



A Case Study on Retinoblastoma Associated Orbital Cellulitis

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Authors' contributions

This work was carried out in collaboration between both authors. Author SCR conceptualized the report, did the literature search, wrote the draft of the manuscript and managed the patient. Author BSM reviewed the draft of the paper and treated the patient with chemotherapy. Both authors read and approved the final manuscript.

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Case Report

ABSTRACT

A 20-months-old male child was brought to the Eye clinic with swelling of right upper eyelid, discharge sticking the eyelids in the right eye and redness in both eyes of three days duration. On detailed examination of anterior segment and fundus, the diagnosis of bilateral retinoblastoma with conjunctivitis was made. The conjunctivitis was cured with ciprofloxacin eye drops and eye ointment. CT scan of orbits and brain confirmed the diagnosis of retinoblastoma with calcification in both eyes. Optic nerve on both sides was normal and there was no metastasis in the brain. Since it was a bilateral case of retinoblastoma, chemoreduction followed by enucleation in the right eye, and salvaging the left eye with chemotherapy in order to save the vision was planned. Intravenous triple drug chemotherapy with carboplatin, etoposide and vincristine (six cycles) was started by pediatric oncologist in pediatric ward. After two weeks of completing the first cycle of treatment, enucleation of right eye was done. Postoperative period was uneventful. The chemotherapy was continued. The child developed marked swelling of left upper eyelid few days before the sixth cycle of chemotherapy. Examination of left eye showed signs of aseptic orbital

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cellulitis which was treated with oral prednisolone and topical eye drops of combination of gentamycin and dexamethasone. The inflammatory signs subsided completely in ten days time. The sixth cycle of chemotherapy was completed. On the follow up visit two weeks after discharge, the left eye ball was normal. In the first follow up, the child could pick up the toys thrown in front of him. Unfortunately the child defaulted follow up. Retinoblastoma should be excluded in all young children with orbital cellulitis because misdiagnosis is life threatening.

Keywords: Retinoblastoma; chemotherapy; enucleation; orbital cellulitis.

1. INTRODUCTION

Retinoblastoma is the most common malignant intraocular tumour in children. Balasubramanya et al. [1] reported fourteen atypical findings in retino-blastoma patients which include endophthalmitis, secondary glaucoma, uveitis, corneal oedema, phthisis bulbi, orbital cellulitis, cataract, pseudohypopyon, iris nodules, hyphema, iris neovascularization, microphthalmos, exposure keratitis and corneal blood staining. In their study, leukocoria was the most common presenting sign (72.2%), followed by proptosis (13%) and strabismus (10%); 1.5% were asymptomatic (detected on screening) and 3.3% had atypical presentations.

Orbital cellulitis is a rare presenting feature of intraocular retinoblastoma in the western world (USA, 0.23%, 3 out of 1265) [2], However, it is not uncommon presentation in the developing nations (Uganda, 2.33% (5 out of 214) [3], Malaysia, 2.85% (3 out of 105) [4]. It is characterized by noninfectious inflammation of the periorbital structures thought to be a result of necrosis of intraocular tumour and accompanying intraocular and periorbital inflammation [5].

A rare case of bilateral retinoblastoma in a young child is reported from Malaysia in which chemoreduction of the tumour followed by enucleation was done in the right eye and the signs of orbital cellulitis were noted in the left eye after few cycles of chemotherapy, with a brief review of literature.

2. CASE REPORT

A 20-months-old male child was brought to the Eye clinic by parents with complaints of swelling of upper eyelid, redness and discharge in the right eye, and redness of left eye for the past three days which was not improving with antibiotic eye drops prescribed by a general practitioner. The child was born by normal vaginal delivery and the developmental milestones were normal. There was no fever or upper respiratory tract infection.

Examination of the right eye showed mild edema of the upper eyelid associated with mucopurulent discharge sticking both eyelids (Fig. 1A). After cleaning the discharge with normal saline swab, the conjunctiva showed diffuse congestion. In the left eye, eyelids were normal without any discharge and conjunctival congestion was present. Rest of the anterior segment was normal in both eyes. Intraocular pressure digitally was normal in both eyes. Fundus examination with direct ophthalmoscope (after dilating pupils with tropicamide eye drops 1%) showed a white reflex with tumour mass protruding into the vitreous on either side of the optic disc, involving the macula in the right eye; and yellowish white reflex with tumour mass on the temporal side of the optic disc up to the macula in the left eye. Vision could not be tested; however, undilated pupil was briskly reacting to light in both eyes.

The diagnosis of bilateral retinoblastoma with conjunctivitis in the right eye was made and the child was admitted for further investigations and treatment. The mucopurulent discharge was sent for Grams stain and culture. The Gram's stain did not show any bacteria. Ciprofloxacin (0.3%) eye drops were put one hourly in the right eye and two hourly in the left eye during day time and same antibiotic eye ointment was put in both eyes in the night time. After two days, oedema of the upper eyelid was less in the right eye. The congestion in both eyes and the discharge in the right eye reduced markedly. The antibiotic eye drops were reduced to two hourly in the right eye and four hourly in the left eye. After two days, the oedema of upper lid was still present; the antibiotic eye drops were further reduced to six times in right eye and four times in left eye, with eye ointment at night time in both eyes. Both eyes became white after one week; and child was opening the eyes well. Left eye after dilating the pupil showed yellowish white reflex with torch light (Fig. 1B).

Conjunctival swab culture was sterile. Blood was sent for full blood counts which showed all the counts within normal limits. The CT scan of orbits and brain was done which showed hyperdense

intraocular tumour mass in temporal and nasal retina extending into vitreous, clumps of calcification in the right eye; and a hyperdense intraocular tumour mass in the temporal retina with calcification in the left eye (Fig. 1C), confirming the diagnosis of bilateral retinoblastoma. The optic nerve was normal on both sides. There was no metastasis in the brain.

The child was examined under general anaesthesia. The tonopen intraocular pressure was 16 mm Hg in the right eye and 15 mm Hg in the left eye. The fundus examination with indirect ophthalmoscope confirmed the retinal findings. Bone marrow aspiration was performed and the smear did not show any malignant cells. Lumbar puncture was done and cerebrospinal fluid did not show malignant cells.

Since it was a bilateral case of retinoblastoma, chemoreduction followed by enucleation in the right eye; and salvaging the left eye with chemotherapy in order to save the vision was planned. The child was referred to pediatric oncologist for advice, and the child was transferred to pediatrics ward for chemotherapy. The topical ciprofloxacin was continued three times daily in both eyes.

A six cycles course of intravenous tripe drugs chemotherapy with carboplatin, etoposide and vincristine was started. After two weeks of completing the first cycle of chemotherapy, enucleation of right eye was performed under general anaesthesia, and the eyeball was sent for histopathology. Post operatively, ciprofloxacin eye drops three times daily and same antibiotic eye ointment in the night time were put in the right eye. The conjunctival wound healed well.

The cut section of the enucleated eyeball showed necrotic tumour in the posterior segment of the eye. Histopathological examination revealed cells with scanty cytoplasm, hyperchromatic nuclei with extensive necrosis and rosettes. There was invasion of choroid with malignant cells at some places. The sclera was intact and free of tumour cells. The cut end of optic nerve did not reveal any infiltration with malignant cells. The chemotherapy was continued in the pediatric ward and followed at scheduled intervals. Eye follow up was done on the day when the child was admitted for next cycle of chemotherapy. The child was doing well and healthy.

Before the follow up for sixth cycle of chemotherapy, the child was brought to the Eye clinic with complaint of swelling of upper eyelid, increasing rapidly, and inability to open the left eye for the past two days. There was no fever or upper respiratory tract infection. Examination of left eye showed no discharge, marked edema of the upper eyelid (Fig. 2A). On separating the upper eyelid with fingers, the conjunctiva was diffusely congested with mild chemosis. Cornea, anterior chamber, iris, pupil and lens were normal. After dilating the pupil with tropicamide eye drops 1%, fundus examination with direct ophthalmoscope showed the yellowish white tumour on either side of the optic disc. The diagnosis of orbital cellulitis in the left eye was made and the child was admitted for treatment.

Moxifloxacin eye drops four hourly in the day time and same antibiotic eye ointment in the night time were put in the left eye. Blood counts were normal. Conjunctival swab for gram stain was negative for bacteria. Nasal swab for culture was sterile. After consulting the pediatrician, a short course of steroids (oral prednisolone 1 mg/kg/day) were given for one week. The upper lid oedema was much less after three days and the same treatment was continued. The CT scan of orbits and brain showed no recurrence of the tumour in the right orbit, and intraocular tumour mass on temporal side with calcification and tumour on the nasal side extending into vitreous in the left eye with periorbital edema (Fig. 2B). The systemic steroids were continued for one week and then tapered in three days. The edema of upper eyelid decreased markedly (Fig. 2C). The conjunctival congestion also much less. The antibiotic eye drops in the left eye were reduced to three times daily for one week, and later on two times daily for another one week. Antibiotic eye ointment was continued in the night time in the left eye.

The child was transferred to pediatric ward and sixth cycle of chemotherapy was completed. At the time of discharge from the ward moxifloxacin eye ointment was continued in the night in both eyes. On the follow up visit two weeks after discharge, the left eye was normal. Moxifloxacin was stopped. He was advised to come for monthly follow up. In the first follow up, the child could pick up the toys thrown in front of him. Vision tested with Catford drum was CF 2 meters. Left eye was white and quiet. Unfortunately the child defaulted follow up later on.

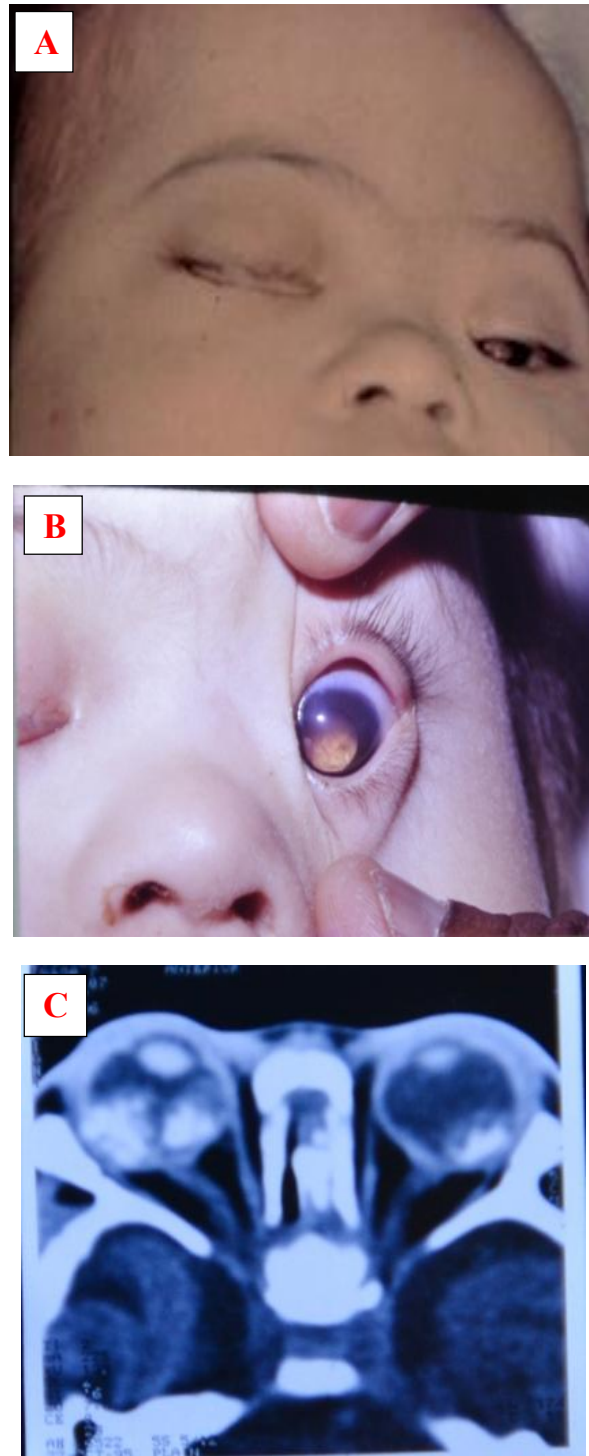


Fig. 1. (A) showing swelling of upper eyelid and discharge in between the lid margins in right eye, and mild conjunctival congestion of left eye; (B) left eye showing yellowish white reflex; and (C) axial CT scan of orbits showing hyperdense intraocular tumour mass in temporal and nasal retina extending into vitreous, clumps of calcification in the right eye; and a hyperdense intraocular tumour mass in the temporal retina with calcification in the left eye.

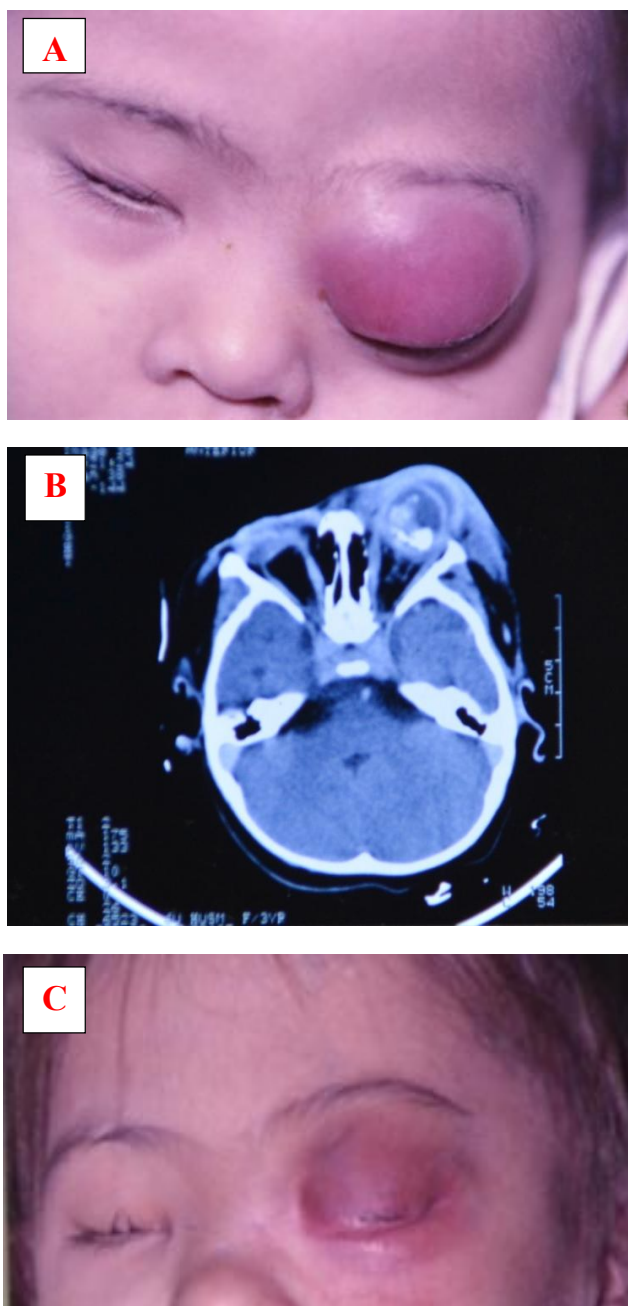


Fig. 2. (A) photo showing sunken right orbit, and marked swelling of the left upper eyelid; (B) axial view of contrast enhanced CT scan of orbits showing no recurrence of tumour in the right orbit, and intraocular tumour mass on temporal side with calcification and tumour on the nasal side extending into vitreous in the left eye with periorbital edema; and (C) photo showing response to short course of systemic steroids treatment in the left eye

3. DISCUSSION

Orbital cellulitis is an uncommon presentation of retinoblastoma. Isolated cases (1 or 2 cases) or case series (4 to 14 cases) of retinoblastoma

associated with orbital cellulitis have been reported in the past two decades.[6-13] The aetiology of orbital inflammation in intraocular retinoblastoma is not clear. Autoinfarction and immune aetiology are thought to be the possible

mechanism of inflammation. An immune mediated response, generated by a contralaterally affected eye or by necrotic tumour by products has been suggested by Shields et al [10].

A rapidly enlarging tumour outgrows its vascular supply, leading to autoinfarction, tumour necrosis and dystrophic calcification. Immune mechanism/activation may induce spontaneous tumour regression and necrosis characterized by calcification [14]. Necrotic tumour products leaching out of the eye may cause orbital inflammation. Infiltration of trabecular meshwork with necrotic cells may cause increased intraocular pressure. Tumour necrosis may be associated with neovascular glaucoma, hyphema and vitreous haemorrhage [12,14].

It is also suggested that necrotic changes occurring in the ciliary body and iris root trigger an inflammatory response in adjacent orbital soft tissues [15]. Orbital cellulitis associated with retinoblastoma may develop during the course of chemotherapy and follow up [16]. Severe pseudo-preseptal cellulitis [17] or aseptic orbital cellulitis [18] following subtenon injection of carboplatin along with systemic chemotherapy for treatment of vitreous seeds in intraocular retinoblastoma have been reported.

Binder [19] after the literature search has mentioned in his paper that tumour necrosis may cause severe inflammation and mask the diagnosis by presenting as orbital cellulitis, exophthalmos, eyelid oedema, conjunctival chemosis and conjunctivitis, endophthalmitis and panophthalmitis.

Differentiation of preseptal cellulitis or orbital cellulitis and retinoblastoma is important because presence of fever, sinusitis, signs of orbital inflammation (severe edema of eye lids, chemosis of conjunctiva, limitation of movements and proptosis), normal fundus appearance, and imaging studies showing sinusitis differentiate orbital cellulitis from intraocular retinoblastoma. On the contrary, patients with retinoblastoma do not show systemic inflammation, while ophthalmoscopic examination reveals leukocoria, buphthalmos, and an intraocular tumor mass. Computerised tomography imaging shows tumour mass in the eye with intralesional calcifications, and soft tissue edema without sinus involvement. Histology confirms the diagnosis [11].

Though the diagnosis by ophthalmoscope is often reliable, imaging is recommended to detect extraocular extension, optic nerve infiltration and intraocular metastasis, and to determine the type of treatment in these patients. Retinoblastoma eyes associated with orbital cellulitis usually have little visual potential if any, and may contain viable cells which may be hard to detect. Thus, enucleation is the treatment usually practiced in these eyes.

For eyes with retinoblastoma and orbital inflammation (preseptal cellulitis or orbital cellulitis), preoperative systemic steroids administration may decrease the signs of inflammation which makes the enucleation to perform easily [12,13]. Preoperative systemic chemotherapy causes tumour regression and may decrease the risk of tumour dissemination into the systemic circulation while decreasing orbital inflammation [7].

In the present case, sterile culture of the conjunctival swab from mucopurulent discharge in the right eye is suggestive of aseptic inflammation of conjunctiva, most probably due to inflammation reaction to the necrosis in the intraocular tumour in the eye. Similarly, the presence of severe upper eyelid edema, chemosis and mild proptosis is suggestive of associated orbital cellulitis in the left eye could probably be due to inflammation reaction to necrosis in the intraocular tumour in the eye [14]. The same tumour necrosis might have initiated immunological response for the orbital inflammation in the left eye at a later date [10]. Another possibility is that the orbital cellulitis in the left eye might have developed following chemotherapy as observed by Roebuck et al [16] and Nalci et al [7]. The oedema of eyelid, chemosis and conjunctivitis may be unusual manifestations of retinoblastoma as mentioned by Binder [19].

4. CONCLUSION

Orbital cellulitis associated with retinoblastoma is uncommon and characterized by noninfectious inflammation of periorbital structures. The underlying mechanism is thought to be necrosis of intraocular tumour. Retinoblastoma should be excluded in young children with signs of preseptal cellulitis or orbital cellulitis after thorough examination of anterior segment and fundus, and by doing imaging studies because misdiagnosis can be life threatening.

CONSENT

As per international standard or university standard, parents' consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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