

# Vincristine Induced Isolated Bilateral Ptosis in a Child with Wilms' Tumour: Case Report with Review of Literature

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## Abstract

Vincristine is used in the treatment of solid tumours, lymphoma and leukemia in children. The dose-limiting toxicity is its neurotoxicity. We describe a three year old girl with Wilms' tumour who developed isolated vincristine-induced bilateral ptosis and recovered on treatment with pyridoxine and pyridostigmine.

**Keywords:** Ptosis; Pyridoxine and Pyridostigmine; Vincristine

## Introduction

Vincristine is used in combination with other agents in the treatment of paediatric malignancies. Cranial nerve palsies involving oculomotor are seen rarely with ptosis and ophthalmoplegias being the most common manifestations, usually associated with polyneuropathy [1]. We herein describe a three year girl with Vincristine-induced isolated bilateral ptosis without associated polyneuropathy causing diagnostic dilemma. Complete recovery of ptosis was achieved following treatment with pyridoxine and pyridostigmine. To the best of our knowledge this is a first case of isolated bilateral ptosis of Vincristine induced neuropathy.

## Case Report

A 3 year girl with Right sided Wilms' tumour stage III was started on DD-4A chemotherapy according to current clinical oncology group chemotherapy regimen following laparotomy and right nephrectomy. Child developed bilateral ptosis following fifth dose of weekly Vincristine (1.5 mg/m<sup>2</sup>) (Figure 1). Neurological examination revealed bilateral ptosis without ophthalmoplegia with normal pupillary and corneal reflexes. Rest of neurological examination was normal. There was no feature of autonomic neuropathy. Cerebrospinal fluid analysis showed normal protein, sugar and no cellular response. She was not on any other drugs. Complete blood picture, serum electrolytes and liver function tests were normal. Chemotherapy was deferred and pyridoxine (3 mg/kg Twice daily, per orally (BID, PO) and pyridostigmine (150 mg/m<sup>2</sup> BID, PO) were started. Bilateral ptosis improved markedly after 10 days of treatment and ptosis completely resolved after 3 weeks (Figure 2). Both the agents were given for 6 weeks and were well tolerated without any side-effects. There was no recurrence following cessation of pyridoxine and pyridostigmine. Vincristine was reinitiated in fifty percent of previous dose without recurrence of ptosis.

## Discussion

Vincristine is commonly used in the treatment of Paediatric solid tumours. Neurotoxicity is most important dose limiting toxicity. Central involvement is rare because vinca alkaloids act by binding intracellular tubulin, and therefore, difficulty in crossing the blood-brain barrier [2]. Incidence of neurotoxicity reported from India (50%) is much higher as compared to other countries (3 to 13%) [3,4]. This may partly be accounted for by the fact that the Indian patients who developed neurotoxicity were all severely malnourished, predisposing them to neurotoxicity [5]. Vincristine-induced neurotoxicity manifests as loss of deep tendon reflexes, neuritic pain, paresthesias and wrist and foot drop. Less frequently, cranial nerve palsies, transient cortical

blindness, oculomotor nerve dysfunction, jaw pain, facial palsy, sensorineural hearing loss and laryngeal nerve paresis have been attributed to vincristine [6].

Time of onset of symptoms and signs is mostly after two weeks or later, with deep tendon reflexes usually first to be involved [7]. Ptosis as initial symptom of toxicity is rare with overall reported incidence of about 2.5% [8]. Isolated unilateral ptosis as first sign of vincristine induced neurotoxicity has been reported only in case previously [9]. The presentation of isolated bilateral ptosis as initial symptom is unique to our case and prompted withholding of drug and early treatment, avoiding severe toxicity.

More than one-third of patients with Vincristine induced



Figure 1: Child with bilateral ptosis.

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**Figure 2:** Complete recovery following treatment.

neuropathy develop signs of autonomic nervous system dysfunction characterized by orthostatic hypotension, constipation, paralytic ileus, urinary bladder dysfunction, and erectile impotence [10]. In our case there was no such involvement. Diagnosis of Vincristine neurotoxicity in this case was made on the basis of the following: exclusion of other causes, the timing of the symptoms (after chemotherapy), negative CSF examination and improvement in ptosis after pyridoxine and pyridostigmine treatment. The neuroprotective effect of pyridoxine against Vincristine-induced neuropathy has been examined in a preclinical murine model, with promising results [11]. Most of the neuropathic symptoms of vincristine toxicity are reversible within months or years after adjusting the dosage or achieving elimination of vincristine, although some are permanent.

## Conclusion

Children receiving vincristine need to be monitored closely for the development of usually reversible neurotoxicity. Combined treatment with pyridoxine and pyridostigmine may hasten the clinical improvement even in severe cases.

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