

CASE REPORT

Orchepididymitis in the context of multisystem inflammatory syndrome in a child with Covid-19 from Syria: a very rare presentation for SARS-Cov-19 in children

M. Haydar^{1,*}, S. Baghdadi¹, M. Taleb¹, B. Al-Dali², H. Badr² and Y. Ghanem³

¹Pediatrics Resident Physician, Pediatrics and Obstetrics Hospital of Latakia, Latakia, Syria, ²pediatrician, Pediatrics and Obstetrics Hospital of Latakia, Province of Latakia, Latakia city, Syria, ³pediatric cardiologist, Pediatrics and Obstetrics Hospital of Latakia, Latakia, Syria

*Correspondence address. Dr Mariana Haydar, Pediatrics and Obstetrics Hospital of Latakia, Latakia, Latakia city, Syria. Tel: +963932216805; E-mail: mariana.haydar.md@gmail.com

Abstract

The coronavirus disease 2019 (COVID-19) is still striking the global population affecting all age groups. So far, many clinical features associated with COVID-19 illness remain under-identified, especially atypical manifestations. It is essential to characterize associated rare symptoms to better recognize complications. As severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes Multisystem Inflammatory Syndrome in children (MIS-C) in severe infection manifesting as a generalized inflammatory reaction and immune response in many body systems, potential involvement of the male urogenital tract by SARS-CoV-2 should be considered. Herein, we report a case of a pediatric patient with orchepididymitis associated with COVID-19 infection, emphasizing the importance of considering other manifestations such as genital involvement of MIS-C in children with COVID-19 and highlighting the need to monitor the genitourinary function after infection. Therefore, andrological consultation is necessary to evaluate fertility as a long-term follow-up, especially as the effects of SARS-CoV-2 on male reproductive function are still to be thoroughly researched.

INTRODUCTION

As the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic continues to spread, rare manifestations rise to our note affecting all age groups. The clinical spectrum of SARS-CoV-2 infection in children is still incompletely described, with many gaps in the course and complications of the disease remaining under-recognized [1]. Only one known case of pediatric orchepididymitis in the setting of confirmed coronavirus disease 2019 (COVID-19) infection has been reported [2], and herein, we report the second of this kind and the first case with orchepididymitis in a child in the context of Multisystem

Inflammatory Syndrome with confirmed COVID-19 infection (MIS-C).

CASE PRESENTATION

A 7-year-old boy without remarkable medical history presented to our hospital on December 2020 complaining of high fever (40°C) for more than 3 days, abdominal pain, loss of appetite, general fatigue and bilateral testicular discomfort developing over the past 2 days. At first, acute appendicitis was suspected but was later excluded. On physical examination he had

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Figure 1: Erythematous rash on the right thigh with mildly elevated borders.

reddish congested oral mucosa, dry cracked lips, pallor, generalized abdominal pain spreading to the iliac fossae, diffuse abdominal tenderness, generalized myalgias, sporadic erythematous rash in the inguinal region, the axilla and on the extremities (Fig. 1). There was left-sided scrotal redness, increased warmth and swelling with testicular tenderness and pain which were worse on the left testis and was relieved with elevation, suggesting acute orchiepididymitis. This was confirmed upon consultation with the Urology department, in the absence of trauma.

Laboratory evaluation revealed lymphopenia: WBC: $7 \times 10^3/\text{ul}$, Plt: $119 \times 10^3/\text{ul}$, Lymphocytes: 7%, Neutrophils: 91%, CRP: 131 mg/L. Urinalysis was normal. Chest X-ray was normal. Abdominal ultrasonography showed a small amount of free peritoneal effusion located in the right iliac cavity and a small amount of clear fluid effusion in the scrotum, multiple hypoechoic spots in the testis, and oedema in the epididymis with enlarged edematous epididymal caput (Fig. 2A–C). Scrotal Doppler ultrasonography could not be done in our hospital because of the pandemic.

The patient was transferred to the Pediatric Intensive Care Unit as he became hemodynamically unstable. Echocardiography showed pleural and pericardial inflammatory reactions. Computerized Tomography of the chest revealed minor alveolar infiltrations in the lower lobes. Differential Diagnosis was mostly suggestive of MIS-C infection with a very rare manifestation, orchiepididymitis. The school our patient attends documented an outbreak of SARS-CoV-2 infections.

Extended laboratory evaluations were consistent with MIS-C, D-dimer: 9400 ng/ml, procalcitonin: 29.8 ng/ml, Ferritin: 757 ng/ml, Antistreptolysine-O: 102 tood units/ml, nasopharyngeal swab (real-time PCR) was positive for SARS-CoV2. The patient was treated as recommended by CDC and WHO Guidelines with Ceftriaxone, Vancomycin, Methylprednisolone (2 mg/kg/day) for 5 days, then Prednisolone for 3 weeks, PPI: Omeprazole IV 1 mg/kg/12 h, IVIG (2 g/kg), Aspirin, Enoxaparin Sodium, Dopamine and Acetaminophen. On Day 3 of hospitalization, symptoms started improving after 12 h of IVIG administration as the generalized pain was lessened, scrotal pain and discomfort decreased gradually. On Day 6, the patient was afebrile, hemodynamically stable and pain-free. Enoxaparin was continued until discharge on Day 10 with a normal blood panel, abdominal and testicular ultrasonography.

DISCUSSION

Acute orchiepididymitis most often presents unilaterally and results after urinary tract infection, viral infections (such as mumps, rubella, coxsackievirus, varicella, echovirus and cytomegalovirus), trauma or autoimmune disorders [3]. The frequency of orchiepididymitis in children has decreased substantially after the administration of mumps-measles-rubella vaccination [3, 4].

Coronaviruses in pediatric patients cause either self-limiting mild infection or more severe infection that affects the whole body. MIS-C can be the severe manifestation in acute infection in children, or it can follow it as an autoimmune response with a severe clinical picture. Although rare, several genitourinary presentations have been reported, in addition to a few complications as a result of hypercoagulable states, such as priapism [1].

One case of orchiepididymitis secondary to SARS-CoV2 has been reported in a previously healthy 14-year-old male in Italy [2]; our case is the second orchiepididymitis to be reported so far secondary to COVID-19 infection and is the first to be represented in the context of MIS-C.

Genomic analysis has shown that SARS-CoV-2 is 76% identical to SARS-CoV, and they both share the main mechanism for invading cells through Angiotensin-Converting Enzyme-2 (ACE2) [4–6]. ACE2 is mostly expressed in cells of the kidney, gastrointestinal tract and bladder, while the highest mRNA expression of ACE2 is in the testes suggesting that testicular cells might be the potential target of COVID-19. Some studies documented that SARS-Cov was detected in testicular epithelial cells and Leydig cells and caused orchitis, testicular lesions and widespread testicular germ cell destruction over a decade ago with subsequent spermatogenic tubule destruction, oligospermia and azoospermia [4, 5]. SARS-CoV-2 RNA has been found in the semen and testes and has been successfully isolated from the urine of COVID-19 patient [6, 7, 9]. This might lead to orchiepididymitis by vas deferens reflux [8]. Nevertheless, there are reports of scrotal discomfort and pain in males with COVID-19 [4, 5, 7, 10].

During active viremia and persistent fever, the blood–testis barrier is tampered, thus raising the possibility of viral access to the male reproductive tract, notwithstanding, the systemic infection condition that causes an immunocompromised state could be responsible for the orchiepididymitis and other genitourinary manifestations or at least facilitate its presentation [2, 5]. One study showed that COVID-19 caused immune impairment similar to the autoimmune orchitis observed previously in SARS-CoV patients [4, 9] and documented impaired spermatogenesis in COVID-19 patients, which could later impair gonadal function and impact fertility in adults [9]. However, ‘are these results applicable to pediatric patients’ is an important question to be addressed. While complications of orchiepididymitis in normal children are infertility, testicular atrophy, and less commonly abscess formation, testicular infarction and reactive hydrocele [3], studies should investigate possible future complications of the genitourinary implication on patients infected with SARS-CoV in their childhood, especially as the role of ACE2 receptors is still incomplete at a young age and the gonadal function is yet to develop.

CONCLUSION

As the SARS-CoV2 pandemic continues, clinicians should be aware that unusual presentations and rare complications

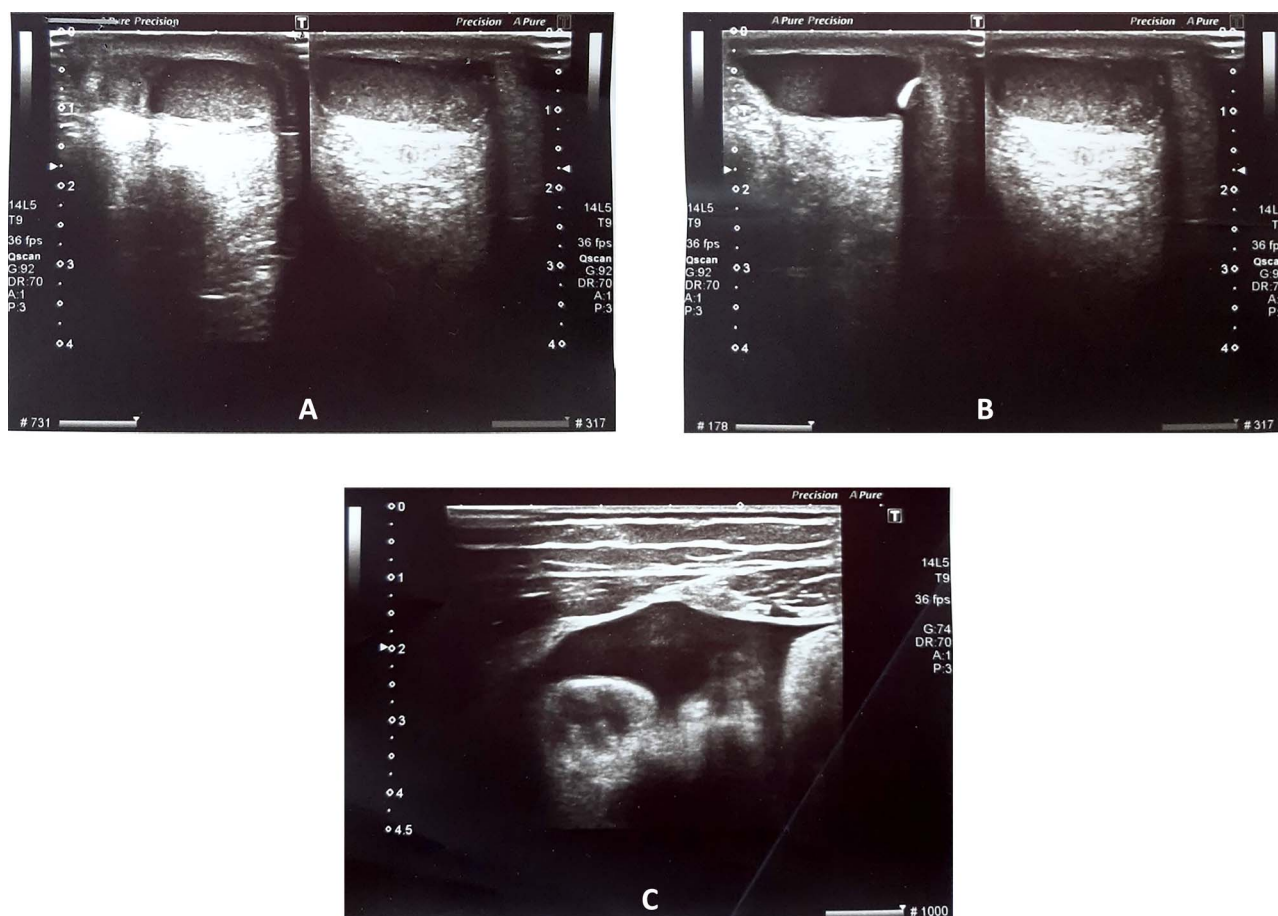


Figure 2: Ultrasonography of the testis shows inhomogeneous structure on echo, multiple hypoechoic spots in the testis (A,B) and edema in the epididymis with enlarged edematous epididymal caput (C).

are mostly under-recognized. The virus exhibits possible pathogenicity to testicular tissues; therefore, clinicians should pay attention to testicular complaints and must conduct future clinical follow-up and gonadal function evaluation, especially in patients who are at reproductive age.

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CONFLICT OF INTEREST

No conflicts of interest.

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CONSENT

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GUARANTOR

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