

Anaphylactic reaction to methylprednisolone in multiple sclerosis: a practical approach to alternative corticosteroids

Sir – We report a case of anaphylactic reaction to intravenous methylprednisolone (IVMP), a rare complication in multiple sclerosis (MS) [1–3]. A 21-year-old female, with no history of infection or immunization during the six months prior to the neurological event, developed, over two weeks, severe cognitive, corticospinal, cranial nerves and cerebellar deficits. The Expanded Disability Status Scale (EDSS) score was 4.0. Cerebral magnetic resonance imaging (MRI) revealed 30 T2 hyperintense lesions – located in the corpus callosum, periventricular and infratentorial areas – with 26 enhancing after T1 gadolinium administration. Cerebrospinal fluid (CSF) examination showed 7 leukocytes/ μL with 1.5% plasmacytes, no brain-barrier disruption, and a strong intrathecal production of oligoclonal immunoglobulin G. Metabolic, infectious and autoimmune disorders were ruled out, and the diagnosis of possible MS was retained. The patient received IVMP (Solu-Medrol®) 1 g/day for three days, tapering the dose over the next 12 days. Although the response was initially satisfactory, the patient worsened after stopping MP and became rapidly bedridden (EDSS 8.0). A second cerebral MRI showed new gadolinium-enhancing T1 lesions, but the CSF remained unchanged. The diagnosis of MS was thus sustained by these repetitive findings, excluding reasonably other demyelinating disorders. Although IVMP (1 g/day) was restarted, the clinical status worsened and, therefore, plasma exchange was performed every other day with a rapid favorable response. Mitoxantrone (10 mg/m^2) was then initiated on a monthly basis for three months, then every three months. As requested per protocol, mitoxantrone injections were preceded by IVMP (Solu-Medrol®) 125 mg. Significant improvement in the patient's condition was noted after the second injection. She was able to walk for an unlimited distance after the fourth injection (EDSS 3.0). However, while the patient was receiving IVMP 125 mg before her fifth mitoxantrone injection, she developed a facial and truncular itching erythema, which evolved towards urticarial maculo-papules persisting over 40 minutes before spontaneous resolution. There was no history of atopy, asthma or

previous allergic reaction to drugs. Prick and intradermal tests for immediate allergic reaction were performed for five different corticosteroids (CS; HP, hydrocortisone, prednisolone, betamethasone and dexamethasone) and interpreted according to international guidelines [4,5]. The patient was only reactive to MP (Solu-Medrol®). Since tests for reactivity to dexamethasone (Mephasone®) were negative, dexamethasone was used instead of MP at an equivalent potency before each subsequent mitoxantrone injection without any side-effects.

Anaphylactic or anaphylactoid reactions following CS administration include pruritic rashes, urticaria, angioedema, bronchospasm, hypotension and possibly death [4,6]. Immunologic and non-immunologic mechanisms are probably involved. Specific IgE has been demonstrated in a few cases, suggesting an immediate, type I allergic reaction [1,3]. Excipients and salt formulations have also been implicated, which was ruled out in our case. Reactions have been described for all CS active ingredients and administration routes, although iv injection seems to pose the greatest risk, and MP and hydrocortisone are the compounds most frequently involved [4]. Twelve cases of death due to CS allergy have been previously reported, therefore re-administration of the same CS is not an option. Reintroduction-desensitization protocols may be applied for drugs that are administered continuously, but are not advised in MS, since CS are used as pulse therapy. In addition, these protocols are also not devoid of risk. Thus, if the use of CS cannot be avoided, skin tests, by prick or intradermal injection, should be performed to find a substitutive CS devoid of cross-reactivity [7]. In our case, only the skin test for MP was positive, indicating a specificity for this compound. Still, it should be borne in mind, that false negative results with skin tests are relatively frequent, especially in immunosuppressed patients, and the introduction of a new compound should, therefore, be performed in a controlled environment [6].

References

1. Burgdorff T, Venemalm L, Vogt T, Landthaler M, Stolz W. IgE-mediated anaphylactic reaction induced by succinate ester of methylprednisolone. *Ann Allergy Asthma Immunol* 2002; **89**: 425–28.

2. **van den Berg JS, van Eikema Hommes OR, Wuis EW, Stapel S, van der Valk PG.** Anaphylactoid reaction to intravenous methylprednisolone in a patient with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1997; **63**: 813–14.
3. **Pryse-Phillips WE, Chandra RK, Rose B.** Anaphylactoid reaction to methylprednisolone pulsed therapy for multiple sclerosis. *Neurology* 1984; **34**: 1119–21.
4. **Kamm GL, Hagmeyer KO.** Allergic-type reactions to corticosteroids. *Ann Pharmacother* 1999; **33**: 451–60.
5. **Malling HJ.** Methods of skin testing. *Allergy* 1993; **48**: 55–56.
6. **Butani L.** Corticosteroid-induced hypersensitivity reactions. *Ann Allergy Asthma Immunol* 2002; **89**: 439–45.
7. **Venturi M, Lobera T, del Pozo MD, González I, Blasco A.** Immediate hypersensitivity to corticosteroids. *J Invest Allerg Clin Immunol* 2006; **16**: 51–56.

CA Deruaz¹, F Spertini¹, F Souza Lima²,
RA Du Pasquier^{1,2} and M Schluep²
¹Division of Immunology and Allergy,
Centre Hospitalier Universitaire Vaudois,
Lausanne, Switzerland
²Department of Neurology,
Centre Hospitalier Universitaire Vaudois,
Lausanne, Switzerland