

Trilateral Retinoblastoma-A Case Report

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Abstract

A sporadic case of trilateral retinoblastoma in a male child of 20 months is described using clinical and imaging approaches. Attempts were made to find out a tumour marker by analysing human chorionic gonadotrophin (hCG), alpha-feto protein (AFP), carcinoembryonic antigen (CEA), and lactic dehydrogenase (LDH) in blood and cerebrospinal fluid (CSF). Only LDH was elevated in CSF and the rest were normal. Retinoblastoma gene could not be isolated in this patient. It is proposed that LDH in CSF should be analysed in patients with bilateral retinoblastoma who had normal brain scan initially. If LDH level in CSF is elevated, the patient should be periodically monitored by non-invasive imaging of the brain to detect intracranial tumour at an early stage.

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Key words: Lactic dehydrogenase, Pineoblastoma, Retinoblastoma gene

Introduction

Retinoblastoma is the third most common tumour in childhood. It is inherited genetically. It is the first human cancer for which the gene 13q14.11 has been isolated.¹ Development of a midline intracranial tumour in association with bilateral retinoblastoma is known as trilateral retinoblastoma, which is a rare tumour. Here we report a sporadic case of trilateral retinoblastoma in a male child. Attempts were made to find out a tumour marker for trilateral retinoblastoma.

Case Report

In July 1995, the parents of a 12-month-old male child noticed a white reflex in the left eye. Ophthalmological examination showed periorbital oedema, buphthalmos with corneal oedema, extensive rubeosis, white reflex at the pupil and a retinoblastoma mass superiorly in the left eye. The right eye had multiple retinoblastoma tumours which were multifocal. General and neurological examination revealed no abnormality. He was the first child born to non-consanguineous parents. None of the family members of the patient in the past three generations had suffered from any tumour involving the eyes or nervous system.

Ultrasonogram of both eyes showed evidence of calcification. Computed tomographic (CT) scan of the orbit showed bilateral retinoblastoma (Fig.1). CT scan of the

brain did not show any intracranial tumour. The left eye was enucleated. The optic nerve was invaded by the tumour beyond the lamina cribrosa but not upto the line of transection. Histopathological report confirmed the diagnosis of retinoblastoma. External beam radiation treatment was given for the right eye. Two months after radiation, an area of retinal detachment was noticed which indicated that the tumour was not quiescent. The patient was reviewed periodically.

Eight months after the first symptom, the child was referred to the neurosurgeon, for decreased physical activity, inability to stand or walk and associated urine and faecal incontinence for a duration of ten days. It was noted that he was drowsy, dehydrated and had tachycardia. In the right eye, there was no perception of light, had white reflex and multiple retinoblastoma tumours. The child had normal power in all four limbs. He had spasticity with hyper-reflexia in both lower limbs. There was no evidence of metastases in other systems.

Complete blood count and blood biochemistry were normal. Radiographs of the skull, spine, chest and ultrasonogram of the abdomen were normal. Follow-up CT scan of the brain revealed a hyperdense circular homogeneous enhancing lesion in the region of the pineal gland with hydrocephalus (Fig.2).

Ventriculo-peritoneal shunt was done to relieve the hydrocephalus. Only CT scan-guided biopsy of the pin-

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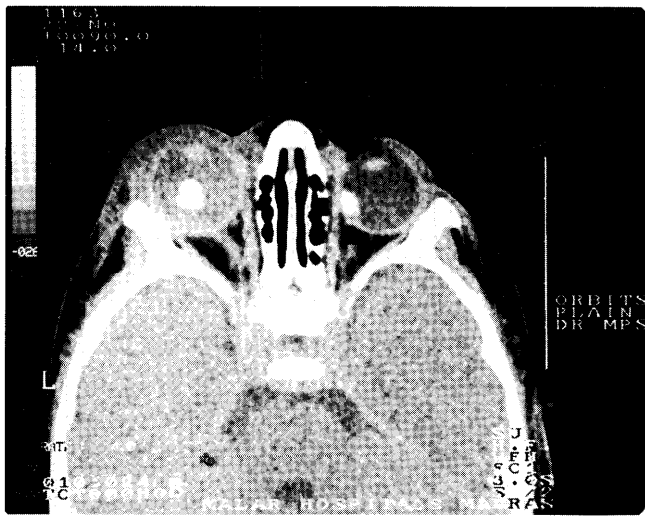


Fig. 1. Computed tomographic scan of the orbit showing bilateral retinoblastoma.

real gland tumour was done, since consent could not be obtained for craniotomy. Histopathology report showed a poorly differentiated pineal gland tumour. The blood and cerebrospinal fluid (CSF) were analysed for lactic dehydrogenase (LDH), human chorionic gonadotrophin (hCG), alpha-feto protein (AFP) and carcinoembryonic antigen (CEA). Raised levels of LDH were found in the CSF of about 158 u/100ml (normal range 20 to 45 u/100ml). Levels of other tumour markers, hCG, AFP and CEA were within normal limits. The blood of both parents were analysed for CEA and was found to be normal. Using Giemsa-Terminal-Gene (GTG) conventional banding techniques, the blood was analysed for retinoblastoma gene but it could not be isolated. The child gradually deteriorated and lapsed into coma and expired in July 1996.

Discussion

Sixty-four cases of trilateral retinoblastoma have been reported in literature. A few reports showed that retinoblastoma was unilateral.²⁻⁴ Midline intracranial tumour was reported to be located commonly in the pineal gland region. It was also reported in other regions like the sellar, suprasellar and parasellar areas.⁵⁻⁷ The majority was hereditary. Sporadic occurrence has been reported in a few reports.⁷ Incidence of trilateral retinoblastoma in children with bilateral retinoblastoma varied from 3% to 6%.^{7,8}

In those with a family history of retinoblastoma, the incidence was around 8% to 10%.^{7,8} Bilateral retinoblastoma occurred at a younger age group in those who developed trilateral retinoblastoma. The mean age at diagnosis of retinoblastoma varied from 3 to 7.2 months.^{7,8} In our patient it was diagnosed at 12 months. The mean interval between diagnosis of retinoblastoma and the development of intracranial tumour was 18 to 33 months

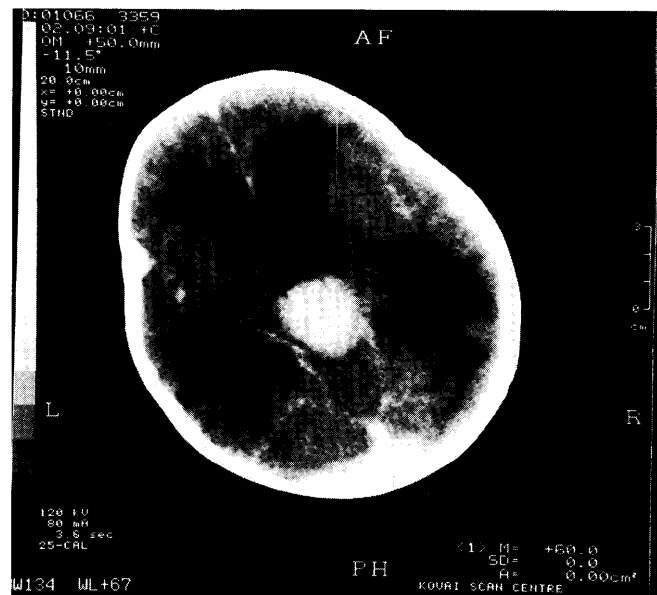


Fig. 2. Computed tomographic scan of the brain showing pineal gland tumour

(range 0 to 48 months). In our patient it was diagnosed after a period of 8 months.⁷

The mean time interval from diagnosis of trilateral retinoblastoma to death was between 6.6 and 11 months.^{7,9} The major cause of death was spinal metastases. Our patient expired after a period of 5 months probably because definitive therapy for brain tumour was not initiated. Mortality rates range from 70% to 100% despite aggressive therapy.⁶⁻⁹ It was reported that three children who were treated aggressively with systemic (cyclophosphamide and vincristine) intrathecal (methotrexate, hydrocortisone and cytarabine) chemotherapy and craniospinal irradiation in addition to therapy of the eye lesions had no active disease 1 to 8 years after diagnosis of the lesions.¹⁰ It was also reported that five patients who had shown complete or dramatic response to therapy as documented by CT scan of the brain, had local intracranial tumour present at autopsy, suggesting the need for more aggressive local therapy.⁹

Raised levels of plasma CEA in unaffected family members of presumptively sporadic cases of retinoblastoma have been reported.⁷ In our case the plasma CEA levels were normal in both parents. Analysis of tumour markers, hCG, AFP, CEA and LDH in blood and CSF of the patient showed increased levels of LDH in the CSF while the rest were normal. Elevated levels of LDH in aqueous are suggestive of retinoblastoma in the eye.¹¹ In our case LDH was significantly elevated in CSF. Hence, it is proposed that elevated levels of LDH in CSF in patients with bilateral retinoblastoma may be taken as an indicator of development of intracranial tumour and may be used as a tumour marker.

It was reported that most patients whose karyotypes

have been examined showed no evidence of chromosomal defects.” In our patient using banding techniques, the retinoblastoma gene could not be isolated. Review of literature showed that the retinoblastoma gene in cases of trilateral retinoblastoma was not isolated in a single case.

It is suggested that in patients with bilateral retinoblastoma, whose brain imaging is normal, LDH level should be analysed in CSF and a genetic screening should be done to identify the retinoblastoma gene. If LDH level in CSF is elevated, the patient should be periodically monitored by non-invasive imaging of the brain to detect the occurrence of brain tumour at an early stage. Early detection of intracranial tumour and immediate aggressive treatment of the lesion may reduce the mortality rate of trilateral retinoblastoma.

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