

Case Report

Vincristine-induced unilateral ptosis in a child with Wilms' tumor

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This report describes the successful management of vincristine-induced unilateral ptosis with pyridoxine and pyridostigmine in a three year old girl with Stage 2a Wilms tumor. Vincristine as an antineoplastic drug causes neurotoxicity frequently. We report here about a 3-year-old girl having a vincristine-induced cranial polyneuropathy and a complete remission due to the therapy with pyridoxine and pyridostigmine. The 3-year-old girl was diagnosed with a Wilms tumor. Following nephroureterectomy she was treated with four cycles of actinomycin D (250 mg/m²), six cycles of adriamycine (20 mg/m²), six cycles of etoposide (100 mg/m²) and nine cycles of vincristine sulphate (1.4 mg/m²). One day after the last vincristine sulphate treatment, she developed unilateral ptosis without pupillary or other oculomotor dysfunction. A neuroprotective and neuroregenerative treatment of this vincristine-induced cranial neuropathy was attempted with pyridoxine (150 mg/m²/dayper oral bid) and pyridostigmine (3 mg/kg/dayper oral bid). The unilateral ptosis markedly improved after two weeks of pyridoxine and pyridostigmine treatment and completely resolved after 4 weeks.

Key words: Ptosis, vincristine sulphate, Wilms' tumor, pyridoxine, pyridostigmine.

INTRODUCTION

Vincristine sulphate (VCR) is a vinca alkaloid widely used in the treatment of neoplastic diseases, including lymphoma, leukemia, and solid tumors. The neurotoxicity of VCR is well recognized and is a limiting factor for the administration of the drug (Ozyureket al., 2007; Mulleret al., 2004). In a previous Pediatric Oncology Group study, 3.6% patients had significant toxicity (Chauvenet et al., 2003). The pathogenesis of neuropathy is primarily due to the structural changes in the microtubules of peripheral nerves induced by VCR which interferes with axoplasmic transport leading to a loss of neuronal reflexes (Moudgil and Riggs, 2000). Here, we describe the treatment of a 3-year-old girl with Wilms' tumor who showed complete recovery of vincristine-induced unilateral ptosis.

CLINICAL CASE REPORT

A 3-year-old girl presented with a left upper abdominal mass. The mass was palpable and elicited no pain on palpation. Her past medical history was unremarkable. There were no previous clinical symptoms of neuropathy or family history of Charcot-Marie-Tooth or other hereditary neuropathies. Computed tomography (CT) scan examinations revealed a mass in the left kidney. Left-sided nephroureterectomy was performed and pathologic examination revealed Wilms' tumor. All of the pretreatment hematological assessments were normal. The patient was treated with four cycles of actinomycin D (250mg/m²), six cycles of adriamycine (20 mg/m²), six cycles of etoposide (100 mg/m²) and nine cycles of VCR (1.4 mg/m²). One day after the last VCR treatment, she developed unilateral ptosis without pupillary or other oculomotor dysfunction (Figure 1). The cumulative VCR dose was 7.5 mg (12.6 mg/m²). The neurologic examination revealed a unilateral ptosis without ophthalmoplegia. Pupillary and corneal reflexes were

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Figure 1. Unilateral ptosis developing after an accumulated dose of 7.5 mg of vincristine.



Figure 2. Complete resolution of unilateral ptosis after 4 weeks of pyridoxine and pyridostigmine treatment.

normal, as were as the remaining neurologic findings, including deep tendon reflexes and sensibility. Ophthalmologic/ophthalmic examination confirmed that visual acuity and fundus region were normal. Cerebrospinal fluid was clear with normal pressure (80 mmH₂O), glucose (72 mg/dl), and protein (30 mg/dl) levels and no atypical cells. Magnetic resonance imaging of the brain was normal. VCR toxicity was suspected. Pyridoxine (150 mg/m²/day per oral bid) and pyridostigmine (3 mg/kg/day per oral bid) were used in the treatment of VCR-neuropathy. There was considerable reduction in ptosis following two weeks of pyridoxine and pyridostigmine treatment. The therapy was continued and there was complete resolution within four weeks (Fig. 2).

DISCUSSION

VCR is a commonly used chemotherapeutic agent for different malignancies; neural toxicity is a limiting factor for the administration of the drug (Duman et al., 2005). The neurotoxicity is dose related and cumulative with repeated dosage such that the drug therapy has to be stopped after a cumulative dose of 30 to 50 mg. Symptoms usually appear 2 to 19 weeks after the commencement of VCR (Bay et al., 2006). The neurotoxicity is usually reversible on interruption of the therapy, but the recovery is slow and takes several months (Legha, 1986). Severe neurotoxicity is rarely seen with current chemotherapy regimens, although severe neurotoxic reactions may be seen if the patient is hypersensitive to this drug, if there is pre-existing liver dysfunction or a hereditary neuropathy, or if other drugs (such as isoniazid, allopurinol, erythromycin, phenytoin and itraconazole) are concomitantly administered (Duman et al., 2005; Schiavetti et al., 2004). However in

the present case, the cumulative dose of VCR was fairly low, with no apparent drug interactions. Familial history was insignificant and did not reveal any hereditary disorders/conditions.

Bilateral ptosis is the most common feature of VCR-induced cranial neuropathy (Ozyurek et al., 2007; Muller et al., 2004; Bay et al., 2006). Recently, several authors reported unilateral ptosis as one of the features of VCR-induced polyneuropathy (Dejan et al., 2009; Lash et al., 2004; Gursel et al., 2009). Gursel et al. (Gursel et al., 2009) reported a case of 4-year-old girl who developed unilateral palpebral ptosis during chemotherapy for acute lymphoblastic leukemia. Ptosis was noted on the 45th day of therapy and VCR was last administered on the 28th day of the protocol (17 days following the last injection (sixth/cycle) of VCR). VCR-induced unilateral palpebral ptosis is a novel finding. According to our knowledge, our case is the third instance of VCR-induced unilateral ptosis without other clinical signs of cranial or peripheral neuropathy in the literature. Ptosis can restrict and even block normal vision, and if a dropping eyelid is left uncorrected, it can lead to amblyopia (Lash et al., 2004). Neuroprotective and/or neuroregenerative agents have been sought after as an effective therapy for treating such complications. Recently, several authors reported full recovery of VCR-associated bilateral ptosis after treatment with usual dose of pyridoxine (150 mg/m² orally twice daily) and pyridostigmine treatment (3 mg/kg orally twice daily) (Ozyurek et al., 2007; Muller et al., 2004; Bay et al., 2006). Pyridoxine and pyridostigmine revealed to be a successful combination for unilateral ptosis which developed as a side effect of vincristine sulphate administration for Wilms tumor. The patient completely recovered 4 weeks after initiation of pyridoxine and pyridostigmine. Both agents were given for 4 weeks and were without any side effects. Even though a spontaneous recovery cannot be excluded, the fast reco-

very after the mentioned treatment leads us to believe that it was attributed to pyridoxine and pyridostigmine.

CONCLUSION

We suggest that pyridoxine and pyridostigmine treatment may safely and effectively be used in the treatment of VCR-induced ptosis.

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