Chemotherapy Related Optic Neuritis

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ABSTRACT

In children, most cases of optic neuritis are immune-related. Less frequently, it may also be due to demyelinating disorders. Other secondary causes such as infection of adjacent structures or infiltration are even rarer. The occurrence of optic neuritis in children on chemotherapy also has not being extensively reported. We report a case of bilateral optic neuritis in a young girl with subacute visual loss after receiving systemic chemotherapy for embryonal ovarian carcinoma.

Keywords: Optic neuritis, bilateral, paediatric, subacute visual loss, chemotherapy

INTRODUCTION

Optic neuritis is an acute inflammation involving the optic nerve.[1] The incidence in children is relatively rare with an onset at the mean age of 9-10 years old.[1] In the post puberty period, it is twice more common in females but shows no sexual preferences in the prepubertal children.[2] There are usually secondary causes for optic neuritis in children with antecedent systemic viral infections being the most common.[1] Two thirds of patients had viral illnesses before the symptomatic visual loss.[2] In general, paediatric optic neuritis has good visual prognosis, particularly when in the young less than 6 years of age and with normal finding on magnetic resonance imaging (MRI) of the brain. Paediatric optic neuritis which occurs after systemic chemotherapy is not extensively reported in the literature. This ocular toxicity might be underestimated and overlooked by physicians as there are many other toxicities of chemotherapy that have to be managed first. Chemotherapy agents such as paclitaxel, carboplatin, cisplatin and etoposide have been reported to have caused many ophthalmic side effects.[3] Peripheral neuropathy is more common in cisplatin administration and central nervous system effects are rare.[4] Apart from chemotherapy, tumour metastases to the eye or paraneoplastic syndrome served as other diagnostic differentials. Breast and lung carcinoma are the most common primary tumours that can metastasize to the eye, specifically to the choroid and adnexa. Paraneoplastic syndromes are the least common effect and usually cause cancer associated retinopathy (CAR). Most common causes are small cell carcinoma of the lung and neuroblastoma in adult and children respectively.[5] Other carcinomas such as ovarian and breast cancers, have also been reported to cause CAR.[6] In paraneoplastic syndromes, the symptoms usually precedes months to years before the first manifestation of the primary carcinoma itself.[7]

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Case Report

A 12-year-old Iranian girl with underlying right embryonal ovarian carcinoma presented with sudden onset of bilateral eye pain and redness for 2 weeks. The pain was aggravated by eye movement. Prior to these acute symptoms, she experienced gradual blurring of vision after she was started on chemotherapy which consists of bleomycin, etoposide and cisplatin four weeks ago. There was no ophthalmic assessment done prior to chemotherapy and this was the first presentation. There was no history of viral illnesses prior to the onset of symptoms. She was newly diagnosed with embryonal carcinoma of the right ovary when she presented with acute abdomen. At presentation, there were metastases to both her adrenal glands and breasts.

Ocular examination revealed reduced visual acuity of 6/24 and N12 for both eyes with absence of relative afferent pupillary defect (RAPD). Anterior segment findings were normal bilaterally and there are no lens opacities. There were bilateral optic discs swelling with blurred disc margins (Figure 1). No other abnormalities were noted in the posterior segment. Confrontation visual field testing revealed generalized constriction of the visual field bilaterally and this corresponded with the findings on Goldmann perimetry. The colour vision test via D15 is normal. MRI of the brain and orbits revealed heterogenous signal in the left optic nerve

within the optic canal which showed subtle enhancement on post-gadolinium (Figure 2). No abnormal signal in the brain parenchyma to suggest demyelinating disease.

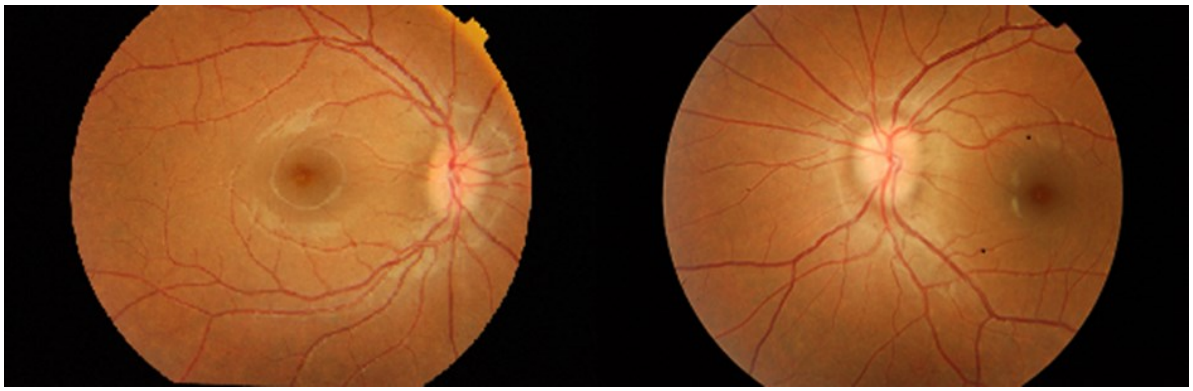

Figure 1 Bilateral optic discs swelling with blurred disc margins

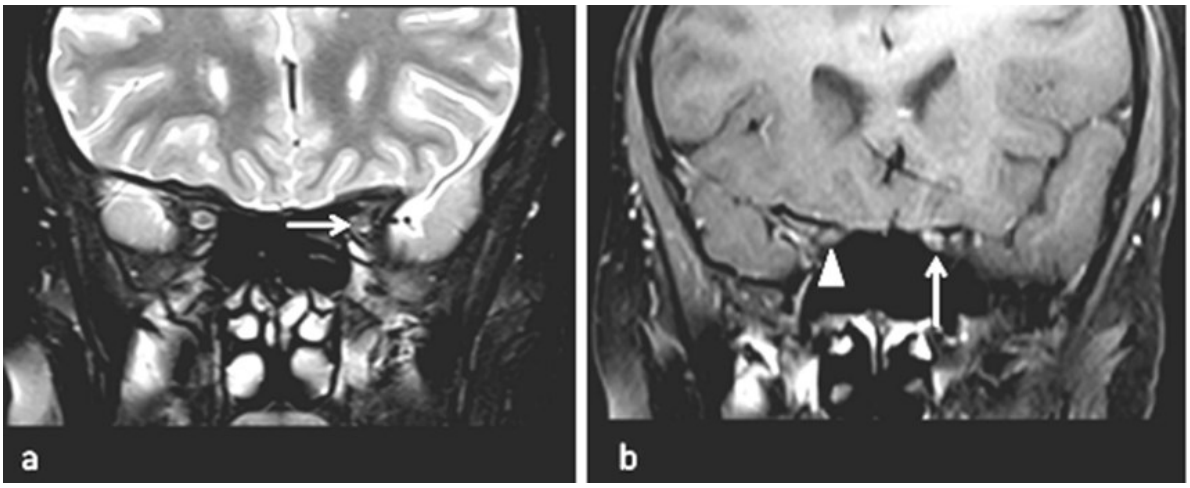

Figure 2. MRI brain and orbit of the patient on (a) coronal T2 fat saturation amd (b) coronal post-gadolinium T1 fat saturation showing heterogenous signal in the left optic nerve within the optic canal with subtle enhancement of the nerve on post-gadolinium (white arrow) as compared to the right optic nerve (white arrowhead).

The decision to treat was made after discussion with the oncology team involved in managing this patient. She was admitted and started on intravenous methylprednisolone 250 mg four times a day for 5 days. Subsequently, she was switched to oral prednisolone 55 mg daily (1 mg/kg/day) followed by a slow tapering dose over 2 months duration. After a week of treatment, her visual acuity improved to 6/9 bilaterally with improvement in her visual fields by confrontation test and Goldmann perimetry (Figure 3).

Discussion

Optic neuropathy, specifically optic neuritis, is one of the rare toxic effects of systemic chemotherapy. It is not being extensively reported in the literature particularly pertaining to the paediatric age group. In children, optic neuritis is usually bilateral and occurs following common viral infection in childhood. This patient had received systemic chemotherapy which consists of cisplatin, etoposide and bleomycin. Among these three agents, cisplatin is the mostly likely culprit to cause toxic optic neuritis. Despite being more common compared to other chemotherapy agents, only few literature reported optic neuritis as being a rare side effect of cisplatin.

Cisplatin is an alkylating agent with an established role for the treatment of ovarian carcinoma. With high single dose and cumulative dose, optic neuritis as well as retrobulbar neuritis have been reported. This is particularly with intra-carotid administration that can lead to severe toxicity to the eye and the orbit.[3] Cisplatin is thought to cause neurotoxicity through neuronal apoptosis when it enters the dorsal root ganglia. In this patient, her symptoms appeared 6 weeks after initiation of cisplatin based chemotherapy. The absence of intraorbital tumour and the timing of chemotherapy prior to symptoms, suggests that cisplatin is implicated in her diagnosis of optic neuritis. Cisplatin has been reported to cause delayed optic neuritis with onset at 13 weeks after it was discontinued.[4] It is postulated in this case that cisplatin induce neuropathy by causing microvascular damage and hence the possible role of angiogenic agents for prevention. There is no single and specific case report that looked into etoposide and bleomycin as causing optic neuritis.

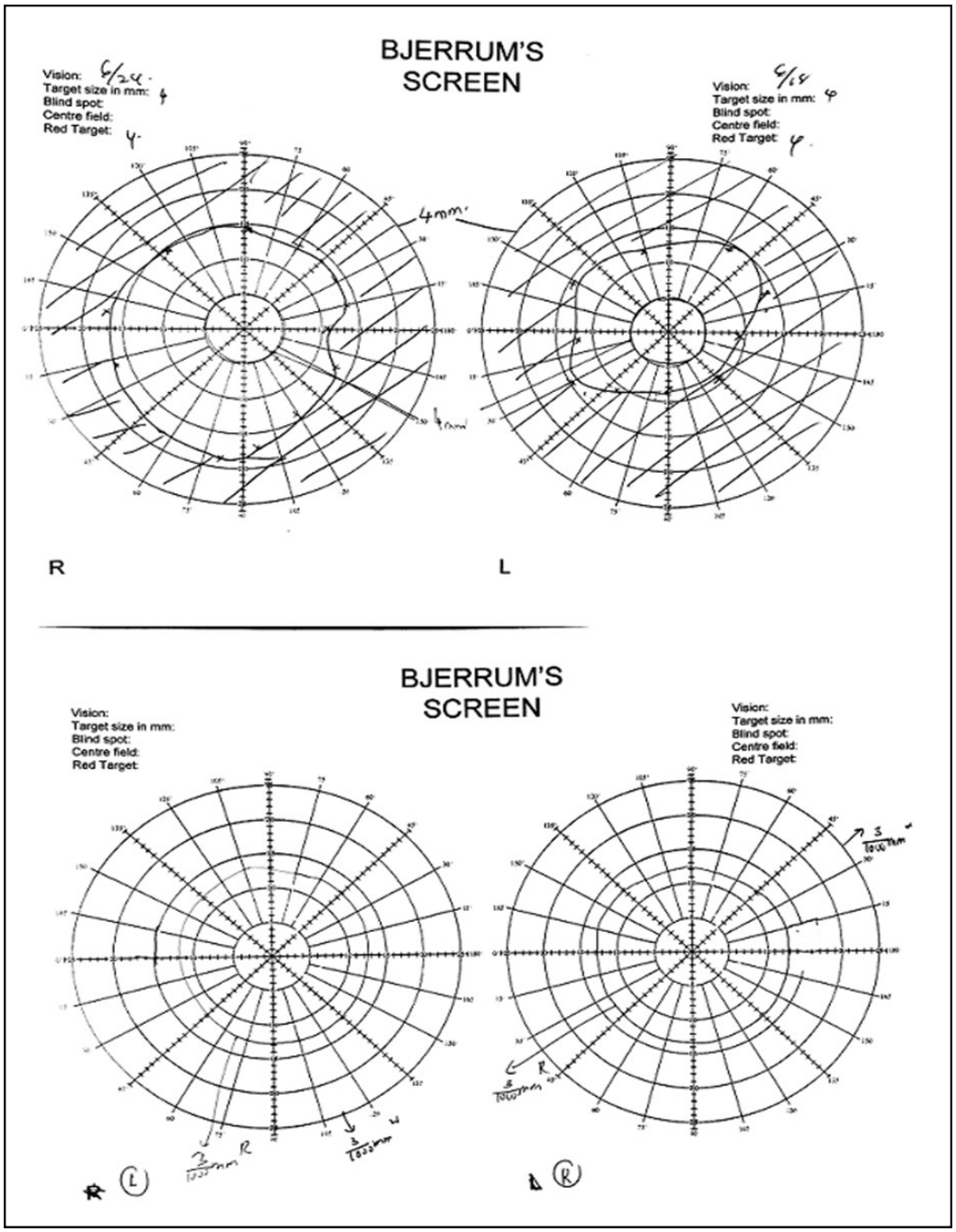

Figure 3. Pre-treatment (top) and post treatment (bottom) Goldmann perimetry showing marked improvement in patient's visual field

However, etoposide has been reported to cause central retinal artery occlusion secondary to thrombosis when given intra arterially. In combination with cisplatin, it exerts synergistic effect and causes retinal toxicities.[8] Meanwhile for bleomycin, it is noted to cause cortical blindness with concurrent usage with cisplatin.[9]

Currently, there are no guidelines for monitoring of visual system when patient is on cisplatin. However, being vigilant about the possibility of optic neuritis and careful follow up are essential for prevention of side effects. The reduced vision in this patient developed after she started receiving chemotherapy for her ovarian carcinoma. However, she did not seek opinion from an ophthalmologist as she did not complain of eye pain at that point in time. Although no eye assessment was done prior to chemotherapy, the findings of bilateral optic discs swelling with blurred disc margins were suggestive of optic neuritis. MRI orbit was done to exclude possibility of metastases to orbit and optic nerve compression by tumour cells. The imaging study showed changes suggestive of optic neuritis without metastatic lesion. Hence, patient was diagnosed as having optic neuritis and treatment with steroids was commenced.

There is no specific treatment guideline for paediatric optic neuritis. Treatment is mainly based on The Optic Neuritis Treatment Trial (ONTT) although this treatment guideline is focused on adults.[10] In severe cases involving both eyes, treatment with intravenous methylprednisolone 10-30 mg/kg/day is proposed to speed up the recovery process. Slow tapering of oral prednisolone

over 1-2 months duration is recommended in children because of high rates of relapses if tapering being made too quickly. According to this regime, more than half of those children affected recovered to 6/6 vision earliest within 72 hours of initiating therapy up to several weeks after prolonged steroid tapered.[1]

In this patient, visual acuity improved from 6/24 and N12 for both eyes to 6/6 and N6 after one week of treatment. She has since completed a total of 8 weeks of oral prednisolone. The bilateral optic disc swelling has completely resolved when she was seen 2 months later.

Conclusions

Optic neuritis is rare in children. However, this diagnosis should still be considered when they present with visual loss while receiving systemic chemotherapy. Visual acuity should be monitored when patient is on chemotherapy and any deterioration should alert the attending physician the possibilities of optic neuritis.

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