Letter to the Editor

Bilateral epiretinal membranes in nevoid basal cell carcinoma syndrome

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Sir,

Nevoid basal cell carcinoma syndrome (NBCCS) is a dominant, autosomal disorder linked to chromosome 9q 22.3-q31 and is caused by mutations of the patched homologue (PTCH) gene (Gorlin & Goltz 1960; Hahn et al. 1996). PTCH mutations can be tumorigenic and cause developmental anomalies by affecting the sonic

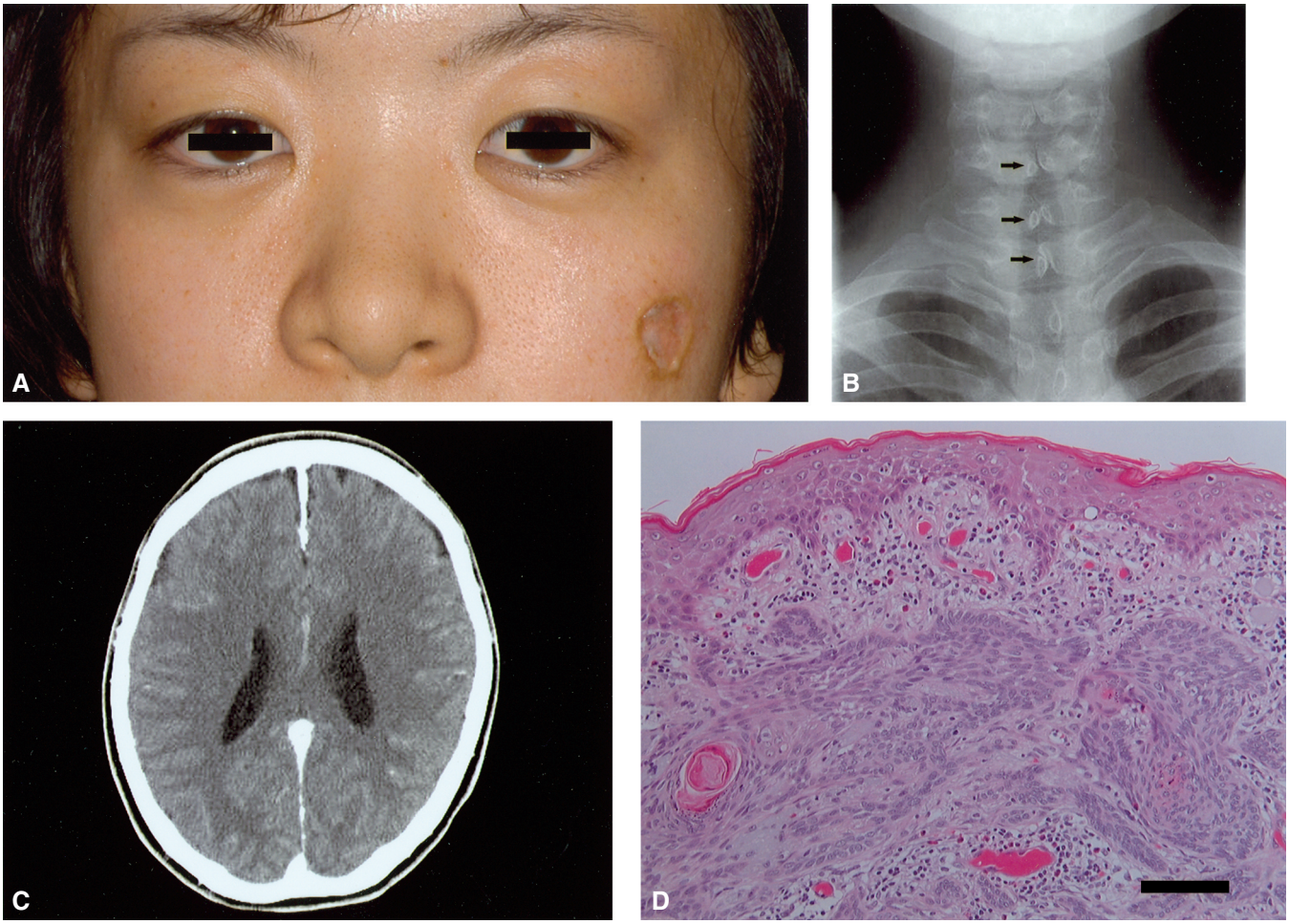

Fig. 1. (A) Photograph of the patient at age 27 years showing an ulcerating mass measuring 2.0 × 2.0 cm on the left cheek. A marked hypertelorism can also be noted. (B) Chest radiograph showed bifid cervical vertebrae, some of which are indicated by arrows. (C) Computed tomographic scan of the patient's head showing calcification of the falx cerebri. (D) Histological section of the specimen removed from the cheek showing proliferation of basaloid cells with severe atypia in the fibrous dermis. Parts of the nests show peripheral nuclear palisading. Focal keratinization is also seen. These findings are characteristic of BCC.

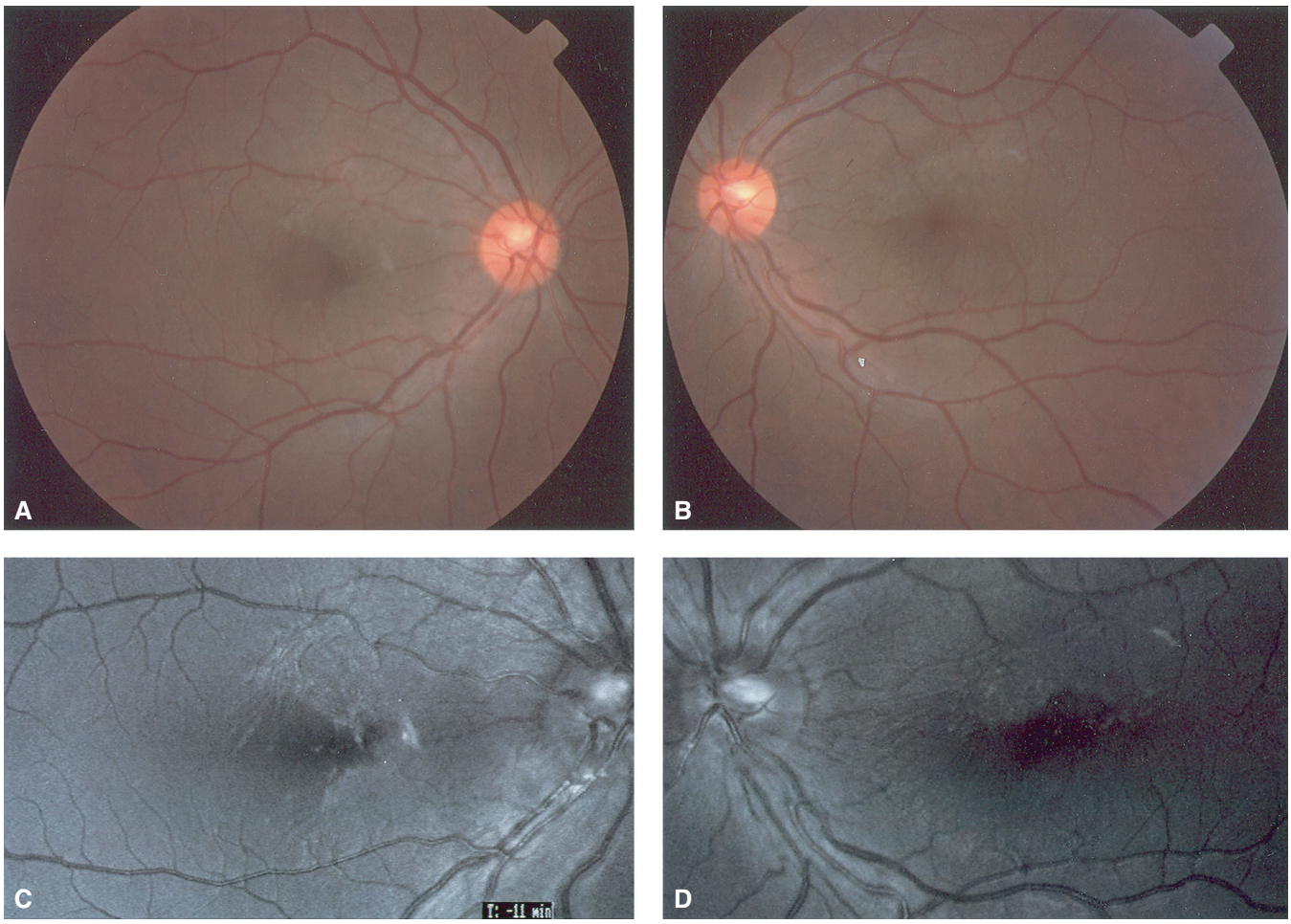

Fig. 2. (A, B) Fundus photographs. Both right and left eyes show a white preretinal membrane. In the left fundus, a distortion of the retinal vasculature can be seen. (C, D) Confocal images of the right and left fundus obtained by scanning laser ophthalmoscope. A well demarcated dense epiretinal membrane is observed above the fovea with radial folds of the internal limiting membrane.

hedgehog/patched signalling pathway (Hahn et al. 1999). This syndrome is characterized by multiple basal cell carcinomas (BCCs), odontogenic keratocysts of the jaw, congenital skeletal anomalies, ectopic calcification, palm and/or sole pits, and ocular abnormalities (Kimonis et al. 1997). The ocular abnormalities include hypertelorism, strabismus, eyelid papilloma, medullated nerve fibres, and hamartoma of the retina (De Potter et al. 2000).

The presentation features of this syndrome are variable both within and between families (Black et al. 2003). We describe a case of NBCCS with bilateral epiretinal membranes (ERMs).

A 27-year-old Japanese woman was seen at Kyushu University Hospital. She had had a tumour on her left cheek (Fig. 1A) and another on her right lower abdomen since the age of 25 years. She also had hypertelorism (Fig. 1A), bifid vertebrae (Fig. 1B), jaw cysts, and palmar/plantar pits. A computed tomographic scan showed intracranial calcification of the falx cerebri (Fig. 1C). She was operated on for the jaw cysts, and the lesions on her cheek and abdomen were removed. A diagnosis of BCC was made from the histopathological findings of the specimens (Fig. 1D).

Her family history revealed that both her father and brother had odontogenic keratocysts of the jaw and that her grandfather had undergone a tumour resection, the histological findings of which are unknown. Based on the family history and the systemic features, a diagnosis of NBCCS was made.

Ophthalmologically, the subject's best corrected visual acuity was 20/25 OD and 20/20 OS, and the anterior segments of both eyes were unremarkable. Fundus examination showed an ERM around the fovea in both eyes (Fig. 2A, B). Scanning laser ophthalmoscopy with an argon blue laser (Rodenstock Instruments, Munich, Germany) revealed a well defined, fibrous-like tissue with folds of the internal limiting membrane (Fig. 2C, D). There was no evidence of a posterior vitreous detachment.

Epiretinal membranes are a common finding in elderly patients but are rare in young patients. Juvenile ERMs are usually unilateral and occur as secondary phenomena, for example after ocular trauma, ocular toxocariasis, Coats disease and pars planitis (Benhamou et al. 2002). In our case, none of these findings was present. We also carefully searched for a hamartoma of the retina and retinal pigment epithelium (RPE) by fluorescein and indocyanine green angiography. No hamartoma was found. Thus, we suggest that this was a case of primary ERM.

It has been recently reported that the retinas of PtchlacZ+/−mice exhibit Muller cell-derived gliosis and that, in NBCCS patients, the intraretinal glial response results in ERM formation (Black et al. 2003). This report and our own case lead us to believe that, rather than being coincidental, the ERMs instead represent an intraocular manifestation of NBCCS, and may have developed because of the tumorigenic condition induced by the abnormal hedgehog/patched signalling caused by the PTCH mutation. Molecular analysis of the PTCH gene and phenotype− genotype correlations might thus provide insights into the mechanisms responsible for the ERM in cases of NBCCS. We recommend a careful fundus examination in patients with NBCCS even if they have good visual acuity.

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