



## Acquired factor VIII haemophilia following influenza vaccination

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

A seventy-two-year-old woman suffered from spontaneous bruises of the wrists at the end of October, 2009. She had been exposed during 31 years (1977-2008) to prednisone for a pulmonary sarcoidosis. She was also treated by L-thyroxine for Hashimoto's thyroiditis, amlodipine for essential arterial hypertension and paroxetine for depression. The patient was vaccinated against seasonal influenza (MUTAGRIP®) eight days before the first haemorrhagic symptom. No local complication was noted during the intramuscular injection. She had never been vaccinated by seasonal influenza vaccine before. Clinical examination was normal except the haemorrhagic syndrome. Platelet count was **320.000/μL**, activated cephalin time (equivalent to activated partial thromboplastin time) was 72 seconds (indicator: 28 seconds) and prothrombin time 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 hours. Due to ineffectiveness of prednisone (one week at 1 mg/kg/d), rituximab was introduced (375 mg/m<sup>2</sup>/week, 4 infusions) and clinical and biological remission was observed: after the last infusion of rituximab, factor VIII and its auto-antibody (Bethesda units) were respectively 8 % and 4 three weeks after and 48 % and no detectable four months after.

According to WHO-UMC criteria [1], the score of causality assessment was considered as "possible".

Acquired haemophilia is a very rare disorder due to an anti-factor VIII antibody: its incidence is estimated 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, methyl dopa, interferon-α, fludarabine, levodopa, clopidogrel) [3-5]. **None of the drugs taken by our patient was known to induce acquired haemophilia.** In our knowledge, no post-vaccination acquired haemophilia has been described in the literature for influenza vaccine. The profile of adverse reactions of vaccines against seasonal influenza remains similar to other vaccines and could lead to auto-immune disorders (Guillain-Barré syndrome, encephalomyelitis, idiopathic thrombocytopenic purpura...) [6-7]. Two mechanisms are proposed: 1) an antigenic mimicry, but the delay is usually about several weeks, except in case of previous sensitization; 2) more often, a non specific activation of quiescent auto-reactive T and B cells; then, the delay is about several days [6]. This second hypothesis could be suggested for in our observation.

Then, in front of an auto-immune disorder without any known aetiology, a recent vaccination should be searched.

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