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SHORT REPORT



Considerations on COVID-19 pregnancy: a cases series during outbreak in Bergamo Province, North Italy

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ABSTRACT

Background: COVID-19 has rapidly spread worldwide, with severe complications affecting particularly elderly and compromised subjects. Less information about COVID-19 in pregnancy has been reported so far in the literature.

Methods: Case series on pregnancies complicated by COVID-19. All cases were diagnosed at Bolognini Hospital, Seriate, Italy. These cases are presented to clarify the features of COVID-19 occurring in pregnancy.

Results: Four women had symptoms of COVID-19 during pregnancy or immediately after delivery. All cases were confirmed by oropharyngeal swab. All patients presented with fever and low saturation levels at the diagnosis. One case was transferred after diagnosis to a tertiary referral center and delivered the day after for worsening clinical conditions. In the other three cases, bilateral pneumonia was documented at the admission. Antithrombotic therapy was used in most cases. No cases of the infected neonate was reported. At 2 month follow-up, all patients were alive, three were asymptomatic while one presented neurological complication. One more case was described because suspicious for COVID-19, however, it was not confirmed by oropharyngeal swab.

Conclusions: In pregnant women, the peripheral nervous system could be affected. No case of trans-placental passage was reported. The swab could be helpful in diagnosis. The antithrombotic therapy could play a role in the positive course of COVID-19 also in pregnant women.

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COVID-19; new coronavirus-19 infection; pregnancy infection; fetal infection

Introduction

COVID-19 has spread pandemically since it was first documented in Wuhan during December 2019, showing the second epicenter in North of Italy (Lodi and Bergamo) in February 2020 [1].

Few and contrasting data were reported so far in the literature about the disease occurring in pregnancy [2–10], hence strong evidence about the optimal management is lacking.



Our aim was to report maternal/neonatal outcomes of pregnancies complicated by COVID-19 that occurred in the Bolognini Hospital, with the intent to expand information on disease features during pregnancy.

Methods

Cases series of pregnancies complicated by COVID-19 diagnosed in a single center who delivered and completed 2 months follow-up.

Bolognini Hospital is a “spoke center” for COVID 19 in pregnancy in Seriate (Bergamo, Italy). According to national policy, pregnancies suspected for or affected by COVID-19 infection should be referred to HUB-Hospital. Nevertheless, “spoke” Departments are asked to manage more severe patients unsuitable to be transferred.

Suspected cases were defined according to a check-list and oropharyngeal swab for COVID-19 was undertaken [10] to make the diagnosis. COVID-19 RNA was assessed by real-time amplification kit.

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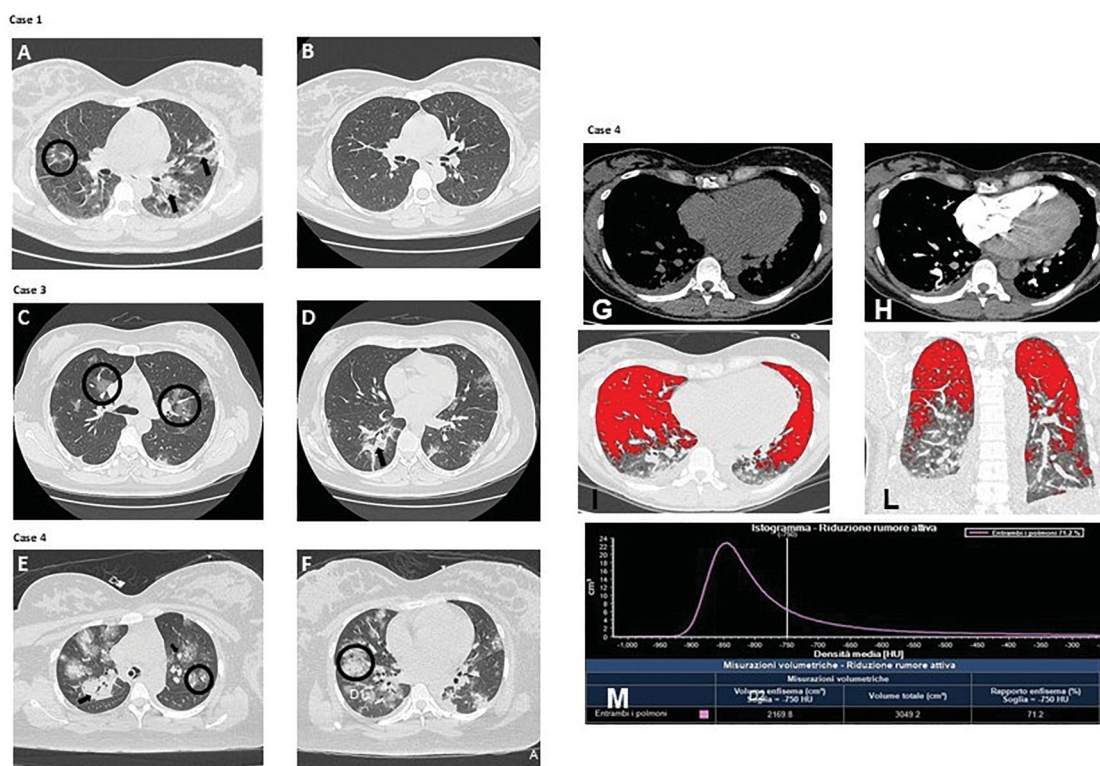


Figure 1. Computed tomography images-Bilateral interstitial pneumonia, with ground glass opacity (black circles), and consolidation areas (black arrows). (A,B) Case 1 (A: at diagnosis; B: complete regression 40 days after). (C,D) Case 3. (E,F) Case 4. (G,H) Case 5 basal and intravenously contrasted computed tomography, which excluded embolism. (I,L,M) elaborated images with in red the normal functioning lungs and calculation of %aerated parenchyma.

In order to increase the knowledge on maternal, fetal and neonatal outcome, we described all cases of pregnancies complicated by COVID-19 that were diagnosed in our department, who delivered and completed a 2 months follow-up.

A maternal follow-up was performed by phone interview; 1 month after delivery, all neonates were reassessed for evaluation and repetition of oropharyngeal swab.

Cases

Case 1–4 performed oropharyngeal swabs for symptoms and resulted positive for COVID-19 during hospitalization.

Neonatal swabs for cases 1–4 were performed both at birth and 1 month after birth, all turned out to be negative for COVID-19.

Maternal and neonatal characteristics are provided in the [Supplementary material](#).

Case 1. 36 + 0 weeks

Induction of labor was performed for insulin-treated gestational diabetes mellitus. Patient's husband developed COVID-19 pneumonia three days before. At admission, no clinical signs of COVID-19 were

detected. The woman had an uncomplicated vaginal birth. After delivery, she developed fever (39°C), cough, asthenia and diarrhea. A computed tomography (CT) scan detected interstitial pneumonia (Figure 1(A)). Thrombocytopenia and lymphopenia ($0.76 \times 10^9/L$) occurred, thus antiviral, antibiotics and Hydroxychloroquine were administered. Given the onset of desaturation (93%) and tachypnea, O₂ therapy was started. Nine days after delivery, her clinical conditions were stable, and she was transferred in a longterm supporting center. The CT-scan performed 40 days after delivery (Figure 1(B)) showed a complete regression. Two months after delivery, the patient was asymptomatic at home.

The neonate presented no symptoms and no adverse outcomes.

Case 2. 27 + 4 weeks

Presented to the emergency room for fever and cough. At admission, the cardiac frequency was 120 min, respiratory frequency 18 min, temperature 37.9°C and saturation 92%. O₂ therapy improved saturation levels (95%). She was then transferred to HUB-hospital and an urgent C-section was performed for worsening maternal conditions.

Excepted for iatrogenic severe-prematurity, the neonate did not present complications.

The maternal condition improved after she gave birth.

Case 3. 38 + 4 weeks

Admission for rupture of the membranes with no signs of infection. A C-section was performed due to a not-reassuring cardiotocography, associated with fever (38.2 °C) and CRP 7 mg/dL (other blood tests were normal). The neonate was fine. The placental bacterial culture was negative. The placental histology did not report signs of infection/inflammation. The patient was treated with antibiotics, for suspected chorioamnionitis, but despite therapy, she presented fever (39.2 °C) and general malaise. She developed thrombocytopenia and lymphopenia ($0.8 \times 10^9/L$). Interstitial pneumonia was diagnosed at the CT-scan (Figure 1(C,D)). The patient fully recovered 5 days later, then she was discharged with antibiotic and antithrombotic.

Two months later she presented completely recovered; husband and neonate remained both asymptomatic.

Case 4. 37 + 3 weeks

Presented for fever, dyspnea, and reduced fetal movements. At admission, she showed fever (38.4 °C) and desaturation (96%). Cardiotocography showed fetal tachycardia (180 bpm) and a reduction in the short term variability. Her clinical condition rapidly worsened, with tachypnea (44/min) and severe desaturation (86%), without response to O₂ therapy. Thus, an emergent C-section was performed. The newborn was fine. A CT-scan detected interstitial pneumonia (Figure 1(D,E)). The saturation remained low despite intubation, ventilation and prone position, therefore she was transferred to HUB-Hospital, extracorporeal circulation undertaken and removed 15 days later. At 1 month follow-up, she was still in hospital because of the onset of an ascending Guillan Barré Syndrome. Two months after delivery she was transferred to a long-term supporting center.

The neonate showed no complication.

Case 5. 35 + 6 weeks

Dichorionic-diamniotic twin pregnancy admitted for rupture of the membranes. One week before she developed a Bell's paralysis (treated with oral dexamethasone).

She underwent a C-section with no complications. Neonates were in wellbeing. One day later, exactly the day of Italian COVID-19 alert, the patient presented with retrosternal and inter-scapular pain, desaturation (78%) and bradycardia (50 bpm). No laboratory signs of myocardial infarction. At the CT-scan, interstitial pneumonia was suspected and cardiomegaly was described. No pulmonary embolism was observed (Figure 1(G,H)). Legionella and Pneumococcus antibodies were negative. Antibiotic therapy was started in association with Enoxaparin. A progressive prolongation in QT interval (658 msec) was detected (interpreted as a possible effect of antibiotic). She presented thrombocytopenia, elevated liver enzymes and increased creatinine. She never developed fever. She progressively improved and was discharged 9 days later, in good clinical condition under enoxaparin and cortisone.

At 2 months follow-up, she declared her suspicion to have had COVID-19 infection during her hospitalization. Therefore, she stayed in a spontaneous quarantine. Her family remained asymptomatic. Accordingly, we proposed to the women a serological evaluation for COVID-19: a rapid test (DiaSorin test) showed IgG+ (with a subsequent serologic dosage of 16,9 AU/mL) and IgM-. We reviewed her CT-scan and observed a 30% of not aerated lung parenchyma, with no sign of embolism, in keeping with COVID-19 lungs involvement (Figure 1(I,L,M)).

Discussion

Even if more information are required to place any conclusions, we would like to make some considerations in the light of our experience:

1. Iatrogenic preterm delivery for maternal condition is likely in severe COVID-19 [7,8].
2. Consider C-section in case of necessity of rapid ventilator support even if COVID-19 is not an indication itself [2,5,6,9].
3. Possibility of rapid worsen. Speculating on that, young and a preexisting good condition might be correlated with a postponed arrival to hospital, with a more severe disease [11].
4. Due to absence/delayed symptoms and the possible absence of typical symptoms, consider all patients potentially infected, test all patients and equip with appropriate personal protection devices all medical/paramedical staff [5]. In the aftermath, case 5 was our first case of COVID-19 in pregnancy.

5. Treat symptoms, despite of swabs results: in case of symptoms the patients should start the therapy even if the swab was negative (30% false negative rate).
6. Transplacental transmission was not documented, according to the literature [7,9]
7. Enoxaparin was safe and could prevent and treat pulmonary vascular impairment also in pregnancies [12–14]. Another speculation: considering the progressive hypercoagulable pattern in pregnancy, an early administration should be suggested.
8. Consider COVID-19 neurotropism [15]. Two of our cases presented involvement of nervous system (at onset as a Bell-paralysis and as complication of systemic disease).

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