

Trilateral retinoblastoma with unilateral eye involvement

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Abstract

Trilateral retinoblastoma (TRb) is a rare combination of unilateral or bilateral retinoblastoma with an ectopic midline intracranial neuroblastic neoplasm (primitive neuroectodermal tumour) usually in the area of pineal gland or sellar region. TRb can occur with both familial and sporadic forms of retinoblastoma. An occurrence of this rare tumour in a 12-year-old boy who had unilateral retinoblastoma in association with ectopic suprasellar primitive neuroectodermal tumour (PNET) is reported here. To the best of our knowledge, this is the first case report in Pakistan on TRb with suprasellar mass.

Keywords: Retinoblastoma, Trilateral retinoblastoma, Primitive neuroectodermal tumour.

Introduction

Retinoblastoma (Rb) is the most common intraocular malignancy in children caused by inactivation of both copies of the tumour suppressor gene Rb1, located on chromosome 13q14.¹ Rb may be hereditary or non-hereditary, familial or sporadic, unifocal or multifocal, and unilateral, bilateral or trilateral (TRb).² Children with hereditary type usually have bilateral and multifocal disease, while unilateral Rb is generally sporadic and non-hereditary with unifocal presentation.³

Trilateral retinoblastoma (TRb) is a well-known multifocal syndrome in which unilateral or bilateral Rb occurs in association with an intracranial neuroblastic lesion, which arises in the area of pineal glands, but can also be seen in suprasellar or parasellar region. It is considered an independent primary lesion, which is histologically similar to Rb.¹

It was first reported in 1971 and was differentiated from cerebral metastasis in 1977. The term 'trilateral retinoblastoma' was first used in 1980.² Although it traditionally refers to the association of bilateral Rb with the intracranial primitive neuroectodermal tumour (PNET), it has been reported with the unilateral form of

the intraocular tumour as well.²

Case Report

A 12-year-old boy, who was a diagnosed case of Rb in the right eye and was advised for enucleation twice but refused by the parents, came to us with the signs and symptoms of raised intracranial pressure. He had no associated positive family history. Examination of the eyes revealed an enlarged and distorted right eye with leucocoria. The left eye appeared normal. Visual acuity was found to be 6/60; there was loss of temporal field of vision, with sluggish pupillary light reflex, and normal extraocular muscles along with slight papilloedema.

Magnetic resonance imaging (MRI) of the brain with contrast showed a well-enhanced mass in the suprasellar region, extending posteriorly into interpeduncular cistern and compressing the posterior cerebral arteries. Anteriorly, it was causing severe compression on the optic chiasma. Another hyperdense mass was seen in the posterior part of the right eyeball invading the optic nerve; the right eyeball also appeared distorted (Figure).

Because of raised intracranial pressure and progressive visual deterioration, surgery was planned after counselling the attendants of the patient. After optimisation, the patient was taken for surgery. Tumour debulking was achieved through the right sub-frontal approach. Post-operative course was uneventful.

Histopathology revealed multiple fibrous tissue fragments extensively infiltrated by sheets of small cells exhibiting indistinct cellular borders, scant cytoplasm and hyperchromatic nuclei. The tumour cells were focally positive for para-amino-salicylic acid (PAS). Immunohistochemical staining revealed the following reactivity pattern: synaptophysin - positive; CD 56 - positive; glial fibrillary acidic protein (GFAP) - negative; and desmin - negative.

A metastases work-up was done which was normal at the time. Subsequently, he was referred to the radiotherapist. Stereotactic radiation therapy for the residual intracranial mass was conducted. Enucleation of the involved eye was recommended, but the attendants refused to go ahead with the advice.

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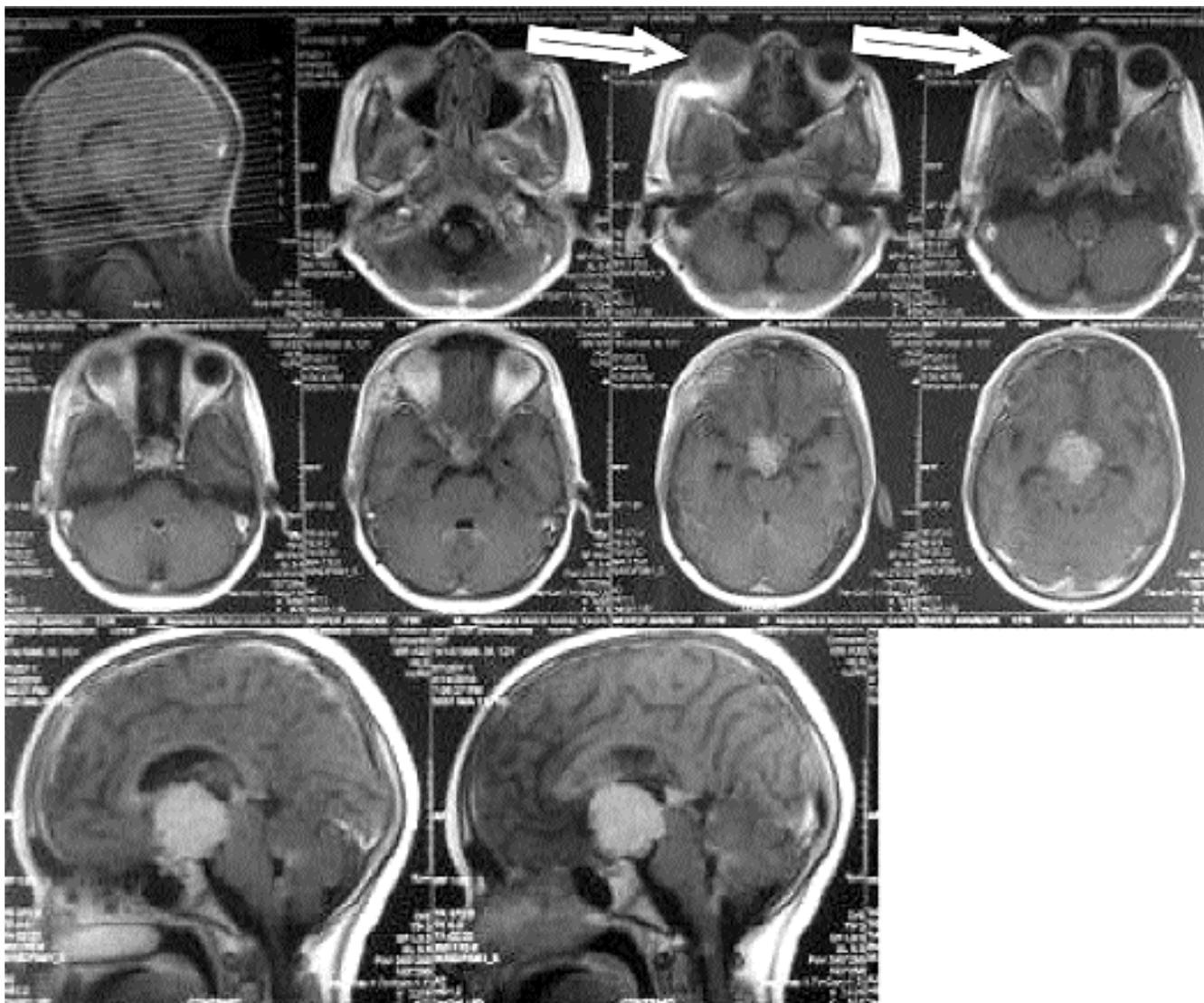


Figure: Axial and sagittal magnetic resonance imaging showing a mass in the suprasellar region. Involvement of right eye can also be noted.

After two months of radiation therapy, he returned with bilateral leg weakness, along with upper motor neuron clinical manifestations. MRI revealed multiple metastatic lesions in the dorsal spine. The patient died a week later.

Discussion

TRb is the occurrence of a primary, intracranial PNET in a patient with unilateral or bilateral Rb.⁴ It is found in approximately 3% of all the patients with Rb. The association of intracranial lesion with unilateral ocular Rb is less common than bilateral ocular Rb - the incidence is 0.5% and 2%-11% respectively.⁵ A series of 94 patients were searched on Medline data over 27 years (1970-1997), and it was found that this rare syndrome had a slight female predominance and that unilateral ocular Rb was

associated with a lesion in the sellar region. It was further added that the intracranial lesion was in the pineal region in 83% of the cases, and was found in the suprasellar area in 17% of the cases.

Most cases of TRb are diagnosed within one year after the diagnosis of ocular Rb.⁵ The latent period may range from one to several years, and by the time a diagnosis is made, the treatment of Rb is often completed.¹ These tumours generally develop before four years of age with a peak incidence in the second year of life. According to literature, patients with familial, bilateral Rb are found to be at higher risk for developing TRb.^{1,2,5}

The ocular signs and symptoms may include a decrease in

visual acuity, leucocoria, ophthalmoplegia, and coloboma of the iris. Patients may have bilateral glaucoma, micro- or macrophthalmia, a large vitreous seeding, a vascularised fluffy mass in the posterior pole, and/or papilloedema. Intracranial lesion presents with signs and symptoms of raised intracranial pressure, i.e., headache, nausea, vomiting, lethargy, irritability, hydrocephalus and somnolence.²

Diagnosis can be made on the basis of eye examination, ultrasound, computed tomography (CT) scan and MRI.² Histologically, these tumours are shown to be undifferentiated and considered to be PNET, while pathologically, they are similar to Rb.² Dissemination of these tumours occurs in the sub-arachnoid space as PNETs spread via cerebrospinal fluid (CSF).⁶ MRI may show a midline mass that is relatively isointense with grey matter and shows enhancement with contrast. CT scan may also show it to be isodense with grey matter on dense contrast enhancement.⁶

The treatment of patients with TRb is usually multidisciplinary - enucleation of the affected eye is the mainstay. The treatment of intracranial mass varies from biopsy to complete resection. Radiosurgery of the cranial lesion and or craniospinal irradiation, with or without concurrent chemotherapy, may be used for residual, inoperable or metastatic lesions.² For effective treatment, close evaluation of leptomeningeal dissemination is required. Recent data suggests that the chances of the intracranial PNET may be reduced with neoadjuvant chemotherapy in the treatment of Rb, and may also diminish the size of the intracranial mass in cases of TRb.^{5,6} According to another study, TRb is potentially curable with conjugate intensive chemotherapy.⁷

The prognosis of the survival rate in unilateral Rb is 93% at 5 years and 92% at 10 years, while for bilateral Rb it is 92% at 5 years and 87% at 10. However, the risk of developing secondary non-ocular malignancy is higher in those with bilateral Rb.⁸ TRb has poor prognosis, especially when the tumour has distant metastasis. Once a lesion in the pineal

or sellar region is diagnosed, the average survival is 9.7 months in those treated adequately, whereas it falls to 1.3 months in those not properly treated.⁸

Several studies have found that patients who were diagnosed earlier and were asymptomatic at the time of diagnosis had a better survival rate than the symptomatic ones.^{1,3,4,7} Thus, it appears that screening all patients with Rb, especially those with the bilateral variety, may be beneficial. Cranial scanning is also advised in all those having positive family history.

Conclusion

Our patient was a rare presentation of the deadly syndrome, having sporadic, unilateral eye involvement with suprasellar neuroblastic lesion. He was inadequately treated due to lack of health awareness, and the refusal of the mother to proceed with enucleation of the affected eye. They left against medical advice, re-visited with dorsal spine metastases, and the child died due to aggressive extension of the disease.

References

1. Kivelä T. Trilateral retinoblastoma: a meta-analysis of hereditary retinoblastoma associated with primary ectopic intracranial retinoblastoma. *J Clin Oncol* 1999; 17: 1829-37.
2. Mouratova T. Trilateral retinoblastoma: a literature review, 1971-2004. *Bull Soc Belge Ophthalmol* 2005; 297: 25-35.
3. Ibarra MS, O'Brien JM. Is screening for primitive neuroectodermal tumors in patients with unilateral retinoblastoma necessary? *J AAPOS* 2000; 4: 54-6.
4. Paulino AC. Trilateral retinoblastoma: is the location of the tumor important? *Cancer* 1999; 86: 135-41.
5. Shields CL, Meadows AT, Shields JA, Carvalho C, Smith AF. Chemoreduction for retinoblastoma may prevent intracranial neuroblastic malignancy (trilateral retinoblastoma). *Arch Ophthalmol* 2001; 119: 1269-72.
6. Provenzale JM, Gururangan S, Klintworth G. Trilateral retinoblastoma: clinical and radiologic progression. *AJR Am J Roentgenol* 2004; 183: 505-11.
7. Dunkel IJ, Jubran RF, Gururangan S, Chantada GL, Finlay JL, Goldman S, et al. Trilateral retinoblastoma: potentially curable with intensive chemotherapy. *Pediatr Blood Cancer* 2010; 54: 384-7.
8. James SH, Halliday WC, Branson HM. Best Cases from the AFIP: trilateral retinoblastoma. *Radiographics* 2010; 30: 833-7.