Neuroradiology. **a–c** MRI at presentation: **a** axial T2-weighted image, **b** sagittal T1-weighted image, **c** contrast-enhanced sagittal T1-weighted image. A huge neoplasm involves the pineal region and posterior third ventricle. There are a large, anterior cystic component (*asterisks*, **a**, **c**) and a posterior solid component (*thick arrows*, **a**, **c**) containing multiple necrotic areas, visible as T2-hyperintense areas that do not enhance with contrast. Along the posterior aspect of the cyst there are a larger, T1-isointense, superior nodule and a smaller, T1-hyperintense, nodule (*thin double arrows*, **b**). **d–f** MRI after treatment: **d** axial T2-weighted image, **e** sagittal T1-weighted image, **f** contrast-enhanced sagittal T1-weighted image. Marked reduction of the cystic component (*asterisks*, **d**, **e**) and complete resolution of the large posterior solid component. The only solid remnant is the double nodular component along the posterior aspect of the cyst (*thin double arrows*, **e**, **f**)

It is unlikely that the tumour had started as a mixed pineoblastoma/pineocytoma. Firstly, infantile mixed tumours are extremely rare. Secondly, despite adequate sampling, there was neither a differentiated component in any of the first biopsies, nor any undifferentiated components in the following ones. Moreover, spontaneous maturation seems unlikely, since tumours with long survival show stable morphology [6].

Neuronal maturation is a biological phenomenon described in embryonal tumours, such as medulloblastoma and PNET, occurring spontaneously or induced by chemotherapy [1, 5].

Although neuronal differentiation may occur in pineoblastoma, such a complete maturation, arguably related to treatment, has never been described [4].

As a consequence of the maturation, the tumour cells became considerably larger: the mean nuclear density in the latest biopsies (276 per 200×, 1.2 mm^2) was significantly lesser than in the first ones (411 per 200×, 1.2 mm^2), while the tumour size reduced, likely owing to a roughly proportional decrease in the number of tumour cells. Therefore, neuroimaging in such cases, where cell enlargement contrasts the effect of cell number decrease, might not accurately assess response to therapy (in this case the response to treatment could have been underestimated).

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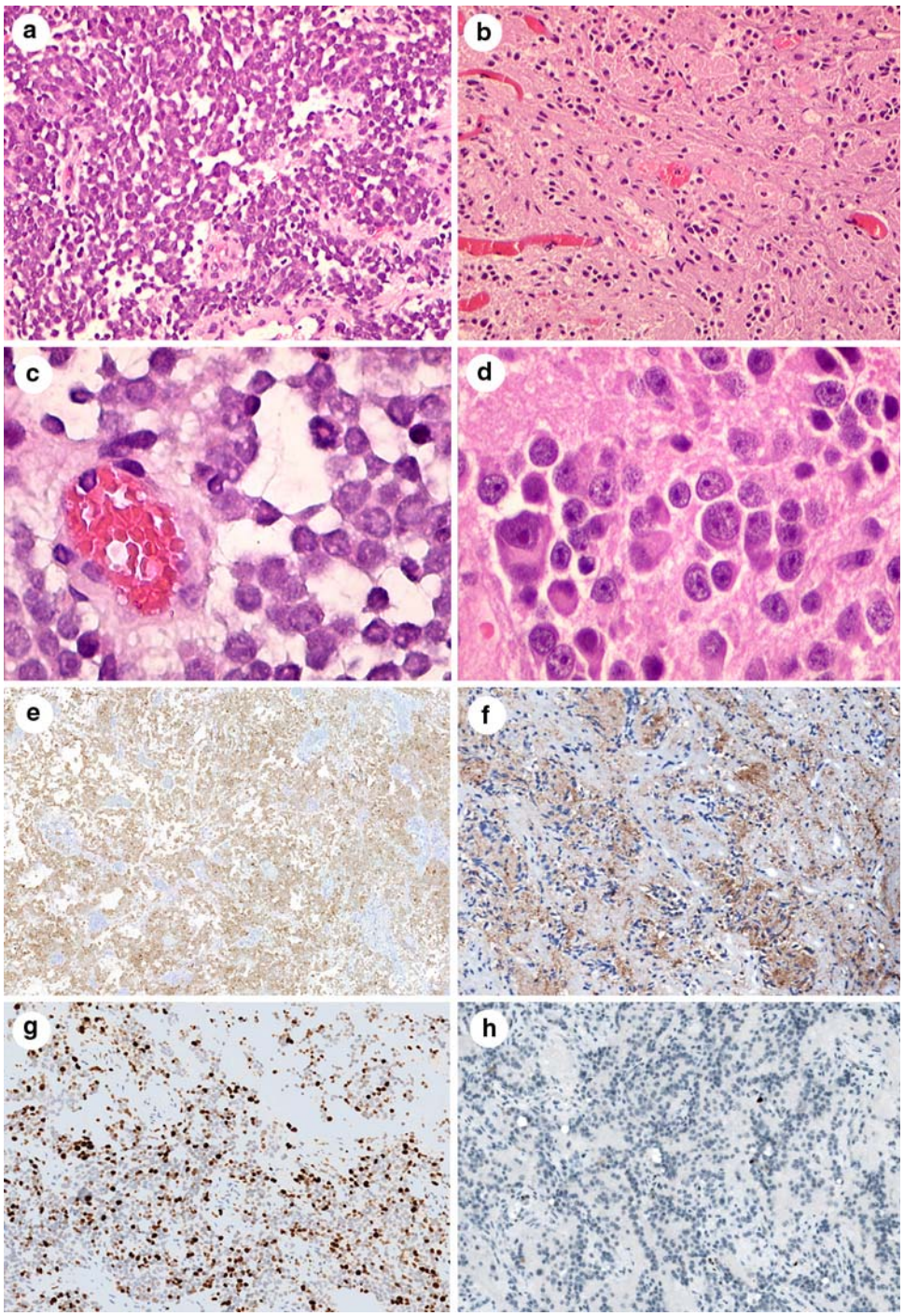

Fig. 2 Neuropathology at presentation (**a**, **c**, **e**, **g**) and after treatment (**b**, **d**, **f**, **h**). **a**, **b** H&E, ×200. **c**, **d** H&E, ×400. **e** Chromogranin A, ×200. **f** Neurofilament protein, ×200. **g**, **h** Labelling index

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