A delayed diagnosis of unsuspected retinoblastoma in an in vitro fertilisation infant with retinopathy of prematurity

Tian Tian, Xun-Da Ji, Qi Zhang, Jie Peng, Pei-Quan Zhao

Department of Ophthalmology, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200082, China
Correspondence to: Pei-Quan Zhao. Department of Ophthalmology, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Kongjiang Road, No.1665, Shanghai 200082, China. zhaopeiquan@126.com
Received: 2015-11-19 Accepted: 2016-01-27

DOI:10.18240/ijo.2016.09.23

Dear Editor,

I am Dr. Tian Tian, from the Department of Ophthalmology, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China. I write to present a rare case report of a delayed diagnosis of unsuspected retinoblastoma (RB) in an in vitro fertilisation (IVF) infant with retinopathy of prematurity. The simultaneous presentation of RB and prematurity of retinopathy (ROP) in an IVF infant is very rare. The relationship between RB and IVF is still indeterminate and mechanisms that lead to ocular or systemic abnormalities remain largely unknown [1]. It has been reported that vitreous haemorrhage is uncommon with RB and occasionally can completely obscure the tumor [2]. However, few literature exists regarding the ocular and life prognosis after vitrectomy or invasive vitreous biopsy for unsuspected RB. Here, we describe another unique case and the youngest reported to our knowledge.

A female baby, the younger of IVF twins, was born at 31wk+1d, with a birth weight of 1200 g. The patient had a history of intravenous transfusion and oxygen supplementation during the two months following delivery. There was no family history of ocular diseases. She was diagnosed with ROP at the first visit (OD: stage 5; OS: stage 4a; Figure 1A, 1B). The right eye received subretinal injections of an anti-vascular endothelial growth factor (VEGF) drug (Lucentis). The left eye underwent laser photocoagulation and lens-sparing vitrectomy (LSV). Unexpectedly, a mysterious lesion was found on the fundus of the left eye after five days of vitrectomy (Figure 1C).

The patient underwent systemic examinations, including routine blood tests, blood bacterial culture, Cytomegalovirus (CMV), Toxoplasmosis (TOX), cerebrospinal fluid, sputum culture, chest X-ray, cerebral magnetic resonance imaging (MRI), and T-spot. All were negative. B-scan revealed an irregular mass, with no calcification. The patient's RB1 gene was wild-type; there was no relevant familial history. The first of two fine-needle aspiration biopsy (FNABs) obtained from the lesion were positive on a fungal smear (Figure 2A, 2B). There was no cytological evidence to support a diagnosis of RB.

Thus, the patient was put on intravenous anti-fungal therapy and received two intravitreal injections of anti-fungal drugs. Unfortunately, the lesion got bigger, even under timely and aggressive anti-fungal therapy (Figure 1D).

Given the diagnostic dilemma, FNAB was attempted for a third time and the result indicated RB (Figure 2C-2F). The antifungal therapy was terminated and six cycles of chemotherapy (vincristine+etoposide+Carboplatin) were administered. During follow-up of 17mo, the tumour in the left eye regressed and there was no sign of orbital or systemic metastasis. The right eye exhibited no RB (Figure 1E, 1F).

In this case, the tumor was inconspicuous and veiled by the fundus haemorrhage, which could easily be ignored by the surgeon, and vitrectomy was inadvertently performed. In 1989, Stevenson et al [3] reported three patients who underwent vitreous biopsy in eyes with unsuspected RB. Developed recurrences were found in the orbit (two patients) and lymphnodes (one patient), even with enucleation. Shields et al [4] reported eleven patients who were referred soon after vitrectomy and suspicion for RB. Ten patients survived who treated with enucleation and prophylactic chemotherapy, radiotherapy, or both at a mean follow-up of 7y. The only patient to die was because of later referral and found to have metastatic disease. The patient in our case received six cycles of chemotherapy without enucleation, because the patient's right eye had total retinal detachment with poor prognosis and her parents firmly refused...
enucleation of the left eye. The clinical appearance of RB may be atypical when combined with ROP. FNAB can be a useful tool when a diagnostic dilemma exits. However, it may also yield misleading information when insufficient material is obtained. It has been reported that FNAB can be expected to give useful information only when lesions are more than 3 mm thick [5]. Inadequate samples may be obtained from compact or cystic lesions, even if the thickness is >4.5 mm[6]. In our case, the lesion was cystic and flat when the first two FNABs were performed, insufficient material was got and leaded to misleading result and increasing risk of metastasis. To confess, it was an inappropriate medical behaviour caused by misleading diagnosis. We strongly advise the contraindication of FNAB under suspicion of RB. The patient in our case was referred to specialist as soon as the diagnosis of RB was made and treated with chemotherapy. We used standard instead of aggressive chemotherapy considering the classification of the tumor and prematurity of the baby. Fortunately, no evidence of orbital recurrence and distant metastasis was found at a follow-up of 17mo. It has been reported that the lack of metastasis after 12 to 15mo generally indicates that the

Figure 1 The fundus photographs A: The right eye was total retinal detachment before treatment; B: The left eye was partial retinal detachment with fundus hemorrhage and an inconspicuous lesion (arrow); C: The lesion was cystic with cheese-like appearance after LSV; D: The lesion got bigger continuously even under aggressive anti-fungal therapy; E: The tumor regressed after six cycles of chemotherapy; F: During the follow up of 17mo, the right eye was total retinal detachment without RB being found.

Figure 2 The results of fungal smear and immunohistochemistry A, B: The result of fungal smear was positive. Spores were seen out of the cell (Arrow). C-F: The results of immunohistochemistry indicated the diagnosis of RB. C: CD 56 (+). D: Ki-67 (35%). E: NSE (+). F: Syn (+).
patient with RB is cured \cite{4}. Through the case, we advise that RB should be excluded in any baby with unexplained vitreous haemorrhage before vitrectomy and RB should always be ruled out before FNAB is performed.

Neither reported studies nor our case proves whether this is a true phenomenon associated with IVF or merely a sporadic occurrence. To prove this crucial question, large-scale studies regarding the ocular and systemic abnormalities of IVF offspring should be conducted. We should raise concerns about the IVF babies’ ocular health in the world.

ACKNOWLEDGEMENTS

Conflicts of Interest: Tian T, None; Ji XD, None; Zhang Q, None; Peng J, None; Zhao PQ, None.

REFERENCES


