

Severe thrombocytopenic purpura after meningococcal C vaccination in a woman affected by systemic lupus erythematosus

Sirs,

Patients with autoimmune rheumatic diseases (AIRD), immunosuppressed for both the disease itself and immunosuppressive drugs, are generally more vulnerable to infections, which, in these patients, are more frequently severe and have a complication rate roughly twice than the general population (1, 2).

The problems concerning vaccines and autoimmunity are manifold: the possibility that the vaccine, particularly if made up of live and attenuated microorganisms, could represent a trigger for the exacerbation of the disease (3, 4), the ability of the vaccines to induce an effective and protective immune response and to be also safe and well tolerated in patients with autoimmune diseases.

In 2010 a committee of experts under the aegis of the EULAR (European League Against Rheumatism) drew up the recommendations on the use of the vaccines in patients with systemic autoimmune diseases. In conclusion, on the basis of these guidelines, many of the vaccinations, that are commonly performed in healthy subjects, may also be used in patients suffering from AIRD. Indeed, some vaccinations are particularly recommended in these patients in the light of a greater risk of infection (5).

From Jan. 2015 to Feb. 2016, 43 laboratory-confirmed cases of invasive meningococcal disease (*i.e.* meningitis and sepsis) due to serogroup C *N. meningitidis* (31 in 2015, 12 in 2016) were reported by the Regional Health Authority of Tuscany (RHAT) to the Italian National Surveillance System for Invasive Bacterial Disease (IBD). The incidence rate (IR) of serogroup C cases was higher compared with the previous years (31 cases in 2015 compared to 2 in 2014 and 3 in 2013) and these cases have also involved people of a more mature age of the population (6, 7).

These infections presented high mortality: of the 31 cases of IMD occurred in 2016, 6 have been fatal, and so did 4 of the 12 of 2016 (6, 7).

Tuscany has therefore undertaken control measures both with immediate chemoprophylaxis of cases and a vaccination campaign offered to adolescents, adults and the elderly (8, 9).

There are two types of anti-meningococcal vaccine: the polysaccharide-one and the conjugated-one. The polysaccharide vaccine, with serogroups A, C, W135, Y, since polysaccharides are "weak" antigens, is not able to effectively stimulate the immune system, especially in children under the age of two years and in patients with asplenia, and it fails to induce immunological memory in people of any age (10).

The conjugated vaccine, with only serogroup C, consists of capsular polysaccharides conjugated with highly immunogenic proteins, like diphtheria toxoid, tetanus tox-

oid or diphtheria toxin protein Cross-Reactive Material CRM 197: the conjugation of these two antigens improves the immune response, confers immunological memory, prolonged protection and booster effect and allows the use of these vaccines also in the child under 2 years old (10).

Menjugate vaccine consists of oligosaccharide *Neisseria meningitidis* group C (strain 11) conjugated with *Corynebacterium diphtheriae* CRM protein-197. For its antigenic nature, it is considered safe by Scientific Society in patients with systemic autoimmune diseases (11).

Most of the reported adverse events in healthy people were mild and self-limiting, more often occurred in combination with co-administration of other vaccines. The most common were reactions at the injection site (including redness, swelling and tension/pain), fever (usually the temperature does not exceed 39°C), rash, gastrointestinal symptoms (overall vomiting) and arthromyalgia. Rare and very rare were anaphylaxis, anaphylactic shock and seizures. In the period of post-marketing surveillance from 2005 to 2012 in Tuscany, were reported two cases of thrombocytopenic purpura, including one classified as idiopathic, and a case of ataxia. Of the 2 cases of thrombocytopenic purpura, one appeared after co-administration with the MMRV vaccine (10).

However, we would here report the case of a rare adverse event to meningococcal C conjugated vaccine occurred in a patient with systemic lupus erythematosus (SLE).

The patient is a 36-year-old woman, suffering from SLE in remission, treated with low doses of corticosteroids and anti-malarial drugs, who performed active immunoprophylaxis with *menjugate* as current indications of the Scientific Society. Ten days after administration of the vaccine, the patient experienced severe metrorrhagia and skin purpura. The blood count examination highlights a severe thrombocytopenia, with a platelet count of 5000/mcl. The patient was therefore treated with high-dose steroids and intravenous immunoglobulins (400 mg/kg/die for 5 days) with good clinical and humoral response (platelet count of 150.000/mcl after 1 week). Thrombocytopenia is defined as a clinical condition in which platelet counts are less than 100 x 10⁹/L. Vaccine-related thrombocytopenia is considered to be of immune origine because antibodies can be detected on platelets in about 79% of cases. These autoantibodies, in fact, cross-react with the naturally present antigenic targets on platelets. It is more frequent in young children because their idiotypic network is still forming (12, 13). Immune thrombocytopenic purpura (ITP) is an adverse event that can follow vaccine administration, although so far the only vaccine for which there is a demonstrated cause-effect relationship is the measles, mumps and rubella (MMR) vaccine, that is made by live and attenuated viruses. However the risk of ITP is lower than that due to these wild viruses and the clinical picture is less severe (12, 14).

In conclusion, it seems appropriate to report the occurrence of autoimmune thrombocytopenic purpura as a possible adverse event due to the administration of anti-meningococcal C conjugate vaccine in patient with systemic autoimmune disease, since it is a potentially severe condition which, if not diagnosed and promptly treated, might become fatal.

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