Oculomotor Nerve Palsy Associated with Vincristine Treatment

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Neurotoxicity is a dose-limiting side effect of vincristine. It may be divided into four groups: peripheral neuropathy, autonomic neuropathy, encephalopathy and cranial neuropathy [1]. Cranial nerve palsies are seen less often than peripheral or autonomic neuropathies in patients treated with vincristine [2]. Although vincristine-induced neurotoxicity has been reported to affect nearly all the cranial nerves, effects on the trigeminal and vagus nerves have been reported most frequently [1]. Among the ocular findings, ptosis and ophthalmoplegias are the most frequent presentations in the majority of cases being affected bilaterally [3, 4]. In this article we report a case of unilateral oculomotor nerve palsy occurring after vincristine administration. A 62-year-old white woman was referred to our Hematology Clinic in November 1990 for evaluation because of a skin infiltration of her right leg which was diagnosed as a non-Hodgkin's lymphoma. The patient did not have any B symptoms and the skin lesion was of 3 months' duration. Previous medical history was unremarkable. Physical examination revealed a nodular-ulcerated lesion 6 cm in diameter surrounded by a diffuse erythema on the right leg. There was neither superficial lymph node enlargement nor organomegaly. Laboratory data showed: hemoglobin 10 g/dl, leukocyte count $5 \times 10^9/l$ with a normal differential, thrombocytes $2 \times 10^{11}/l$, ESR 62 mm/h. BUN, creatinine, uric acid, serum proteins and liver function tests and OGTT were within normal ranges. Blood haptoglobin, β_2 -microglobulin and fibrinogen levels were slightly elevated. With the reevaluation of the skin biopsy material, the lesion was diagnosed as a high-grade, T-cell, immunoblastic lymphoma. A CT examination of thorax, abdomen and pelvis was normal. Bone marrow biopsy excluded bone marrow involvement. The disease was diagnosed as a primary high-grade lymphoma of the skin and chemotherapy was initiated with a m-BACOD regimen with previously reported doses [5]. At the end of three courses of this treatment there was a partial regression of the tumor and then the patient received local-field radiotherapy resulting in further tumor regression. Because of poor patient compliance, further treatment had to be given as CHOP combined chemotherapy, instead of m-BACOD regimen [6]. A few days after the completion of the sixth course of CHOP treatment, the patient began to complain of peripheral paresthesias, which was followed by ptosis

of the right eyelid in a week. A neurological examination showed that the patient had a right oculomotor paralysis involving the levator, superior, medial, inferior rectus and the inferior oblique muscles, sparing the pupil. There were also signs of peripheral neuropathy with depressed deep tendon reflexes. An electromyographic study of the extremities also revealed findings consistent with peripheral neuropathy. To exclude any lymphomatous or other intracranial pathologies, a magnetic resonance imaging examination of the brain was made and it was found to be normal. Vincristine neurotoxicity was diagnosed as the cause for the peripheral neuropathy and oculomotor nerve functions returned to normal within 3 weeks, confirming our initial diagnosis of vincristine neurotoxicity.

This patient who had a high-grade immunoblastic lymphoma developed a unilateral oculomotor nerve palsy in addition to peripheral neuropathy while receiving a chemotherapy regimen which included cyclophosphamide, adriamycin, vincristine and prednisone. Among these, vincristine is the only agent known to frequently cause neurological complications [2,4,7]. Most of the reported cases with oculomotor involvement of vincristine neuropathy had bilateral ptosis [3,4,8]. In all these cases the diagnosis depended on the exclusion of meningeal tumor infiltration

and the improvement of the abnormalities when vincristine dosage was reduced or discontinued. In our patient, the occurrence of a unilateral oculomotor palsy raised the possibility of a lymphomatous involvement of the central nervous system but the magnetic resonance imaging study of the brain and the resolution of symptoms after discontinuation of vincristine therapy led us to diagnose the situation as vincristine neurotoxicity. In conclusion, we would like to repeat that the development of oculomotor or other cranial nerve palsies in a patient receiving vincristine should raise the suspicion of vincristine neuropathy in addition to central nervous system infiltration or other intracranial pathologies where the neuropathy is unilateral or bilateral. Before deciding on drug toxicity, it is obvious that other causes should be excluded.

References

- McCarthy GM, Skilling JR: A prospective cohort study of the orofacial effects of vincristine neurotoxicity. *J Oral Pathol* 1991;20:345-349.
- Rosenthal M, Kaufman S: Vincristine neurotoxicity. *Ann Intern Med* 1974;80:733-737.
- Vize M, Oster MW: Ocular side effects of cancer chemotherapy. *Cancer* 1982;49:1999-2002.
- Sandier SG, Tobin W, Henderson ES: Vincristine-induced neuropathy. *Neurology* 1969;19: 367-374.
- Miller TP, Dana BW, Weick JK, Jones SE, Coltman CA, Dahlberg S, Fisher RI: Southwest Oncology Group clinical trial for intermediate-and high-grade non-Hodgkin's lymphomas. *Semin Hematol* 1988;25:41.
- McKelvey EM, Gottlieb JA, Wilson HE, Haut A, Talley RW, Stephens R, Lane M, Gamble JF, Jones SE, Grozea PN, Gutterman J, Coltman C Jr, Moon TE: Hydroxydaunomycin (adriamycin) combination chemotherapy in malignant lymphoma. *Cancer* 1976;38:1484.
- Weiss HD, Walker MD, Wiernik PH: Neurotoxicity of commonly used antineoplastic agents. *N Engl J Med* 1974;291:127-133.
- Albert D, Wong V, Henderson E: Ocular complications of vincristine therapy. *Arch Ophthalmol* 1967;78:709-713.