Brain Imaging Findings in COVID-19 Positive Newborns

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7.1 Introduction

Only limited data regarding COVID-19 infection in paediatric and neonatal population are available yet: COVID-19 tends to spare newborns and risk of severe disease in infected patients is low [1].

A retrospective review of 1099 cases of COVID-19 in China identified nine children [2] and, according to a retrospective study of 266 hospitalized children in Wuhan, the virus was isolated in only six children [range 1–7 years age]: only one child had severe disease requiring intensive care [3]. After an outbreak of Kawasaki disease in paediatric patients, some colleagues from our hospital in Bergamo, have suggested in a recent work that also children can be affected by SARS-CoV-2 even if not directly for pulmonary involvement at least with endothelial damage. Moreover, SARS-CoV-2 epidemic was associated with high incidence of a severe form of Kawasaki disease [4].

About newborns, since SARS-CoV-2 is contained in most body fluids and secretions, faecal-oral transmission can occur, raising the possibility of transmission from mother to baby at birth, although not prenatally.

Few data on CNS involvement by COVID-19 infection in paediatric and neonatal population are reported in the literature [5, 6]: in a study of children with respiratory disease and acute encephalitis-like syndrome, in approximately 12% of cases there was evidence of an acute coronavirus infection [7].

Few reports of encephalitis [8] including Bickerstaff’s encephalitis [9] are available regarding MERS: MRI showed hyperintense signal abnormalities on T2-weighted imaging in deep and subcortical white matter, corpus callosum and basal ganglia [8].

In a 5-year-old child with lower extremity pain, impaired walking, peripheral facial weakness and bulbar palsy, HCoV-OC43 infection has been found [8]. MERS can also trigger a post-infectious brainstem encephalitis and Guillain-Barre syndrome [10]. Regarding COVID-19, there are Chinese reports of transverse myelitis [11].

There are three main ways in which COVID-19 could affect newborns:

1. Newborns might be infected by COVID-19 before, during or soon after birth: this may lead to breathing or feeding problems, requiring hospitalization.
2. COVID-19 could affect newborns already hospitalized for other medical conditions (like prematurity) that increase the risk of severe infection.
3. COVID-19 can modify the clinical management of mothers during pregnancy or labour, leading to indirect problems to some babies although not directly infected by the virus [1].

7.2 Case Description

Between February and May 2020, seven all term neonates with adequate Apgar score (age range 44–118 days, average 81 days; three males and four females) were evaluated at the Neonatal Intensive Care or Sub-Intensive Care Unit and Neuroradiology Department of our hospital (Papa Giovanni XXIII Hospital in Bergamo, Italy), mainly due to fever and feeding impairment. All patients had a positive swab therefore they were considered as proved cases of SARS-CoV-2 infection and hospitalized in COVID-19 dedicated wards. Only three mothers had a positive SARS-CoV-2 nasopharyngeal swab at the NICU admission of their babies: mothers weren’t tested for COVID-19 at the time of labour.

The medium age of nasopharyngeal swab normalization was 38.5 days.

7.2.1 Magnetic Resonance Imaging (MRI)

In all patients, no morphologic anomalies nor qualitative and quantitative signal alterations in grey and white matter on all the sequences performed in particular on T1 and T2-w sequences (data not shown).

In four cases (patients 3, 4, 5, 7) we visually found a mild to moderate reduced diffusion in the genu of the corpus callosum (hyperintensity in DWI and hypo intensity on the ADC map): this finding was confirmed on quantitative ROI-based (see methods) analysis of the genu of the corpus callosum (example of patient 4 in Fig. 7.1).

ADC and FA values were compared to normal ones (corrected for age) reported in the literature [12–17].

Regarding the splenium of the corpus callosum, no signal alterations on DWI were found at visual inspection: quantitative ADC ROI analysis revealed mild diffusion reduction compared to the literature, especially in patient 2.

In six out of the seven COVID-19 neonates, there was a mild diffusion reduction in the genu of the corpus callosum. In five cases restriction can be appreciated both on visual inspection and with a quantitative analysis while in one case only ROI-based approach was able to highlight this finding. Only by quantitative assessment a slight diffusion restriction in the splenium of the corpus callosum can be picked up. FA and T1-T2 signal were in normal ranges in the corpus callosum.

Well-known entities associated with involvement of the splenium of the corpus callosum include the reversible splenial lesion syndrome (RESLES) and MERS, which is a clinical-radiological entity characterized by mild encephalitis or encephalopathy associated with reversible lesion of the splenium of the corpus callosum. Transient lesions in the splenium of the corpus callosum can occur in several conditions such as epilepsy, following the sudden withdrawal of antiepileptic drugs, influenza encephalitis, and other conditions such as haemolytic-uremic syndrome, subarachnoid haemorrhage, trauma (diffuse axonal injury), hypoglycaemia, hypernatremia, osmotic myelinolysis, Wernicke encephalopathy, Marchiafava–Bignami disease and haemolytic-uremic syndrome [18–20].

In addition, isolated involvement of the splenium of the corpus callosum may also occur in patients with ADEM [21]. We can consider that the lesion in the splenium of the corpus callosum in our patients is of demyelinating nature (likely post-viral).

The pathogenesis can be related to markedly increased levels of cytokines and extracellular glutamate, leading to dysfunction of the callosal neurons and microglia. Cytotoxic oedema develops when water becomes trapped in these cells [18, 19].

Cytotoxic lesions of the corpus callosum (CLOCCs) are areas of low diffusion, equal or slightly low T1 signal, high signal on T2-FLAIR sequences and no enhancement after paramagnetic contrast agent injection. It is also possible to observe only diffusion reduction without any
abnormal signals under conventional sequences. These lesions tend to be midline and relatively symmetric [18–22].

Viral aetiologies represent the most common cause of CLOCCs callosal lesions, which usually become evident from as early as 2 day of onset of symptoms. Among all the possible viral agents (influenza, rotavirus, mumps, E. coli, adenovirus), rotavirus and Parechovirus have peculiar imaging pattern [18, 22, 23]. To date, both in adult and in paediatric/neonatal population, no cases of selective genu involvement have been described [18–22].

Then, our findings of selective moderate diffusion reduction in the genu (and, in a lesser extent, in the splenium) of the corpus callosum might represent a different type of CLOCCs possibly related to COVID-19 CNS neonatal infection. Larger studies are needed to confirm and better understand these findings and the appearance of these data in this atlas is just to be aware of these possible findings.

Fig. 7.1 Qualitative and quantitative assessment of the genu and splenium of the corpus callosum in patient 4 (the most significant) on morphologic, diffusion and diffusion-tensor imaging. (a, b, g): T2-weighted and T1-weighted (3D Ax T1 and Sag SE T1) sequence for genu and splenium of the corpus callosum (separated enlarged view). (c, d): DWI and ADC with diffusion restriction in the genu of the corpus callosum. (e, f): Quantitative ROI-based evaluation of corpus callosum on coloured FA and ADC map, respectively, in which an ADC reduction and mild FA increase compared to the literature can be appreciated (see text). (h): DTI reconstruction of corpus callosum (deterministic tractography) with normal findings.

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