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Short communication

COVID-19 reinfection after pregnancy

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ABSTRACT

Background: There have been reports of COVID-19 reinfections, but the immunological characterization of these cases is partial. We report a case of reinfection with SARS-CoV-2, where the first infection occurred in the course of late pregnancy.
Case presentation: On May 27, 2020, a 37-year-old woman gave birth at full term, 3 hours after full dilatation. She developed fever (38.3 °C) after delivery. Mild biological anomalies compatible with COVID-19 were observed: lymphopenia, thrombocytopenia, elevated D-Dimers, CRP, and LDH. At 6-month follow-up, she reported having contracted COVID-19 with high fever, rhinorrhea, hand frostbites, cough, headache, dysgeusia and anosmia.
Conclusions: We report a case of COVID-19 reinfection with a first mild infection during late pregnancy and a more aggressive second infection 5 months later.

1. Background

The SARS-CoV-2 virus is the third known coronavirus after SARS-CoV and MERS-CoV. It was identified on January 9, 2020 and is responsible for severe lung damage with pneumonia in humans. For some viruses, the first infection can provide lifelong immunity; for seasonal coronaviruses, protective immunity is short-lived [1]. Duration of protection after COVID-19 is unknown and correlates of protection after SARS-CoV-2 vaccination need to be defined. There have been reports of COVID-19 reinfections, but the immunological characterization of these cases is partial [2]. The role of protective antibodies is probably essential, but protective cellular immunity could also play a role.

COVID-19 and acute respiratory distress syndromes (ARDS) are both characterized by an exacerbated inflammatory response related to macrophage activation syndrome and the ensuing "cytokine storm". For ARDS, the viral load does not correlate with worsening clinical signs [3]. A dual therapeutic approach (antiviral and anti-inflammatory) has been proposed [4]. Due to the exacerbated inflammatory response to the virus, it is necessary to better understand the various cellular pathways leading to this immune response dysregulation. Among the immunological checkpoints of the immune response, the HLA-G molecule – a non-classic HLA class 1 molecule – is a well-known checkpoint [5] for its tolerogenic role, initially described for fetal-maternal tolerance [6]. We report a case of reinfection with SARS-CoV-2, where the first infection occurred during the course of late pregnancy.

2. Case presentation

On May 27, 2020, a 37-year-old woman gave birth at full term in our facility, 3 hours after full dilatation. She developed fever (38.3 °C) 2 hours after delivery. She had no comorbidity related to severe COVID-19 infection such as obesity, diabetes, or hypertension. The patient carried heterozygous Factor V Leiden mutation and had a family history of thromboembolism carrier and had received low-molecular-weight heparin prophylaxis (enoxaparin sodium) from 30 weeks of amenorrhea onwards. She also received valaciclovir from 36 weeks up until delivery for herpes recurrence during pregnancy.

In line with the recommendations, a nasopharyngeal SARS-CoV-2 RT-PCR test (Allplex2019-nCoV, Seegene, Seoul South Corea) was immediately performed and returned positive. The patient developed no other symptom subsequently, and fever disappeared. Blood oxygen saturation was 99% while breathing ambient air. Mild biological anomalies compatible with COVID-19 were present:

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Table 1
Blood test results (bold characters for out-of-range results) (May 27, 2020).

	Hematology		Biochemistry		
Hemoglobin	12.2 g/dL	Normal			
WBC count	19.8 10^9/L	+	Procalcitonin (PCT)	0.0974 µg/L	
Lymphocyte count	1. 10^9/L	–	Ferritin	45 µg/L	Normal
Neutrophil count	17.8 10^9/L	+	D-dimer[a]	5.565 mg/L	+
Hematocrit	35.5%	–	INR	< 1 normal	< 1 normal
Platelets	143. 10^9/L	–	CRP	26.1 mg/L	+
Monocytes	0.9 10^9/L	+	LDH	271 UI/L	+

+: increase values; –: decrease values.
[a] 9 hours after enoxaparin sodium injection.

lymphopenia, thrombocytopenia and elevated D-Dimers, CRP and LDH (Table 1).

On May 30, 2020, the anti-SARS-CoV-2 IgG test (Abbott) was negative. Negative anti-SARS-CoV-2 IgG was confirmed 4 months later on September 29 by Roche Cobas® 6,000 diagnostic test (IgG index: 0.07).

At 6-month follow-up, the patient reported having contracted COVID-19, with symptoms from November 8 to 15, 2020 (high fever, rhinorrhea, hand frostbites, cough, headache, dysgeusia, and anosmia). She had a positive RT-PCR test on November 9 (SARS-CoV-2 multiplex, Eurobio Scientific). Serology for SARS-CoV-2 was strongly positive on December 7, 2020 by Roche electrochemiluminescence diagnostic test with total antibody index at 86.3 (negative < 1.00).

3. Discussion and conclusions

We report a case of COVID-19 reinfection with a first mild infection during late pregnancy and a more aggressive second infection 5 months later. Both episodes of COVID-19 were confirmed by positive nasopharyngeal RT-PCR tests.

The only signs of the first infection were brief acute moderate fever and mild blood test anomalies. Pregnant patients present with the same clinical characteristics of COVID-19 as the general population, but they may be more often asymptomatic [7]. This pauci-symptomatic COVID-19 case would not have been diagnosed if it were not for the systematic screening of febrile patients implemented during the first epidemic wave in France.

Fever is a frequent condition in postpartum women especially with long delivery.

A meta-analysis covering 10,491 patients suggested that CRP, PCT, LDH, and D-dimer could be early biomarkers of COVID-19 severity [8].

Elevated D-dimer concentrations usually reflects active coagulation and fibrinolysis, especially in case of COVID-19 infection during late pregnancy [9]. In our case, this condition could be linked to the heparin therapy received at the same time as the SARS-CoV-2 infection [9]. Indeed, D-dimer concentrations exponentially increase in pregnant women receiving heparin, peaking at the time of delivery [10].

Similarly, the increased CRP level observed in our patient after delivery may not be specific of SARS-CoV-2 viral infection; nevertheless, the rate observed in our patient is much higher than those reported by Mertens (around 10 mg/L) [11].

If recent data seem to show a low risk of maternofetal transmission for the fetus [12], more severe cases of COVID-19 were described during the third trimester of pregnancy with a higher risk of ARDS, cesarean section [13], and premature birth [14]. The pathogenic thrombotic consequences of SARS-CoV-2 infection may threaten the pregnancy with maternal increase risk of thrombosis, intrauterine growth retardation, preeclampsia, and placenta thrombosis [13]. In our case, the use of low-molecular-weight heparin prophylaxis, administered for another reason, may have improved the outcome of the patient and her baby.

Titers, evolution, and the protective role of antibodies against SARS-CoV-2 reinfection are subjects to fierce debate. After mild or asymptomatic infection, low or undetectable titers or antibodies have been reported [15]. Recent data showed only 4.7% of positive anti-SARS-CoV-2-IgG antibodies among 529 pregnant patients systematically tested during labor between April and June 2020 in Paris [16]. Our patient's serological tests performed in May and September were indeed both negative, but SARS-CoV-2 serology was strongly positive after the second COVID-19 episode. Similar cases have been reported [17]. A negative serology three days after delivery could be associated with infection that occurred several days or weeks before, with an unrelated fever during delivery, or could be related to the pregnancy-related immunodeficiency.

Persistent or fluctuant expression of SARS-CoV-2 RNA in the oropharyngeal swab test was reported, but this was reported in case of severe clinical symptoms or immunosuppressive conditions [2].

A few papers reported reinfection with SARS-CoV-2, but none related to a first episode occurring in a pregnant patient. Modulation of the maternal immune system during pregnancy and hormonal variations may affect the response to various infections, and more specifically to viruses. These alterations could be mediated in part by a decreased antibody level and could explain the negative serology after the first episode, contrasting with the strongly positive test after the second episode [18].

However, reinfection due to a variant viral strain could be a possibility as numerous new and more aggressive variants are described [19]. Several cases of reinfection were fully documented, but with respect to the millions of infected patients, those cases are rare. Selvaraj [20] described a clinical case of severe symptomatic reinfection and presented a summary of reported reinfection cases. He stated that there is an apparent paradox between declining antibody levels and low incidence of reinfection, implying that other immune mechanisms are at work, including T lymphocytes. Our case questions pregnancy as inhibitor of antibody production. To our knowledge, it is the first case of reinfection after pregnancy. The role of HLA-G immuno-inhibitor may be questioned and may be a possible treatment.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

Contribution of authors

AL, AV, and DZ wrote the article. MC, JL, OB, AM, JMA, and EF contributed to re-writing the article. All authors read and approved the definitive version of the manuscript.

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Disclosure of interest

The authors declare that they have no competing interest.

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