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LETTER TO THE EDITORS

Acquired factor VIII haemophilia following influenza vaccination

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Autoimmune diseases should present or be worsened by vaccination due to the pharmacological properties of vaccines. We report a case of acquired haemophilia mediated by anti-factor VIII antibody following a vaccination against influenza.

A 72-year-old woman suffered from spontaneous bruises of the wrists at the end of October, 2009. She had been exposed for 31 years (1977–2008) to prednisone for a pulmonary sarcoïdosis. She was also being treated with L-thyroxine for Hashimoto's thyroiditis, amlodipine for essential arterial hypertension and paroxetine for depression. The patient was vaccinated against seasonal influenza (MUTAGRIP) 8 days prior to the first haemorrhagic symptom. No local complication was noted during the intramuscular injection. This was the first time she had been vaccinated with a seasonal influenza vaccine. The results of the clinical examination were normal, except the haemorrhagic syndrome. Platelet count was 320,000/μL, activated cephalin time (equivalent to activated partial thromboplastin time) was 72 s (indicator: 28 s) and prothrombine time was 100%. The amount of factor VIII was 1%, and antibody directed against factor VIII was detected at 8 Bethesda units, without any von Willebrand factor deficiency. There was no clinical or biological evidence for any haematopoietic malignancy or systemic disease. Antinuclear antibodies were detected at the limit of significance (titre: 1/160), without any specificity (anti-DNA nor anti-extractable nuclear antigens). Symptomatic treatment with activated prothrombin complex concentrates (FEIBA) was prescribed for 24 h. Due to the ineffectiveness of prednisone (1 week at 1 mg/kg/day), rituximab was introduced (375 mg/m^2/week, 4 infusions), which resulted in clinical and biological remission: 3 weeks after the last infusion of rituximab, factor VIII and its auto-antibody were 8% and 4 Bethesda units respectively; 4 months after the last infusion, these values were 48% and not detectable, respectively.

According to World Health Organization–Uppsala Monitoring Centre criteria [1], the score of causality assessment was considered to be "possible".

Acquired haemophilia is a very rare disorder due to an anti-factor VIII antibody: its incidence is estimated to range from 0.2 to 1.9/million/year [2]. An underlying cause is present in approximately half of cases: solid tumours, haematopoietic malignancies, auto-immune diseases, pregnancy and post-partum, infections, drugs (penicillins, sulfa antibiotics, phenytoin, chloramphenicol, methyldopa, interferon-α, fludarabine, levodopa, clopidogrel) [3–5]. None of the drugs taken by our patient were known to induce acquired haemophilia. To the best of our knowledge, no post-vaccination-acquired haemophilia has

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been described in the literature for influenza vaccine. The profile of adverse reactions of vaccines against seasonal influenza remains similar to that of other vaccines and could lead to auto-immune disorders (Guillain-Barré syndrome, encephalomyelitis, idiopathic thrombocytopenic purpura, among others) [6, 7]. Two mechanisms have been proposed. The first is an antigenic mimicry, but the delay is usually about several weeks, except in case of previous sensitization. the second—and more often—cause is a non-specific activation of quiescent auto-reactive T and B cells, with a delay of about several days [6]. This second hypothesis could be possible in the case of our patient.

When a patient presents with an auto-immune disorder without any known aetiology, the clinician should search the medical history for a recent vaccination.

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