

Vincristine Induced Bilateral Ptosis in Wilms' Tumor: Youngest Case Report

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Received: December 17, 2017; **Published:** January 25, 2018

Abstract

Neuropathy is a known side effect of vincristine. This reversible neurological dysfunction is often missed and not treated. Here, we describe the youngest case of bilateral ptosis in an 8-months-old female child diagnosed with Wilms' tumor of right kidney.

Keywords: Wilms' Tumor; Vincristine; Neuropathy; Ptosis

Introduction

Wilms' tumor is a common malignant tumor of kidney in childhood. It has multimodal treatment in form of chemotherapy, surgery and radiotherapy. Vincristine and actinomycin D form backbone of chemotherapy regimens. Peripheral and autonomic neuropathies are common side effects of vincristine therapy. Here, we present an interesting case of bilateral ptosis in an 8-months-old female child diagnosed with Wilms' tumor (WT) of right kidney on United Kingdom Children's Cancer Study Group (UKCCG) protocol.

Case Report

An 8-months-old female infant presented with right flank mass, discovered incidentally by mother one day back while giving bath to the baby. The mass occupied right lumbar, right hypochondrium, umbilical and right iliac regions, with fullness of right renal angle; fingers could be insinuated under right costal margin. No evidence of calcification was present on plain abdominal roentgenogram. Ultrasonography showed a heteroechoic mass replacing the right kidney. A tru-cut biopsy was taken from right renal angle and was suggestive of Wilms' tumor. Contrast-enhanced computer tomography (CECT) showed heterogeneous enhancing solid lesion arising from mid and lower pole of right kidney. The patient was started on actinomycin D and vincristine based neo-adjuvant chemotherapy for 4 weeks. She later underwent right nephroureterectomy and lymph node berry-picking. On post-operative day 3, after auscultation of bowel sounds, vincristine dose was administered. On post-operative day 5, mother complained of baby not opening eyes properly. On examination, patient had bilateral ptosis (Figure 1). Other general physical and neurological examination were within normal limits. There was no peripheral neuropathy and tendon reflexes were normal. CECT brain was also normal study. Cerebrospinal fluid (CSF) and fundus examinations were within normal limits.



Figure 1: Bilateral ptosis.

Discussion

Vincristine is a chemotherapeutic agent, belonging to the class of vinca alkaloids (plant alkaloids). It acts by inhibiting tubulin polymerization, thus blocking mitosis. It is known to cause neuropathy, alopecia, anti-diuretic hormone secretion and a known vesicant. Neurotoxicity caused by vincristine may be peripheral, autonomic, encephalopathic or cranial. The autonomic and peripheral neuropathies are most commonly presented. All cranial nerves may be affected but Trigeminal and Vagus nerves are frequently implicated [1]. Among ocular findings, ptosis and ophthalmoplegia may serve the clue. In our patient, there was no history of familial neuropathy and the rest of the neurological examination was normal.

The exact pathophysiology for vincristine induced neurotoxicity is not known, but vincristine causing axonal degeneration by binding and inactivating tubulin has been proposed [2]. The vincristine induced neurotoxicity is usually mild. Its symptoms usually start after 2 to 19 weeks of vincristine therapy [3]. The neurotoxicity has been implicated to be more severe, if cumulative dose exceeds 12 mg [4].

Our patient had stage 2 intermediate risk Wilms' tumor and was treated as per UKCCG protocol [5]. She had a retroperitoneal biopsy proven Wilms' tumor, followed by 4 weeks of neoadjuvant actinomycin D and vincristine based chemotherapy and then surgery. She had symptoms after receiving 3.5 mg of vincristine @ 1.5 mg/m². She developed bilateral ptosis after completion of 5th week (4 pre-op and 1 post-op) of chemotherapy. There are various situations in which neurotoxicity caused by vincristine may be increased, like hereditary neuropathy, liver dysfunction, hyper-sensitivity to drug and concomitant use of allopurinol, isoniazid (INH), erythromycin, phenytoin, mitomycin C or itraconazole [6]. Our patient was on allopurinol (@ 100 mg/m²) and isoniazid [INH] (5 mg/kg/day) in view of our department protocol to give these drug chemoprophylaxis to all cancer patients so that to avoid side effects of hyperuricemia and prevent tuberculosis risk. The finding of bilateral ptosis may be attributed to side effect of vincristine. But before deciding upon drug toxicity, other causes should be excluded. The concomitant use of INH and allopurinol in our case, may have led to presentation at a lower cumulative dose of 3.5 mg of vincristine. Isoniazid can cause neuropathy by interfering with vitamin B6 and may have been the primary cause in this patient, or certainly contributed.

Pyridoxine (150 mg/m²) and pyridostigmine (3 mg/kg) based therapy has shown good results albeit depending on severity and duration of vincristine [7]. The neurotoxicity is generally reversible but may be slow to respond. Our patient was started on these agents; stopped INH and allopurinol and chemotherapy dose was reduced to two-third. Vincristine was not stopped completely as it forms part of complete chemotherapy schedule and also patient showed response to initiation of therapy. She showed good response and had complete resolution of bilateral ptosis in 3 weeks of therapy (Figure 2). She was given total 6 weeks of therapy and has been recurrence free. She has completed 17 weeks of post- op chemotherapy and is in close follow up.



Figure 2: Complete response.

The utility of modafinil, nescapine and glutamic acid in vincristine neuropathy has been reported but mechanism is uncertain [8]. The combination of thiamine and pyridoxine has been used for same [9,10]. Thiamine has role in nerve conduction and neural transmission and has been reported to reduce hyperexcitability and decrease alterations in sodium transport in injured dorsal root ganglion neurons in rats [11]. Thus, thiamine has role in neuronal regeneration and aids in balancing sodium transport. Pyridoxine has essential role in various biochemical synthetic pathways of neural function, including amino acid metabolism, neuronal protein and sphingolipid synthesis. Pyridostigmine is a quaternary synthetic ammonium agent, which increase acetylcholine concentration at neuromuscular junctions.

From 2008 to 2017 literature survey, to best of our knowledge, three cases of vincristine induced neurotoxicity presenting as ptosis has been reported in Wilms' tumor patients [12-14]. One of them had unilateral ptosis and all three showed good response to pyridoxine and pyridostigmine regimen. We followed the same therapy and had complete response. Also, our reported case is youngest in age so far reported in literature.

Conclusion

We propose to keep vincristine induced neuropathy as a differential in any cancer patient receiving vincristine and who develops neurological signs on chemotherapy. The pyridoxine and pyridostigmine regimen has shown good response in vincristine induced neuropathy and is the recommended therapy at present.

Conflict of Interest

None declared.

Source of Support

Nil.

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Volume 7 Issue 2 February 2018

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