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Case Report

Hoigne Syndrome Caused by Intralesional Meglumine Antimoniate

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Abstract

Hoigne syndrome (HS) is the term coined to describe an acute, non-allergic, psychiatrically based reaction occurring with a wide list of medications, mainly antibiotics. Since its first description by Hoigne and Schoch in 1959, few cases have been reported in medical literature and, although antimicrobials are commonly used, very rarely in dermatology. The authors describe the first case occurred after intralesional administration of meglumine antimoniate and briefly discuss the pathogenetic hypotheses on this atypical adverse drug reaction.

Introduction

Hoigne syndrome (HS) is the term coined to describe an acute, non-allergic, psychiatrically based reaction [1] occurring with a wide list of medications, mainly antibiotics (thus the other terms used as “pseudoanaphylactic reaction to procaine penicillin” [2], “acute psychotic syndrome after penicillin” [3] or “antibiomania [4]).

Since its first description by Hoigne and Schoch [5] in 1959 few cases have been reported in medical literature and, although antimicrobials are commonly used, very rarely in dermatology. No reports of HS with the use of antiparasitic drugs have also been found.

A 56-year-old woman sought attention because of an erythematous-infiltrative slowly progressing lesion of the medium dorsal third of the right forearm present for the last four months. At he beginning of the disease, the patient noticed a small red, itchy papule, which he treated as a mosquito bite using betamethasone/fusidic acid cream, with no significant improvement. A complete clinical evaluation showed the patient in good health, with a history of cutaneous superficial spreading melanoma seven years ago.

A 3 mm punch-biopsy was performed for diagnostic assessment and histologically stained with haematoxylin and eosin. Microscopic examination revealed a granulomatous dermic infiltrate, consisting of lymphocytes, histiocytes and multinuclear giant cells, being coherent with the clinical suspect of cutaneous leishmaniasis. Touch imprint from the biopsy specimen and microscopic examination (Giemsa stain) confirmed the diagnosis through the evidence of Leishmania amastigotes. Therapeutic regimen with N-methylglucamine antimoniate, 1 ml twice a week was proposed and the drug administered intralesionally at our clinic.

Immediately after the fourth injection of the drug, the patient presented confusion, disorganised

thinking, visual and auditory hallucinations. She also reported exaggerating anxiety and psychomotor agitation.

We provided laboratory tests including thyroid levels and toxicology, electrocardiogram together with neurological and psychiatric evaluation, all resulting within normal limits. A computer tomography of the brain was also unremarkable. In the further two days, the patient referred sleep disturbances with underlying anxiety and fear.

Antimonials were withdrawal, and a significant improvement of these symptoms was seen in the following days. The patient denied any previous similar manifestations to drugs as well as the personal and familial history of allergic/anaphylactic diseases in the past. He refused any further drug administration, including replacement with oral itraconazole, and the cutaneous disease remained unchanged.

HS is a sort of acute pseudoallergic reaction having psychiatric symptoms, disturbances of perceptions and intense anxiety as main clinical features, occurring with the administration, especially infusion, of a series of drugs, varying from anaesthetics to intralesional steroids and oral antibiotics.

Neurological signs and symptoms may present at a different degree, most cases including panic, fear of death, alteration of consciousness, hallucinations, accompanied by tachycardia, tachypnea, hypertension and numbness in the extremities [7].

Usually, the withdrawal of the offending drug leads to the rapid attenuation of symptoms, with excellent prognosis [1,3,5]. As many different drugs, with different pharmacodynamics and ways of administration, have been reported to cause acute psychiatric reactions, the complete improvement of the condition occurs in minutes to days [4,7,8].

The exact mechanism by some drugs may induce these effects remains largely unexplained and more than 200 pharmacological agents have been claimed as causative.

Local anaesthetics (lidocaine, procaine, cocaine) have been involved in the majority of case reports and suspected to be responsible for the development of limbic kindling through the facilitation of excitatory N-methyl-D-aspartate receptors [6,9] and a reduction in the inhibitory activity of gamma-aminobutyric acid (GABA) transmission [6,10]. This theory, however, requires previous sensitization to the anaesthetic that is not met in all cases of HS described in the medical literature [11].

Alternatively, it was speculated that drug microcrystals injection might cause microembolization of small vessels of the brain and/or lungs [12]. In fact, an embolism is a well-known biological phenomenon representing a possible complication of a variety of conditions [13,14], which can also involve any organ or apparatus with drug administration as well as it occurs locally with Nicolau syndrome [15] at the cutaneous level. Depending upon the size of these particles and their solubility in the blood, they can reach the diverse systems thus explaining such reactions [16]. Lastly, some authors postulated that the inhibition of the hepatic cytochrome P450 (CYP) isoenzymes, subclass CYP3A4, may play a role in the induction of neurological [17] and psychiatric [8] disorders.

Mediterranian basin is an endemic region for several parasitoses [18, 19]. Among these, cutaneous leishmaniasis is relatively frequent, mostly due to *Leishmania infantum* , carried by the female sandflies of *Phlebotomus perniciosus* [20].

Several drug therapies are effective in the treatment of cutaneous leishmaniasis [19] and antimonials have been widely used in localized forms [21]. In our experience intralesional meglumine antimoniate (Glucantime®) is useful and manageable, through the selective inhibition of enzymes involved in parasite anaerobic metabolism, with rapid clinical response and little discomfort for the patient [22].

To the best of our knowledge this is the first report of HS in course of antiparasitic drugs.

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