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Sir,

Paradoxical vascular–fibrotic reaction after intravitreal bevacizumab for retinopathy of prematurity

Retinopathy of the prematurity (ROP) is the main cause of childhood blindness in developing countries, largely because of the lack of efficient programmes for its detection and treatment. The use of antiangiogenic agents in cases of advanced ROP has been suggested even though the long-term ocular and system side effects of using these medications in premature babies are unknown.[1,2] We report a case of advanced ROP treated with laser ablation and intravitreal injection of bevacizumab (Avastin, Genentech, San Francisco, CA USA), after which the vascular response was paradoxical with significant fibrosis and subsequent traction.

Case report

A 1350-g male baby, born at 31 weeks of gestation, was discharged from neonatal intensive care unit and referred to ophthalmological evaluation at 36 weeks postmenstrual age (PMA) without a specific time for follow-up recommendation. The baby's first ophthalmic examination was performed 4 weeks later (40 weeks PMA). Funduscopic examination showed circumferential ROP stage 3 in zone II with severe plus disease in both eyes (Figure 1). Information was provided to the parents about the baby's poor visual prognosis, options, advantages, and disadvantages of treatment, and the informed consent was obtained. Under general anaesthesia, photocoagulation with diode laser (810 nm, 3310 burns right eye, and 3405 burns left eye using 200 mW and 200 mS) as well as intravitreal application of 0.4 mg of bevacizumab was performed . Twenty-four hours after the treatment, the plus disease showed some signs of resolution with diminished vascular activity, increased fibrous activity in the region of the ridge (Figure 2). At one week, vascular activity had markedly decreased and the proliferative membrane showed marked fibrous component (Figure 3). At day 8, a vitrectomy was performed in the left eye because of progressive stage 4a. In the right eye, a fibrous ring was noted on day 14 (Figure 4).

Comment

In the majority of the cases treated with laser, the involution of the vascular component (plus disease) correlates to the activity of the fibrovascular ridge of stage 3.[3] However, in the case reported here, the tractional component progressed even without the appearance of vascular activity. This finding is not unique when using intravitreal bevacizumab in vascular retinopathies. Fibrosis, 7 days after intravitreal bevacizumab, had been reported in eyes with proliferative diabetic retinopathy,[4] as well as acute contraction of the fibrovascular membrane in ROP.[5] Kong *et al* reported in a pathologic study that intravitreal bevacizumab in zone I, stage 2 plus ROP did not show inflammation, necrosis, or degeneration.[6] Contraction of large fibrovascular membranes (stage 3, more than 6 h extension) may well lead to a tractional retinal detachment as shown in this case and in two cases in a series by Kusaka *et al*.[1,5]

Antiangiogenic therapy had been proposed as a valuable resource in the treatment of advanced cases of acute phase ROP; however, we must remember that such use is off-label, and long-term ocular and systemic side effects in this population are unknown.[2,6,7] The value of the current report is pointing out that the development of a tractional retinal detachment is a potential complication of such therapy. Postsurgical evolution of these cases differs from the cases treated only with photocoagulation.

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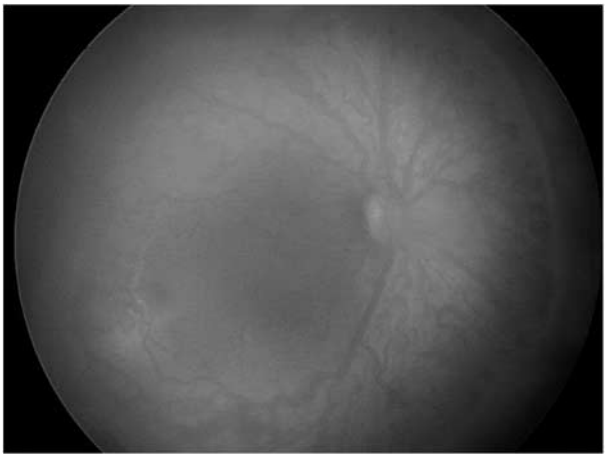

Figure 1 Image of the right eye obtained before treatment show ROP stage 3, zone II, plus disease.

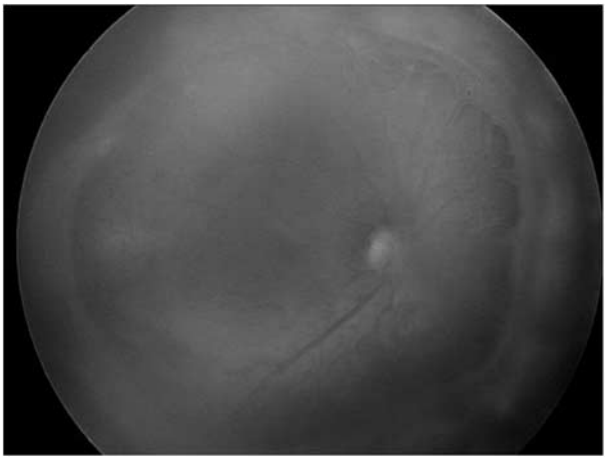

Figure 2 Fundus image of the same eye obtained 1 day after diode laser ablation and intravitreal bevacizumab; notice how plus disease decreased and the elevated membrane.

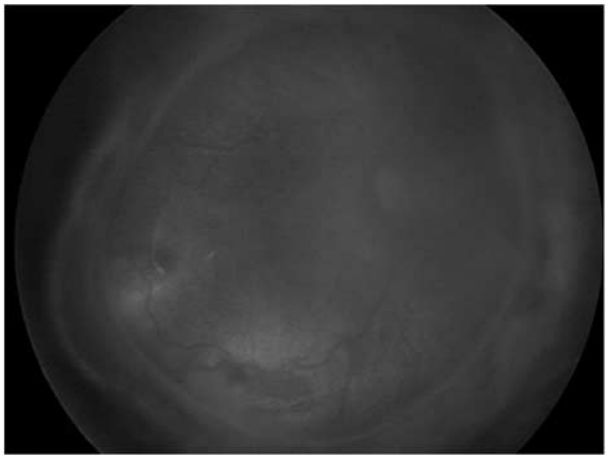

Figure 3 Fundus image of the same eye obtained 1 week after treatment show plus disease residual and vitreous organisation at the edge.

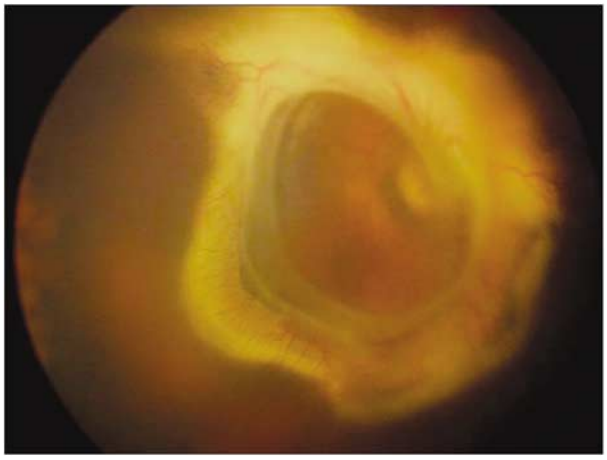

Figure 4 Fundus image of the right eye obtained 14 days after treatment show a ring-shaped fibro-tractional membrane.

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