英文題目：Vincristine Induced Polyneuropathy

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ABSTRACT

Vincristine is a vinca alkaloid used in treatment of lymphoma, and leukemia.[1] The neurological complications of vicristine was dose-limited. The mechanism of neurotoxicity is the result of structural changes in the microtubules of peripheral nerves and the interference of with axoplasmic transport(1). Peripheral, sensory-motor and autonomic neuropathy was common. 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(2).

We described a 55-year-old female who showed vincristine induced cranial and peripheral polyneuropathy and was improved after pyridoxine and pyridostigmine treatment but progressed to laryngeal nerve palsy and respiratory failure.

CASE REPORT

A 55-year-old girl was diagnosed diffuse large B cell lymphoma. She received chemotherapy including prednisolone 25mg (5 tab four times a day[2]), cyclophosphamide 1080(750 mg/m^2), vincristine 2mg (1,4 mg/m^2), and epirubicin 108 (75 mg/m^2) with triple intrathecal therapies . After the eighth dose of vincristine, she was presented with left drop foot (Fig. 1). There were no previous clinical symptoms of neuropathy and no positive history for inherited neuropathies. she cannot look toward right side and Neurological examination revealed right 6th palsy and peroneal palsy with normal pupillary and corneal reflexes. The remaining physical findings were normal. Cerebrospinal fluid examination and cranial MRI were normal. We arranged NCV and showed left peroneal neuropathy on a background of sensory motor polyneuropathy .We arranged PET for excluding lymphoma CNS involvement and showed negative finding. We would like to emphasize that the development of ptosis in the patient receiving a chemotherapy regimen including vincristine should raise the suspicion of toxic cranial neuropathy. She received 16 mg (6 mg/m^2) cumulative dose of vincristine before development of cranial palsy . We gave her treatment for attempt with pyridoxine (20mg p.o. BID) and pyridostigmine (30mg p.o. TID). The right 6 th palsy slightly improved after 7 days of pyridoxine and pyridostigmine treatment But still left drop foot. Both hand and feet numbness, left 3rd nerve palsy, dysphagia, areflexia developed after one week. We arranged brain MRI and CSF study again and showed negative finding. NCV showed extensive multiple mononeuropathy with autonomic dysfunction. We kept
pyridoxine (20mg p.o. BID) and pyridostigmine (30mg p.o. TID). Guillain-Barré syndrome was suspected and we arranged IVIG therapy (19 mg once daily for 5 days) and MTP pulse therapy (1000 mg).No symptom improved and she developed easily choking. She cannot swallow salvia. Then she died of sudden cardiopulmonary arrest.

DISCUSSION

Vincristine-induced neuropathy is usually mild, and severe toxicity is rare. It happened when more than recommended dose is given .Several drug was known to interact with vincristine and enhance its toxicity by inhibiting enzymes of cytochrome P-450 or blocking P-glycoprotein pumps and interfering with the metabolism of vincristine(3).Antifungals(azole), cyclosporine, isoniazid and nifedipine were discussed(3).Our patient did not use above agents. We diagnosed the following vicristine neurotoxicitis, by exclusion of other etiologies, the timing of symptom after chemotherapy, normal MRI and CSF examination and relief of right 6 th palsy after treatment of pyridoxine and pyridostigmine.

Our patient was treated with pyridoxine and pyridostigmine. pyridoxine and pyridostigmine had neuroptotective effect was controversial.Most of neurological vincristine toxicity was reversible within months or years after elimination. However , our patient improved after treatment for one week.(4)

Vincristine may induce cardiovascular automomic neuropathy .Our patient was died of sudden cardiopulmonary arrest. We didn't find any functional cardiac abnormalities but concomitant use of anthracycline and vincrsitine was considered.(4)

Some study recombinant human insulin-like growth factor-I as a potential neuroprotective agent against vincristine induced neuropathy in rat model by ameliorating vincristine induced gait disturbance folinic acid, vitamin B1, B6, isaxonine , glutamic acid were also discussed. Avoiding high peak vincristine concentrations by intravenous bolus injection was recommended.(4)

In conclusion, vincristine neurotoxity was common.We may avoid toxicity by avoiding over recommanded dose and drug interaction with vincristine. We may try pyridoxine and pyridostigmine. And other neuroprotecitve agent for vincristine neurotoxicity needed to be more studied. Some fatal toxicity such as cardiovascular automomic neuropathy, vocal cord palpsy needed to be concerned.

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Figure 1