

## Case Report

# Knee osteonecrosis after COVID-19

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### Abstract

**Background:** COVID-19 is an emergent infection, the long-term complications of which are still under study. While hypercoagulability is a common feature in severe cases, the incidence of ischemic complications such as osteonecrosis remains unknown. Previous studies on SARS-CoV1 found an increase in osteonecrosis 3–36 months after infection, and it is still unclear if this was related to the use of corticosteroids or to the virus itself.

**Methods:** We introduce a 78-year-old woman who complained of right knee pain and swelling a month after COVID-19 infection onset. Her knee radiography showed no significant changes compared to previous ones. MRI, on the other hand, found osteonecrosis in the internal femoral condyle. No coagulation abnormalities were found in blood tests.

**Results:** While knee replacement should be her main treatment, it will be long delayed due to the pandemic. In the meantime, we increased her tapentadol and salicylic acid doses and gave her home exercises to improve functionality.

**Conclusion:** In the follow-up after COVID-19, any muscular or joint pain with unusual characteristics should be carefully examined.

**Key words:** Corticosteroids, COVID-19, hypercoagulability, joint pain, osteonecrosis, SARS-CoV1

### Introduction

After SARS-CoV1 epidemic, an increase in osteonecrosis has been detected, with 5–58% cases in different series (1–5), but this complication has not been studied in the current pandemic (4,5). In SARS-CoV1 cases, osteonecrosis appeared 3 months to 3 years after the infection (2,6). Diagnosis could be delayed when the joint pain was considered a normal convalescence symptom.

Overuse of corticosteroids (1,2,4,5,7), hypercoagulability (8) and a bone resorption mechanism induced through ACE-2 receptor (5) were pointed out as possible causes. All of them are also related to COVID-19 and may lead to this same outcome.

### Case report

We present a 78-year-old woman who, 1 month after the first symptoms of COVID-19, referred increased pain and swelling in her right knee. She also felt dizziness, asthenia, mild dyspnoea and a feverish sensation with normal temperature, as part of a parasympathetic post-COVID syndrome.

Her previous conditions were hypertension, hyperlipemia, a heart stroke with no secondary dyskinesias and AV block treated with an insertable cardiac monitor implant. Her thyroid gland had been removed, with current hypothyroidism and hypoparathyroidism well adjusted with treatment. She required home oxygen therapy and continuous positive airway pressure due to hypoventilation, sleep apnoea and obesity.

Arthrosis and meniscus degeneration were present in both knees, mainly affecting the left one. Surgery had been ruled out in the previous year. She took 200 mg per day of tapentadol to control pain and used a cane for long walks.

On March 26, she referred mild fever and dyspnoea, with cough 5 days later. She was treated with levofloxacin and azitromycin and sent to hospital after 2 days with no improvement. She stayed in hospital for 1 week, treated with hydrochloroquine, lopinavir, ritonavir and an increase of oxygen supply. While she had three negative PCR on the nasopharyngeal tract, her chest X-rays revealed COVID-19-like pneumonia.

## Key Messages

- Physicians should keep aware of ischaemic complications of COVID-19.
- What can we learn from SARS-CoV1 epidemic?
- Any atypical joint pain after COVID-19 should be carefully studied.
- We need to monitor corticosteroids side effects in COVID-19 patients.

Two weeks after discharge, her right knee pain worsened. She also referred a mild increase in dyspnoea, with 92% oxygen saturation. We gave her a total dose of 165 mg of prednisone over 9 days to treat her bronchospasm. One week later, she presented local swelling on the internal side of the knee. X-ray tests displayed on both knees showed no changes since the last control.

The MRI showed a broken internal meniscus, dislodged to femorotibial recess; chronic sprain in collateral internal ligament; and oedema due to osteochondral damage in condyle surface measuring 20 × 28 mm with collapse of the anterior segment of the condyle. No instabilities or loose fragments were found. These findings suggested osteonecrosis of the internal condyle in the right knee.

Orthopaedic surgeons recommended full knee replacement and rehabilitation. Heparine was not prescribed because four different blood tests showed no coagulation or platelet abnormalities. As both surgery and rehabilitation will be long delayed due to the pandemic, primary care professionals gradually doubled her tapentadol and tripled her salicylic acid doses and gave her home exercises to strengthen the muscles.

Both pain and swelling were reduced within 1 month of diagnosis. Our patient is currently waiting for surgery, using tapentadol 300 mg and salicylic acid 300 mg per day. She can walk using a cane, as she did before, but with increased pain and instability.

## Discussion

Osteonecrosis has been thoroughly studied since SARS-CoV1 appeared and is likely to occur after COVID-19. The main risk factor in studies on SARS was the overuse of corticosteroids (1,2), also common in COVID-19. Other drugs used in both infections, such as lopinavir and ritonavir (5), can produce osteonecrosis. Some virus-related mechanisms were also pointed out as possible causes: the hypercoagulability induced both by SARS-CoV1 and SARS-CoV2 (4,5,8) and an increase in bone resorption mediated via ACE-2 receptor (5). Despite all those risk factors, common to both viruses, no cases of osteonecrosis after COVID-19 have yet been reported (4,5). Our patient had other risk factors for osteonecrosis, such as previous arthrosis, age, obesity, high cardiovascular risk and a possible muscular loss during confinement. Her alcohol intake was mild, and she quitted smoking >10 years ago. Nevertheless, the short period between infection and ischaemic complication, shorter than that observed for SARS-CoV1 (2,6), may suggest a correlation.

At the beginning of the current pandemic, caution in the use of corticosteroids was advised (7,9,10). Our patient did receive a small, low-risk dose of oral prednisone when she already had symptoms, but although this might have worsened her osteonecrosis, it is unlikely to be the cause, for her symptoms had already started when they were prescribed. She did take lopinavir and ritonavir at hospital, which also can cause osteonecrosis (5).

Main treatment for her condition should be knee replacement, but it will be long delayed in her case. Alendronate (5) was not a viable treatment as she had already taken it for >5 years before. Enoxaparin (5) was ruled out by both internal medicine and orthopaedic surgery, considering her normal coagulation and platelets in blood test. Extracorporeal shock wave therapy (5) was not available for primary care. Our only non-operative management options were increasing salicylic acid dose, pain management, protected weight bearing and home exercises. Her mild relief may as well be due to those or to spontaneous improvement (3,5) observed in some osteonecrosis cases.

In different studies of SARS-CoV1 epidemic, osteonecrosis was detected in 5–58% of patients (4). Corticosteroids seemed the main related risk factor, as they were widely used on those patients, and the total dose apparently correlated (1,2,5). However, incidence was 45% higher than that found after same-dose corticosteroid treatment for other reasons (3,5), and sometimes even appeared after low-risk doses (3). Other drugs used in both infections, such as lopinavir and ritonavir, can also cause osteonecrosis (5). Hypercoagulability and an increase in lupic anticoagulant are also known osteonecrosis risk factors (1,3,4), associated with both SARS-CoV1 and COVID-19 (5,8). Even an increased bone resorption mediated via ACE-2 receptor was described for SARS-CoV1, having SARS-CoV2 a higher affinity for this receptor (5). Any of those factors can be expected to increase osteonecrosis also after COVID-19.

Unlike in our case, the mean age of osteonecrosis patients during SARS-CoV1 was 32.1 years (6), with a higher incidence in men, appearing even in children (3). The average time lapse since infection was 6 months (91–143 days) (2,6) and up to 3 years (2).

While osteonecrosis has not been reported after COVID-19 (4), there is a high risk of detecting an increase in the former due to hypercoagulability (8), increased bone resorption and the use of corticosteroids in severe cases (9,10). They may occur months to years after the primary infection. Thorough studies to assess incidence and risk factors would help discriminate the usual post-infectious joint pains from severe complications.

The current pandemic has a short history, and many long-term complications are yet unknown. We should be vigilant to assess possible new outcomes, mainly those that can be expected from our knowledge of COVID-19 and SARS-CoV1. Osteonecrosis, an ischaemic illness associated with corticosteroid use and SARS-CoV1, should be something to monitor.

## Patient perspective

A month after COVID-like pneumonia, the patient developed acute pain, swelling and joint failure in the right knee. Currently her pain has lowered to moderate and intermittent, increasing along the day, with some remaining instability. She complains about the lack of information and follow-up by orthopaedists and the delay in surgery, which, despite asking for a second opinion in a different hospital, will be likely to happen a year after diagnosis. On the other hand,

primary care attention, while missing face-to-face appointments, seems adequate and thorough enough to her.

## Declaration

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Ethical approval: verbal consent was provided by the patient for this case report.

Conflict of interest: none.

## Data availability

No new data were generated or analysed in support of this research.

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