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Vincristine Neurotoxicity

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The prognosis for children with malignancies has improved significantly in the past two decades as a result of comprehensive care of these children and increasingly vigorous chemotherapy. Vincristine sulfate (Oncovin [R], Eli Lilly and Company, Indianapolis), a VINCA alkaloid, has been one of the most widely used chemotherapeutic agents in the past decade. Arnold *et al.*(1) noted significant increase in neurotoxicity of vincristine (VCR) since a ready-to-use form of the drug became available. Warrier and Ducos(2) reported a 10-year-old child with severe abdominal pain, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and generalized seizures following the first dose of VCR. We have retrospectively reviewed the charts of all children who received VCR before and after the introduction of the ready-to-use VCR preparation to look for any significant change in the degree of toxicity.

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Material and Methods

Data on all children who received VCR as part of chemotherapy for malignancy from January 1979 to June 1985 at Children's Hospital of New Orleans (CHNO) were reviewed. From 108 charts, the patients were divided into two groups depending on whether they had received the VCR before May 1, 1983 (Group I, 53 patients) or only after the date (Group II, 55 patients). Children who received VCR both before and after May 1983 were included in the first group. Children ranged in age from neonates to 18 years, and the maximum single dose did not exceed 2.0 mg.

Thy lyophilized form was reconstituted with 10 ml of bacteriostatic saline for injection. The drug was prepared according to manufacturer's directions and given by slow intravenous push.

Minimal abdominal pain, decreased deep tendon reflexes (DTR), and jaw and bone pain that resolved spontaneously or with mild analgesics were graded as mild side effects. Absent DTRS, abnormal gait, SIADH, seizures, severe jaw, bone and abdominal pain that required narcotics, and obstinate constipation were considered as severe side effects.

Results

As shown in the *Table*, the total number of cases with toxicity in Group I was 15% whereas the evidence of toxicity in Group II was 30.9%.

This was statistically significantly larger ($\alpha = 0.05$, upper tailed test) than that due to the lyophilized form. The average number of doses received when toxicity was noted was 6.13 (Range: 2-19.00) in Group I and 4.29 (Range: 1-13.00) in Group II. The average number of doses, although larger, was not statistically significantly larger for the lyophilized forms according to the upper tailed modified t-test for unequal variances (5% level of significance was used)(3).

Acute toxicity developed within 3 doses in only three children (3.8%) in Group I, whereas eight children (14.5%) in Group II experienced toxicity within 3 doses. Five children in Group II were noted to have toxicity with just one dose whereas at least 3 doses were administered before any toxicity was reported in Group I.

Discussion

Peripheral neuropathy with loss of deep tendon reflexes and paresthesias with progression to muscle pain, weakness, and gait disturbances have been th. most common dose-limiting factors in the use of VCR(4-7). Severe colicky pain or ileitis due to autonomic neuropathy may occur but central nervous system toxicity is rarely observed because of the inability of VCR

TABLE I—*Toxicity Data on Two Groups of Patients Receiving Different Forms of Vincristine Therapy*

Group	Total	Toxicity	Severe toxicity	No toxicity	Doses*
Group I (lyophilized VCR)	53	8 (15)	2 (3)	45 (85)	6.13
Group II (ready-to-use VCR)	55	17 (31)	5 (9)	38 (69)	4.29

Figures in parentheses indicate percentages.
* Average number of doses received when toxicity occurred.

to penetrate the blood-brain barrier adequately(8,9). SIADH is another rare but well recognized neurotoxic side effect of VCR(10-12). Convulsions after the use of VCR are very rare(13,14). Accidental intrathecal administration(15) or over dosage of VCR(16) with resulting fatal ascending myelopathy and seizures respectively have been described. Recent reports of vincristine toxicity of unusual frequency and severity seem to have coincided with the introduction of the ready-to-use solution of VCR(1,2,17,18). In reply to several inquires, Eli Lilly has maintained that peripheral neuropathy is likely to occur as the cumulative total dosage of VCR increases and that there is no reason to suspect a relationship with the ready-to-use prepared solution(18,19).

The significant increase in toxicity that appears to have coincided with the introduction of the ready-to-use form of VCR is worrisome because VCR is a commonly used and well-tolerated drug in childhood cancer. Careful and continued monitoring of the side effects and studies of pharmacokinetics and bioavailability of the drug should be continued.

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Gingival Fibroma: An Unusual Presentation

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Although fibroma is a common benign soft tissue neoplasm occurring in the oral cavity, it is generally small and occurs most commonly in the third to fifth decades of life(1). We report a case of unusually big fibroma in a child.

Case Report

An 8-year-old male child presented with a peduncular mass in the oral cavity for the last two years. Initially, it was pea sized and had steadily grown to the present size. There was no history of pain, ulceration or discharge, loss of appetite or weight. However, in the preceding few months there was difficulty in speech. The child could not articulate retroflex sounds (*e.g.*, /t/,/th/,/d/) clearly. The child belonged to a village and had never used a brush or "datun" (twig toothbrush).

Examination revealed a peduncular mass, 5×3 cm, normal in color with a lobular surface, firm in consistency, non tender, with no tendency to bleed and showed no ulceration or discharge, arising between the first and second deciduous molars. Major portion of the swelling lay on the lingual aspect (*Fig.*). The adjacent teeth were loose and the oral hygiene extremely poor with heavy plaque accumulation and severe halitosis. The gingiva was highly

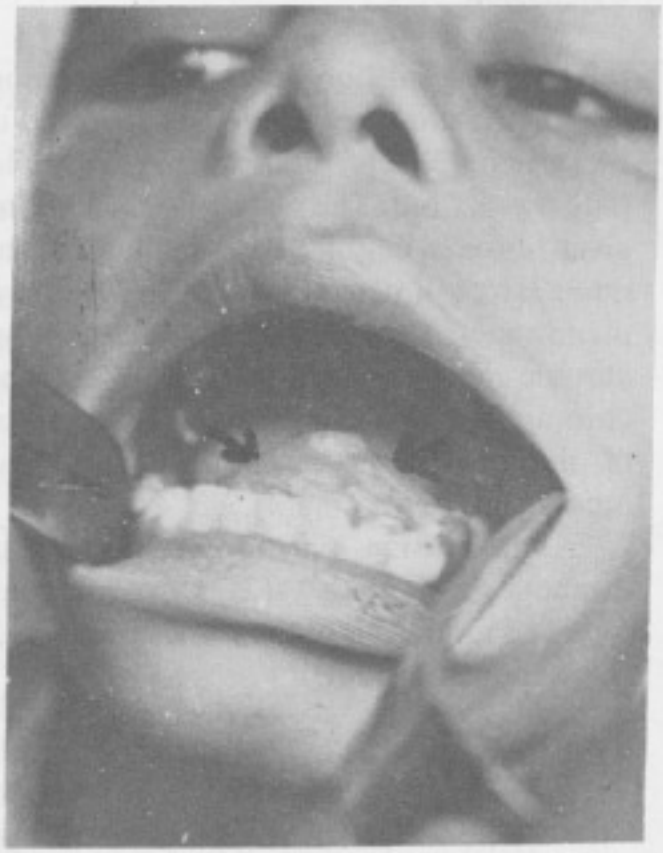

Fig. Photograph of the oral cavity showing the massive gingival fibroma arising between the first and second deciduous molars with a lobulated surface.

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