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Unilateral Ptosis in a Child with Wilm's Tumor Induced by Vincristine

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Abstract

Vincristine is a chemotherapy drug belonging to the group of Vinca alkaloids which also includes vinblastine and vindesine. It is used in hematological malignancies and solid tumors. The Vinca alkaloids are neurotoxic, usually causing peripheral neuropathy, and rarely cranial neuropathies. We report a case of a 33-month-old male child diagnosed with Wilms' tumor, who had an isolated unilateral right ptosis following vincristine, with a good improvement after stopping it.

Keywords

Wilms' Tumor, Vincristine, Neuropathy, Ptosis

1. Introduction

Vincristine is a chemotherapy drug used in combination with other agents for the treatment of solid tumors such as Wilms' Tumor, lymphoma, and leukemia. Neurotoxicity is one of the very common complications of anticancer agents and is therefore a factor dose-limiting. Eyelid damage is frequent and varied, most often represented by ptosis, oculomotor paralysis, facial paralysis, and corneal hyperesthesia [1]. We report the case of a 33-month-old male, who present Wilm's tumor treated with vincristine and dactinomycin, who developed unilateral right ptosis after the fifth dose of vincristine. Complete recovery of ptosis was achieved after stopping the chemotherapy.

2. Case Report

A 33-month-old boy was diagnosed with a right Wilms tumor and treated with chemotherapy according to the medium-risk stage II on GFA Nephro 2005 Pro-

tocol. He received neoadjuvant chemotherapy including vincristine (1.5 mg/m^2) and Dactinomicyn (45 mcg/j) for 6 weeks. A nephroureterectomy was performed later. Vincristine was administered after the operation, following the chemotherapy protocol. One week later, the child was admitted to our department for unilateral right ptosis after 6 doses of weekly vincristine (1.5 mg/m^2). At this time, the child has received a total of 7.5 mg/m^2. There were no previous clinical symptoms of neuropathy and no history of inherited neuropathies.

Neurological examination revealed unilateral ptosis without ophthalmoplegia, and pupillary and corneal reflexes were normal. The remaining physical exam was normal. An ophthalmologic examination confirmed that visual acuity and the fundus were normal. Biological tests including vitamins (B1, B1, B6, and B12) and serum ionogram, also cranial Magnetic Resonance Imaging (MRI) and orbital ultrasonogram to exclude other causes of ptosis were without abnormalities, thus vincristine toxicity was suspected as the cause of the third cranial nerve paresis. In addition to vincristine, the patient was treated with six cycles of etoposide (150 mg/m^2) and carboplatin (200 mg/m^2), five cycles of cyclophosphamide (150 mg/m^2), and adriamycin (150 mg/m^2). The treatment was stopped; therefore the ptosis was completely resolved after 4 weeks.

3. Discussion

The chemotherapeutic effectiveness of vincristine was first reported in 1962 [2], and with its increased use, the incidence of reported neurologic side effects has also increased. Vincristine-Induced Neuropathy (VIN) spans a broad spectrum of dysfunctions that fall into three categories: sensory, motor, and autonomic neuropathy. The most common is peripheral sensory and motor nerve neuropathy characterized by numbness, paresthesia, impaired balance, weakened tendon reflexes, and altered gait [3]. Autonomic dysfunctions include constipation, paralytic ileus, urinary retention, and orthostatic hypotension [4] [5]. Furthermore, several cranial nerve palsies and some Central Nervous System (CNS) toxicities have been reported [6] [7]. All cranial nerves may be affected, trigeminal and vagus nerves are frequently implicated [8]. Among ocular findings, ptosis and ophthalmoplegia may serve the clue [9]. Bilateral ptosis is the most common feature of vincristine-induced cranial neuropathy. Recently, several authors reported unilateral ptosis as one of the features of this polyneuropathy [10]. The pathogenesis of vincristine-induced neuropathy is explained by vincristine which prevents microtubules and separates the chromosome pairs during mitosis. This reduces the rate of cell divisions thereby inhibiting tumor growth. Meanwhile, this causes the microtubules to lose function in the maintenance of cell shape and scaffolding, causing axonopathy through axonal transport impairment, and eventually leading to axonal degeneration and death [11]. Vincristine neurotoxicity is related to the dosage and frequency of administration. Its symptoms usually start after 2 to 19 weeks of vincristine therapy [12]. In children from 3 to 11 years old who receive chemotherapy for Wilms tumor, the predicted neurotoxicity risk at the cumulative dose of 25 mg/m^2 is 30% [13]. Our patient had

developed unilateral right ptosis after completing 6 doses of weekly vincristine (1.5 mg/m^2). He received only a cumulative dose of 6 mg/m of vincristine when the right ptosis developed. This dose was lower than most cases from earlier reports. There are various situations in which neurotoxicity caused by vincristine may be increased, such as hypersensitivity to this drug, if there is pre-existing liver dysfunction, or hereditary neuropathy, or if other drugs (such as isoniazid, allopurinol, erythromycin, phenytoin, and itraconazole) are concomitantly administered [14] [15]. Our patient had no known risk factors as mentioned for vincristine-induced neurotoxicity. There was no history of neuropathy in the family. The patient was not taking any other medications apart from chemotherapy, and his liver function was normal during the course of chemotherapy. The definitive diagnosis of drug-induced neuropathy depends on the exclusion of other etiologies that may produce a similar clinical picture. The neurotoxicity in our patient has been attributed to vincristine, as the neurological symptoms could be temporally linked to its administration. Further, withholding vincristine alone led to improvement in the ptosis. Laboratory testing, magnetic resonance imaging of the brain, and orbital ultrasonogram were normal. Most of the neuropathic symptoms of vincristine toxicity are reversible within months or years after adjusting the dosage or achieving the elimination of vincristine, although some are permanent [16]. In our patient, ptosis improved markedly after 20 days and completely resolved after four weeks. In chemotherapy-induced peripheral neuropathy, there are no general rules as to when the drug therapy should be changed or even stopped. It is considered that if chemotherapy can cure the patient's cancer, chemotherapy-induced neurotoxicity might be tolerated without changing the effective-dose regimen. The present patient had only mild neurologic complications, thus the protocol was continued without modifications and vincristine was discontinued; no drug was administered for ptosis [17]. Recently, several authors reported full recovery of VCR-induced polyneuropathy after treatment with the usual dose of pyridoxine and pyridostigmine [14] [18]. In all of these reported patients, treatment was well tolerated and no side effect was documented. The authors also used the same treatment regimen in the present cases. It was well tolerated without documented side effects by the patient.

4. Conclusion

Ptosis is a rare complication of vincristine chemotherapy. We propose to keep vincristine-induced neuropathy as a differential diagnosis in any cancer patient receiving vincristine and who develops neurological signs on chemotherapy. Other causes of ptosis must be excluded.

Conflicts of Interest

The authors declare there are no conflicts of interest.

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