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Flu-Like Syndrome Due to Tritoqualine in Cutaneous Mastocytosis

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Cutaneous mastocytosis is known to represent the tissue analogue of the basophilic line leukoprolifera-tive disorder. We observed a 22-year-old woman with this disease and with the typical urticarioid macules that flushed at any minimal psychophysic traumatic stimulus. The patient exhibited a huge histamine serum peak, documented by ionic exchange chroma-tography. To improve her symptoms a therapy was administered with tritoqualine, an inhibitor of histamine synthesis which in a single case was reported to be successfully used in mastocytosis [1].

Treatment was started with 100 mg p.o. four times daily but 36 h later the patient complained of typical flu symptoms (fever, malaise, myalgias, headache, conjunctival congestion). The drug was withdrawn and a second attempt was made a few days later, starting with 100 mg twice daily. The flu-like syndrome reappeared and the treatment was once again stopped. Finally only 50 mg three times daily were tried: a milder reaction with fever, myalgias and conjunctivitis developed for the third time so that tritoqualine was definitively abandoned.

The flu-like syndrome is a well-known side effect observed with the use of many drugs, mostly immu-nomodulators. Its appearance is typically induced by interferon administration [2], but it has also been reported for treatments with levamisole [3], interleukin 2 [4], zimelidine [5], allopurinol [6]. Tritoqualine had never been reported as the cause of this syndrome.

The pathogenesis of flu-like reactions is not always clear and would deserve further investigation. Three possible mechanisms are to be considered: (a) the involved drug may form immunocomplexes and/or may complex as hapten with the leukocyte membrane, thus leading to leukocyte lysis and pyrogen release (this phenomenon could virtually happen with any drug); (b) when hyperpyrexia is the leading symptom a direct neurotoxic effect can be envisaged; (c) in most cases the syndrome appears to be related to the interference in the production of prostaglandins and other active compounds.

It is possible that in our patient the very inhibition of histamine synthesis might be interlocked with a cascade reaction of other immunophlogistic mediators and this could trigger the flu-like syndrome. This hypothesis is in keeping with the latency period preceding the clinical onset of the adverse effect, which was longer than that observed for interferons. It is well known, finally, that antihistaminic drugs can directly affect the balance of prostaglandins, along with their effects, and that some histamine antagonists can synergize the action of interferon- α [7].

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