maximally dilated fragile arterioles to direct arterial pressure.⁶ This theory has been used to explain the presence of intracranial haemorrhages in ill neonates. Likewise, in the setting of ROP related vasculopathy, the stress of an ophthalmological examination with the accompanying variations in intraocular pressure and scleral distortion might result in retinal haemorrhages.

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Retinoblastoma and optic nerve enhancement on MRI: not always extraocular tumour extension

Neoadjuvant chemotherapy is useful in the management of extensive forms of retinoblastoma with radiologically detectable optic nerve invasion at diagnosis.¹ Magnetic resonance imaging (MRI) can detect various degrees of optic nerve invasion as enhancement extending from an intraocular tumour into the optic nerve. However, pretreatment false positive MRI findings based on inflammation occur occasionally.² We describe a case of unilateral retinoblastoma and false positive MRI findings of extensive optic nerve involvement.

Case report

A 3 year old girl presented with retinoblastoma of the right eye. Ophthalmic examination revealed a large exophytic growing

Figure 1 A 3 year old girl with unilateral retinoblastoma of the right eye. MRI findings on admission. (A) Axial T2WI (TR/TE, 3000/120) shows an exophytic growing tumour mass combined with a V-shaped retinal detachment and hyperintense (proteinaceous) subretinal fluid. Compared to the normal optic nerve, the affected site shows absence of cerebrospinal fluid in the optic nerve sheath. (B) Contrast enhanced axial fat suppressed T1WI (TR/TE, 575/13) (level corresponding (A)) shows an enhancing tumour mass of the right eye with marked enhancement and thickening of the intraorbital part of the optic nerve (arrows), in continuity with the intraocular mass, being suspicious for extensive tumour invasion.

tumour, a shallow anterior chamber, rubeosis iridis, and an elevated intraocular pressure. T2WI showed a hypointense subretinal tumour mass with similar signal intensity (SI) compared to both optic nerves (fig 1A). No delineation of the ipsilateral optic nerve with surrounding cerebrospinal fluid was possible. On additional short tau inversion recovery (STIR) MRI, the optic nerve showed an increased SI from the postlaminar part to the orbital apex. Contrast enhanced T1WI showed enhancement of the tumour mass (tumour volume 2.1 cm³). Thickening and marked enhancement of the entire intraorbital part of the optic nerve was seen, being suspicious for extensive tumour invasion (fig 1B). Based on these findings, retinoblastoma with

extensive optic nerve invasion was diagnosed, and one course of etoposide-carboplatin chemotherapy was administered. Follow up MRI (fig 2), 4 weeks after admission, disclosed a tumour mass reduction (tumour volume 0.5 cm³, 77% volume reduction), a decrease in range of contrast enhancement of the optic nerve, without evident normalisation of signal pattern on T2WI and STIRWI. Enucleation was performed using an altered surgical approach by the neurosurgeon and ophthalmologist, which allowed 15 mm of optic nerve to be removed under direct vision. Histopathology revealed a largely necrotic intraocular retinoblastoma, without any degree of optic nerve invasion. Normal architecture of the optic nerve was only disturbed at the lamina cribrosa, with

Figure 2 Follow up MRI study and histopathological findings after one course of chemoreduction therapy performed 4 weeks after initial presentation. Axial T2WI (TR/TE, 2200/120) (A) and contrast enhanced axial fat suppressed T1WI (TR/TE, 475/14) (B) show a marked reduction in intraocular tumour volume. The optic nerve shows persisting abnormalities on T2WI (A), with a decrease of enlargement and contrast enhancement (arrow), which was interpreted as residual optic nerve invasion (B). (C) Immunohistochemical staining with CD-45 antibodies for lymphocytes shows positive staining (dark cells) throughout the optic nerve. (CD-45; original magnification 40× objective) (D) Detail of the optic nerve shows endothelial proliferation in a vessel wall (arrows) with total obliteration of the lumen. (Haematoxylin and eosin stain; original magnification 40× objective.)

local presence of reactive gliosis, but without any presence of residual necrotic tumour cells. Immunohistochemistry stains for MIB-1 and CD-45 revealed no tumour cells, but did show a lymphocytic infiltrate throughout the optic nerve (fig 2C). The dura showed no thickening or inflammation. A second uncommon histopathological finding in the optic nerve was endothelial cell proliferation and swelling, with total obliteration of some vessels as a consequence (fig 2D).

Comment

The combination of inflammation and endothelial proliferation in our patient, which are thought to be responsible for at least the residual optic nerve enhancement after neoadjuvant chemotherapy, have never been described before as a possible cause of (post-treatment) false positive MRI. However, a striking discrepancy between pretreatment radiologically detectable extensive optic nerve invasion and post-treatment histopathology, without any remaining signs of a former minimal or extensive post-laminar invasion is left unsolved. Histopathological findings in eyes after multiple courses of chemoreduction therapy for retinoblastoma are well documented and consist mainly of viable and necrotic tumour cells and gliosis, without presence of inflammation or endothelial proliferation.^{3,4} The latter occurs characteristically in brain tissue and is associated with contrast enhancement in brain tumours.⁵ Only Bellaton *et al*¹ published three cases with a comparable discrepancy of extensive optic nerve invasion on pretreatment MRI without any remaining histopathological signs of former extensive tumour invasion after two or three courses of chemotherapy, although a slight residual enhancement is reported in at least one patient. Unfortunately, they did not mention a possible histopathological substrate for (residual) enhancement. In conclusion, optic nerve enhancement on MRI is an indicator for tumour invasion, but it must be taken into consideration that other histopathological changes (inflammation, endothelial proliferation) can occur in combination with retinoblastoma and may mimic (residual) tumour invasion, also after neoadjuvant chemotherapy.

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Cytokeratin subtyping to distinguish reactive and neoplastic RPE cells

Retinal pigment epithelial (RPE) hyperplasia is common in retinal disease, whereas RPE neoplasia is rare. In tissue sections it can occasionally be difficult to distinguish between the two conditions on morphological features alone. In a retrospective case series that addressed this issue, features thought to favour a reactive hyperplasia of the RPE included a history of previous ocular disease in the affected eye, conspicuous elaboration of basement membrane, rarity of mitotic figures, and histological pattern.¹ These features are not

Figure 1 (A) Preoperative fundus photograph of right eye showing foveal choroidal neovascularisation (CNV) with surrounding exudate. (B) Section through the excised CNV stained with haematoxylin and eosin. (C) The cortex of the CNV (haematoxylin and eosin). Note the tubular-vascular arrangement of the cells and their association with basement membrane-like material. Scale bar: 50 μ m. Inset: diastase periodic acid Schiff staining of the CNV cortex demonstrates copious amounts of basement membrane-type material surrounding the RPE cells (haematoxylin counterstain). (D, E) Sections through the CNV stained for cytokeratin 7 and 8/18 respectively, using the immunohistochemical method (red reaction product) and counterstained with haematoxylin. The cells in the CNV cortex demonstrate strong positivity for cytokeratin 7 but not 8/18. A few RPE cells in the surface monolayer do, however, stain for simple epithelial cytokeratins (e). Scale bars: 50 μ m. (F, G) Immunohistochemical stain of hyperplastic RPE cells in a disciform CNV (used as a cytokeratin reference specimen) for cytokeratin 7 (F) and 8/18 (G) respectively. The reactive cells have mostly lost positivity for cytokeratin 8/18 but are immunoreactive for cytokeratin 7 (arrows). Cells in a surface layer mostly express both cytokeratins (arrowheads). (H, I) Immunohistochemical stain of known low grade RPE adenocarcinoma (used as a cytokeratin reference specimen) demonstrating absence of cytokeratin 7 staining (H) but strong cytokeratin 8/18 labelling (I).