Carbamazepine-Induced Generalized "Pseudoleukemia Lymphoma" – Like Syndrome

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Key words: anticonvulsants, pseudolymphoma, splenomegaly, leukopenia, carbamazepine

IMAJ 2003;5:457

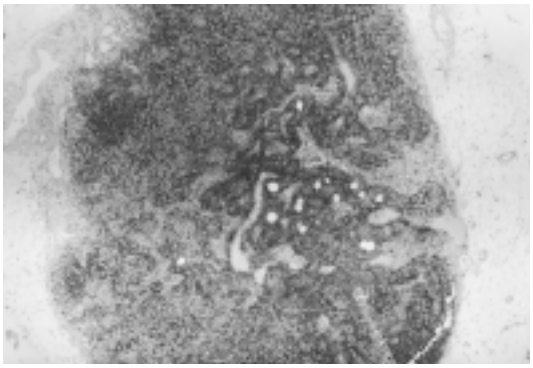
Known adverse reactions of the anti-epileptic drug carbamazepine include the rare carbamazepine hypersensitivity syndrome, characterized by allergic skin reaction, thrombocytopenia and generalized lymphadenopathy with a clinical picture of "pseudolymphoma" [1–3].

The following case report describes an unusual presentation of carbamazepine hypersensitivity, appearing 2 weeks after the drug was given for grand-mal seizures. The clinical presentation included prominent hematologic manifestations mimicking "leukemia/lymphoma."

Patient Description

A 27 year old healthy woman was hospitalized because of lymphadenopathy for 1 week and 2 days of fever and purpura. Nine months earlier she had experienced an episode of grand-mal seizures without neurologic or laboratory abnormalities and no therapy was given. Two weeks before admission she had a second seizure and, once again, no clinical or laboratory abnormality was evident. Investigations included electrocardiography and computed tomography scan of the brain. She was then given carbamazepine 200 mg q.i.d. On admission to hospital she appeared to be in good general condition, her body temperature was 39°C and she had generalized firm non-tender bilateral posterior cervical and axillary lymphadenopathy (2–4 cm diameter) with modest splenomegaly and purpura. The blood count showed normal hemoglobin (12.9 g/dl), mild leukopenia (white blood cells $3.1x10^9$/L) and thrombocytopenia ($20x10^9$/L). The peripheral blood smear was normal apart from marked thrombocytopenia, and no blasts were seen. Biochemistry revealed an elevated lactate dehydrogenase level of 958 IU.

The history of recent administration of carbamazepine was strongly suggestive of a drug reaction. Nevertheless, the absence of typical allergic skin allergy in the presence of the above-mentioned abnormal physical findings and bicytopenia (leukopenia and thrombocotopenia) prompted us to evaluate her lymphadenopathy and an axillary lymph node biopsy was performed. This revealed a reactive lymph node [Figure] without evidence of B cell gene rearrangement. Serology for Epstein-Barr virus, cytomegalovirus and *Toxoplasma* were all negative. Bone marrow aspiration was not done at the time. Discontinuation of carbamazepine resulted in a rapid resolution of the clinical findings within 2 days and platelet recovery ($35x10^6$/L after 1 day and $69x10^6$/L the following day). The lymphadenopathy regressed within a week. The anti-epileptic drug was replaced by valproic acid.



Lymph node biopsy showing hyperplastic lymphoid infiltration of the lymphatic follicles, without invasion into the sinuses and capsule, characteristics for reactive lymphadenopathy.

Comment

In this patient, because of the temporal relationships between onset of the clinical findings and use of carmazepine, and immediate improvement following cessation of the drug, the only acceptable explanation for her acute disease was the ingestion of carbamazepine. This combination of fever, generalized lymphadenopathy, splenomegaly and elevated LDH levels, associated with progressive blood cytopenias, may be termed "pseudoleukemia," analogous to "pseudolymphoma," which was adopted in cases with similar findings but without blood cytopenias.

Although lymph node morphology truly mimicked lymphoma in a few cases [4], even at the immunophenotypic level with the presence of CD30+ lymphoid cells (typical for Hodgkin's disease), gene rearrangement studies for clonality were invariably negative, as in this case. However, chronic antigenic stimulation itself occasionally precipitates true neoplastic transformation, such as Sjögren's syndrome, chronic gastritis and thyroiditis. Fortunately, no true form of lymphoma is associated with carbamazepine, and drug discontinuation results in resolution of all clinical findings in these cases.

References

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LDH = lactate hydrogenase