Acquired factor VIII haemophilia following influenza vaccination

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Acquired factor VIII haemophilia following influenza vaccination.

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Complete List of Authors:	Moulis, Guillaume; Faculté de Médecine, Pharmacology Pugnet, Grégory; CHU Toulouse-Purpan, Université de Toulouse, Service de Médecine Interne Bagueri, Haleh; Faculté de Médecine, Université de Toulouse, Service de Pharmacologie clinique Courtellemont, Claire; CHU Toulouse-Rangueil, Université de Toulouse, Service de Néphrologie et Immunopathologie clinique Huart, Antoine; CHU Toulouse-Rangueil, Université de Toulouse, Service de Néphrologie et Immunopathologie clinique Chauveau, Dominique; CHU Toulouse-Rangueil, Université de Toulouse, Service de Néphrologie et Immunopathologie clinique Pourrat, Jacques; CHU Toulouse-Rangueil, Université de Toulouse, Service de Néphrologie et Immunopathologie clinique Montastruc, Jean-Louis; Faculté de Médecine, Université de Toulouse, Service de Pharmacologie clinique

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Name, affiliations and addresses of the authors:

Guillaume Moulis^{1,2}, Grégory Pugnet^{1,3}, Haleh Bagheri², Claire Courtellemont³, Antoine Huart³, Dominique Chauveau³, Jacques Pourrat³, Jean-Louis Montastruc¹.

¹ Service de Médecine Interne, Centre Hospitalier Universitaire de Toulouse, Université de Toulouse, France

Address: Service de Médecine Interne, salle Le Tallec, CHU Toulouse-Purpan, Place du Docteur Baylac, TSA 40031, 31059 Toulouse cedex, France.

² Service de Pharmacologie Clinique, Centre Midi-Pyrénées de Pharmacovigilance, de Pharmacoépidémiologie et d'Informations sur le Médicament, Unité de Pharmacoépidémiologie EA 3696, Centre Hospitalier Universitaire de Toulouse, Université de Toulouse, Faculté de Médecine, France

Address: Service de Pharmacologie Clinique, Faculté de Médecine, 37 Allées Jules-Guesde, 31000 Toulouse.

³ Service de Néphrologie et Immunopathologie Clinique, Centre Hospitalier Universitaire de Toulouse, Université de Toulouse, France

Address: Service de Néphrologie et Immunologie clinique, CHU Toulouse-Rangueil, Boulevard Ducuing, 31400 Toulouse, France.

Submitting author:

Guillaume Moulis,
Service de Pharmacologie Clinique,
Faculté de Médecine,
37 Allées Jules-Guesde
31000 Toulouse
Phone: +33 5 61 14 59 73
Fax: +33 5 61 14 56 42
e-mail: gmoulis@hotmail.com

Corresponding author:

Jean-Louis Montastruc,
Service de Pharmacologie Clinique,
Faculté de Médecine,
37 Allées Jules-Guesde
31000 Toulouse
Phone: +33 5 61 14 59 73
Fax: +33 5 61 14 56 42
e-mail: montastruc@cict.fr

Keywords: acquired haemophilia; influenza vaccine

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/m²/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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