Case of reactive sacroiliitis possibly induced by an mRNA coronavirus disease vaccine

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SUMMARY
A woman in her 30s received a second dose, first booster, Comirnaty vaccine against the SARS-CoV-2. Three days later, the patient developed unilateral sacroiliitis. A pelvic scan revealed inflammatory joint edges, bone erosion and a heterogeneous mass of 2.5 cm in the psoas muscle. Joint puncture revealed no microcrystalline deposits, but bone marrow cells, erythroblast were identified. The standard bacterial cultures and culture for mycobacteria were negative. HLA B27 was negative, and no seroconversion was identified for the HIV, Epstein-Barr virus, cytomegalovirus, chlamydia or Quantiferon. Two months later, the sacroiliitis resolved. The aetiological approach of this erosive unilateral acute sacroiliitis in a person naïve to rheumatologic pathology was negative for inflammatory or infectious sacroiliitis. Arthralgias after vaccination are expected. Arthritis is less common, and acute sacroiliitis has not yet been described. Acute sacroiliitis may be considered a reactive sacroiliitis to the anti-COVID-19 mRNA vaccine.

BACKGROUND
In view of the COVID-19 pandemic, multiple vaccines for the prevention of COVID-19 were developed and tested. Some rapidly acting vaccines were also available. The first favourable results of phase three vaccine trials were published in November 2020.1

The vaccines were tested on variable populations, including differing age groups (>75 years, 55 years, 18–55 years old, 12–18 years, 5–12 years) and pregnant individuals.2–5 The vaccines’ immunogenicity, efficacy and tolerance were accessed, and the balance benefit risk was evaluated for each vaccine, which was commercialised when this balance proved favourable.

A survey of the pharmacovigilance of each vaccine was initiated. Few side effects were declared considering the magnitude of global vaccination. As with any vaccine, the minor side effects included local pain, myalgia, nausea, headache, fatigue, tinnitus, fever, focal adenopathy and arthralgias, while the major side effects included venous thrombosis, thrombocytopenia autoimmune, thrombocytopenia, myocarditis, pleurisy, pericarditis, Guillain-Barré syndrome and arthritis. Each side effect was also classified as very frequent, frequent, uncommon, rare or undetermined. Some dispositions were established according to the results of a survey on side effects and immunogenicity.6–12 We herein describe a novel case of sacroiliitis that was possibly induced by an mRNA vaccine and that was completely reversible without any sequelae: a reactive arthritis to a vaccine against COVID-19.

CASE PRESENTATION
A woman in her 30s received a Comirnaty vaccination against SARS-CoV-2, including, 3 weeks later, a second dose, and first booster. Three days after her first booster, she experienced acute pain in the right buttock when she attempted to stand from a chair at work. She was unable to stand and was confined to bed. The patient had no medical history. The patient was first considered to have truncated sciatica. No significant lumbar pathology was observed on MRI. The inflammatory biological parameters showed slightly elevated C reactive protein at 70 mg/L. Corticoids and level 2 painkillers (prednisone 1 mg/kg/day postoperative and tramadol 100 mg two times postoperative, respectively) were prescribed but did not improve the patient’s condition. A second consultation with a rheumatologist evoked right sacroiliitis, and the patient was directed to a tertiary rheumatologist centre, where she was hospitalised for 11 days. A body scan identified slight pleuroperticarditis corresponding to the crackles auscultated clinically. Sacroiliitis was confirmed on a scan revealing inflammatory joint edges and a heterogeneous mass of 2.5 cm in the right psoas muscle (figure 1). Bone erosion was identified, explaining the collection by extravasation of the medullary tissue (figure 2). A joint puncture was performed (figure 3), which showed no microcrystalline deposits, but there were bone marrow cells as erythroblast identified. Standard bacterial cultures and culture for mycobacteria were negative. Hemocultures were sterile. C reactive protein 5.5 mg/L, renal and hepatic parameters were normal. HLA B27 was negative, and no seroconversion was identified for the HIV, Epstein-Barr virus, cytomegalovirus, chlamydia or Quantiferon (figure 4). Rest, a level 1 painkiller (paracetamol 1 g by mouth three times daily) use, and non-steroidal anti-inflammatory drug (ketoprofene 100 mg two times a day for 5 days) were sufficient to relieve pain. Two months later, the collection completely disappeared, and the osteitis was rebuilt identically. The sacroiliitis resolved, and the patient recovered and returned to work (figure 5).

The aetiologic approach for acute sacroiliitis in a person naïve to rheumatologic pathology was negative for inflammatory or infectious sacroiliitis. Arthralgias after vaccination often occur as secondary side effects. Arthritis is less common but is well described in any joint. However, acute sacroiliitis is uncommon. A temporal chronology is

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not a strong enough argument for an incriminate vaccine, but the negative aetiologic approach associated may be a strong argument for a possible interaction between the vaccine and the acute sacroiliitis. Seric disease in an mRNA vaccine against SARS-CoV-2 infection was not considered in this case.

INVESTIGATIONS
A pelvic scan and MRI were first performed on the dorsolumbar spine for severe pain in the right buttock without relevant abnormalities.

MRI of the sacroiliac joint demonstrated erosive anterosuperior sacroiliitis with an iliac muscle abscess.

A puncture under scan was performed to determine the nature of the synovial fluid of the sacroiliac joint.

DIFFERENTIAL DIAGNOSIS
An initial diagnosis of truncated sciatica led to erratic treatment and a delay in medical care. Notwithstanding treatment with corticoids for 15 days, systemic manifestations, such as pleuropericarditis, were associated with unilateral sacroiliitis.

The articular puncture disclosed sterile liquid and medullary cells without microcrystalline deposits. Extravasation of the marrow fluid was challenging, explained by a rupture of the cortical bone, as seen on the scan. The aetiologic search for unilateral anterosuperior sacroiliitis excluded a diagnosis with an inflammatory, infectious or autoimmune root cause.

The possibility of a seric reaction or a viscerotropic disease secondary to the mRNA anti-COVID-19 vaccine was rejected based on clinical and biological results.

Non-specific treatments, such as puncture, rest, level 1 painkiller use and non-steroidal anti-inflammatory drugs for a week provided quasi-spontaneous relief of the disease. The restitutio ad integrum of the sacroiliac joint was the last argument for the diagnosis of sacroiliitis.

The triggering factor for reactive arthritis may reasonably be vaccination.

TREATMENT
Initially, the patient was treated for neuralgia sciatica with rest, corticotherapy and level 2 painkillers without efficacy. Later, level 2 painkillers and corticotherapy were discontinued. After puncture, which may relieve local pressure on the joint and/or collection, the anti-inflammatory non-steroid drug ibuprofen was used for 1 week and level 1 painkillers were progressively reduced and then terminated.

No further treatment was provided until restitutio ad integrum of the sacroiliac joint.

OUTCOME AND FOLLOW-UP
The first line of treatment, corticoids and level 2 painkillers, did not improve the patient’s condition. Puncture, rest and level 1
painkiller-use (non-steroidal anti-inflammatory drugs) for 7 days were sufficient to relieve pain and return autonomy. Two months later, the collection completely disappeared, and partial osteitis was rebuilt identically. Inflammation of the sacroiliac joint was resolved.

**DISCUSSION**

We describe a new case of reactive arthritis presenting in a unilateral sacroiliac joint, which was plausibly induced by an mRNA vaccine against COVID-19. Imputability was evaluated using the method by Bégaud. The imputability scores demonstrate the plausibility of an association between the disease and the vaccine. The rechallenge (the third anti-COVID-19 vaccination by Moderna) was prescribed but not done and no reinjection limited the score of imputability.

The COVID-19 pandemic did not induce many rheumatologic symptoms. Myalgias and arthralgias have been well described during the invasive period. Reactive arthritis is defined as aseptic arthritis occurring after infection, at a site distant from the infection. Arthritis attributable to the SARS-CoV-2 infection is rare but perhaps hidden by the fear of a new pandemic disease without recommendations, his major and specific health problem with severe pneumonia, the complex care in intensive care and the high mortality rate. Only two cases of sacroiliitis have been reported that were supposedly induced by the COVID-19 infection.

In addition to severe acute respiratory syndrome, some flares of chronic rheumatic diseases have been attributed to COVID-19. Rheumatologists have made extensive efforts regarding recommendations for the use of disease-modifying antirheumatic diseases and biologic treatments, fearing the impact of modulating immunity with the widespread use of these drugs in rheumatology. The same oversight was implemented through the use of COVID-19 Vaccines Global Access (COVAX) to evaluate the impact of treatment developed to thwart coronavirus: vaccines, monoclonal antibodies and drugs. Furthermore, side effects of vaccines against COVID-19 were monitored closely without deleterious severe side effects.

The key strengths of this case report were the exhaustive overview of the antero-superior erosive sacroiliitis and the follow-up. The imputability of the damage was high, but not definitive. Arthralgias are common but occur as minor side effects of any anti-COVID-19 vaccine (BNT162b2 Comirnaty, mRNA-1273 Spikevax, ChAdOx1 nCoV-19 COVID-19 Vaxzevria, Ad26Cov2.S JM) vaccine and NVX-CoV2373 COVID-19).

Arthritis was described following Vaxzevria, Corona Vac and Sputnik-V which was sometimes severe; however, each case was resolved without sequelae.

The shortcomings of the case study were the absence of an analysis for the SARS-CoV-2 virus in the liquid obtained by puncture of the sacroiliac joint and the absence of histology in this identical joint. However, cytology was normal. Moreover, the delay in current care for the patient in the first hospital, and the identification of inflammation of the sacroiliac joint in the second hospital was over 3 weeks in a patient treated with corticosteroids without benefits. This treatment may disrupt the aetiological process of acute erosive anterosuperior sacroiliitis.

However, systemic manifestations, such as pleuropericarditis, may be integrated into reactive manifestations secondary to vaccines or adjuvants. A seric reaction is formally different, showing no fever, no renal manifestations, a short delay between vaccination and clinical symptoms and no response to corticosteroids. No intercurrent disease was identified through an exhaustive search.

In conclusion, temporal association does not imply causation, and the risk of severe arthritis is very low after a mass vaccination with mRNA vaccines against COVID-19. However, a reactive arthritis on the sacroiliac joint, secondary to vaccine against COVID-19, may be a new aetiology of unilateral sacroiliitis.

**Patient’s perspective**

Pains appeared 3 days after vaccination. At the end of afternoon, I was not anymore, able to walk or dress.

During my stay in hospital, where visits were scary and short, I could not see my young daughter, old of 16 months; the pains were stronger than pains of childbirth contractions and it was difficult to manage stress in the absence of visibility of events.

Back to home, resources were put in place to be able to take care of my daughter. But facing the loss of autonomy, I tried to keep in touch with my daughter who did not understand the situation.

Along weeks and medical examinations, mobility came back slowly. My daughter has adapted herself to this situation. It was a period difficult for me, as a mother not to be able to perform simple gestures, carry, put in bed my child alone…

Today, despite some pain, I have a normal life, taking full advantage of time with my family.

**Learning points**

- Reactive arthritis may follow any vaccination.
- A temporal chronological sequence between vaccination and sacroiliitis is not a sufficient argument for causality.
- Suspected guilty antigen reintroduction is a valuable argument for imputability of side effects but may be dangerous, painful and the patient may be reluctant to reintroduction test.

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Case report

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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