First case of COVID-19 infection in a adult patient with Ellis-van Creveld Syndrome

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Case Report

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Abstract

Background: Ellis-van Creveld syndrome (EVC) is a rare autosomal recessive disorder, the features of the syndrome are: chondral and ectodermal dysplasia characterized by short ribs, polydactyly, growth retardation resulting in dwarfism, teeth and craniofacial abnormalities and heart defects (mostly endocardial cushions and atrial septal defects).

Case presentation: We describe the first case of COVID-19 infection in a 24-years-old girl, diagnosed with EVC syndrome. The patient suffered only from a mild illness, she remained stable with normal saturation without need of neither respiratory support nor specific therapy and she was rapidly discharged.

Conclusions: This case appraises the pathophysiologic interplay between different specific prognostic variable in a syndromic patient with congenital heart disease and COVID-19.

Background

Ellis-van Creveld syndrome (EVC) is a rare autosomal recessive disorder, firstly described in 1940 by Richard W.B. Ellis and Simon Van Creveld. (1) It is caused by mutations in the EVC or EVC2 genes located on the chromosome 4, coding for components of the primary cilia, and is associated to parental consanguinity in about 30% of cases. (2-4)

EVC syndrome, like Jeune asphyxiating thoracic dysplasia (JATD), is part of the skeletal ciliopathies, sharing common clinical and radiological features. There is a large spectrum of severity in skeletal involvement, however, differently from JATD, extreme thoracic hypoplasia is rare in EVC. (5)

The EVC syndrome features include chondral and ectodermal dysplasia characterized by short ribs, polydactyly, growth retardation resulting in dwarfism, teeth and craniofacial abnormalities and heart defects. (6-8) The prevalence of cardiac anomalies in patients with EVC syndrome has been estimated to affect 60% of individuals. (9) The cardiac phenotype in patients with EVC syndrome reveals a characteristic pattern of atrioventricular canal defects (AVCD) with systemic and pulmonary venous connection abnormalities and common atrium (10)

Case Description

We describe the first case of COVID-19 infection in a 24-years-old girl, diagnosed with EVC syndrome. She had undergone ostium primum atrial septal defect repair at age of five, genu valgum deformity correction and tibial lengthening at the age of eleven. (11) At age of ten, she was prescribed growth hormone for GH deficit, that she stopped due to headache. (12) The patient displayed all the somatic syndromic signs, including thet agenesis, short lingual frenulum and obesity. In addition she was on chronic Cortone Acetate because of lichen planus.

The patient presented to the emergency department with fever and dry cough lasting for the last two days. She was eupnoic at rest with normal respiratory rate and chest findings on physical examination. BMI was 28. Oxygen saturation in room air was 98%. Laboratory findings were: Hemoglobin 125 g/L, WBC $5.65 \times 10^9/L$, Na 141 mmol/L, K 4.1 mmol/L, CRP 0.2 mg/dl, creatinine 0.60 mg/dl, GOT 21 U/L, GPT 27 U/L, LDH 202 U/L. The chest-X-Ray beside showing reduced thoracic diameters was unremarkable, in particular lung transparency was normal (Figure 1).

The ECG showed sinus rhythm, first degree AV block, left anterior fascicular block and occasional ventricular ectopics consistent with the underlying congenital anatomy (Figure 2).

During admission the patient remained stable with normal saturation without need of neither respiratory support nor specific therapy. She was discharged after five days and the nasopharyngeal swab became negative after fifteen days.

Discussion

AVCDs and common atria are usually associated with EVC, suggesting a developmental defect in endocardial cushions. Although primary pulmonary involvement has not been reported in association with Ellis-van Creveld syndrome, respiratory function may be affected by skeletal abnormalities of the thoracic cage. Both cardiac and extra cardiac involvement may affect clinical presentation and severity of COVID-19.

This case offer several pathophysiologi cal issues to discuss. The patient had undergone partial atrioventricular septal defect repair at the age of five, therefore we can speculate that exposition to pulmonary over-circulation might have altered vascular reactivity. Furthermore the association of EVC syndrome with pulmonary vascular disease has been reported. (10) So far there are no evidences suggesting increase susceptibility to SARS CoV-2 or a worse prognosis of the infection in adults with CHD. (13.14) More importantly, scheletric chest abnormalities, reduced vital capacity and increased BMI in EVC syndrome are relevant comorbidities which might potentially affect in many different ways clinical course of COVID-19. (15)

Kidneys and liver are other uncommon end organs involved in EVC characterized by glomerular and tubular degeneration and periportal fibrosis, respectively. (16) Although we do not have evidence of renal or hepatic failure in our patient, the aforementioned histologic abnormalities may be subclinical and can be responsible for reduced functional reserve that might be unmasked by COVID-19 infection.

On the other hand the patient displayed some clinical characteristic that might be considered protective. In particular female gender and young age are recognized as aspecific favorable demographic variables. (17) Furthermore chronic steroid therapy with Cortone acetate might have blunted the inflammatory storm which is deemed to be a crucial pathophysiologic mechanism sustaining lung injury (Figure 3). (18)

Conclusion

In conclusion we present the first case of COVID-19 in a patient with EVC syndrome. Data on the impact of CHD and syndromes on COVID-19 clinical course are still very scant. This report support the concept arising from preliminary data suggesting that, among CHD patients, the outcome of SARS CoV-2 infection is shaped by the complex interaction of patient specific variables, rather than by the preexisting cardiac condition. (13)

Abbreviations

EVC Ellis–van Creveld

JATD Jeune asphyxiating thoracic dysplasia

WBC white blood cells

CRP C-reactive protein

AVCD atrioventricular canal defect

ASD atrial septal defect

CHD Congenital heart disease

Declarations

Ethics approval and consent to participate: obtained

Consent for publication: obtained

Availability of data and materials: N/A

Competing interests: none

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Authors' contributions: Dr Isabelle Piazza collects the data and write the paper.

Dr Paolo Ferrero reviewed and approved the final manuscript.

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Figures

Figure 1

Chest X ray at admission

Figure 2

ECG tracing at admission

Figure 3

Figure 3

Diagram summarizing specific variable potentially modulating the risk in EVC syndrome