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ORIGINAL ARTICLE

Omicron virus as a cause of epididymoorchitis in children

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ABSTRACT

Background: This study aims to answer the question of whether Omicron, a variant of Coronavirus, is one of the causes of viral epididymal orchitis in children and to analyze its clinical course with a trial to search for any predisposing factors.

Methods: This study included 76 children who proved to have Omicron infection. Sixty-nine of them had no testicular pain (group A), while 7 had testicular pain and acute scrotum (group B). The two groups were compared regarding history and laboratory findings. Group B patients were analyzed regarding clinical pictures and ultrasonography (US) findings and followed up for one month.

Results: Testicular pain occurred in 9.2% of children with Omicron infection. Clinical presentation and US findings of epididymal-orchitis were evident in 4 boys (out of 7 with testicular pain). No statistically significant difference was reported between groups A and B regarding the patient's age, duration of infection, history, and laboratory findings.

Conclusions: Omicron is one of the causes of viral epididymal-orchitis or testicular pain in children. This study did not find clinical or laboratory data to predict testicular pain or epididymal-orchitis in children with Omicron viral infection.

Keywords: COVID, Testis, Orchitis, Omicron Level of evidence: Level I

INTRODUCTION

Epididymo-orchitis is a relatively frequent diagnosis in adolescents and children (estimated at 1.2%) per year [1]. The most frequent cause of epididymal in children is viral infection, such as mumps, rubella, coxsackie virus, varicella, echovirus, and cytomegalovirus [2-4]. Most mumps orchitis occurs in pre-pubertal (less than ten years), and most cases occur 4-6 days after the onset of mumps [5].

Recently, many published papers reported the relationship between COVID-19 infection, testicular pain, and epididymal orchitis in adults and children [4,6-9].

The Omicron variant of Coronavirus, which is much more transmissible than previous variants, started to affect an increasing number of children in January 2022 [10].

During the Omicron outbreak, we examined some of the children who proved to have Omicron infection, complaining of testicular pain and acute scrotum. We studied these cases to confirm that Omicron may be an additional cause of viral epididymal in children and to study the course of this problem.

METHODS

Written informed consent was obtained from all participant's parents; the study was approved by the research ethical committee of the Faculty of Medicine, Zagazig University (approval number 11203-31-10-2023). The study was done according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. A retrospective clinical study was conducted in Zagazig University Hospitals from January 2022 to March 2022 during the Omicron virus outbreak.

The study included 76 male patients who presented to the pediatric clinic and were confirmed by PCR to have Omicron infection. The patients' ages ranged from 2 to 18.

Seven of these patients were referred to the Pediatric Surgery clinic with testicular pain. The patients were divided into two groups: Group A (69 patients without testicular pain) and Group B (7 patients with testicular pain).

The records of the whole group of patients (76 patients) were reviewed and recorded. Collected data included symptoms at presentation, history of present illness, history (including history of urinary tract infection (UTI), history of urological problems, urological or testicular surgery, and results of the laboratory investigations (including neutrophil count, lymphocytic count, Neutrophil lymphocyte ratio (NLR), C-reactive protein and urine analysis.

Patients with testicular pain (7 patients) were evaluated, examined, and followed in the pediatric surgery clinic. Scrotal examination and scrotal US were done for each patient at the time of presentation and followed up by repeated clinical examination and scrotal US three days, 10 days, and one month after the first visit.

STATISTICAL ANALYSIS

The collected data were computerized and statistically analyzed using the SPSS program (Statistical Package for Social Science) version 25.0. Qualitative data were represented as frequencies and relative percentages. The chi-square test was used to calculate the difference between qualitative variables. Quantitative data were expressed as mean (Standard deviation). The independent t-test was used to calculate the difference between quantitative variables in normally distributed data in two groups.

RESULTS

A total of 76 male patients proved to have Omicron infection were analyzed. Seven of them (9.2%) had testicular pain. Patients enrolled in this study were divided into two groups, group A (69 patients) without testicular pain, and group B (7 patients) had testicular pain. The median age of patients in groups A and B was 10 and 11 years, respectively, without significant differences. There was no significant difference between the two groups in the duration of Omicron infection. The history of urological problems or previous urological surgery in both groups is shown in Table (1).

There was no significant difference in laboratory results between both groups, as shown in Table (2). Group B patients with testicular pain were subjected to physical examination and scrotal ultrasound and followed up three days, ten days, and one month after presentation. Three had no scrotal or testicular inflammation signs, and their US findings were normal. Four patients showed clinical signs of acute scrotum (scrotal edema, redness of scrotal skin, mild hydrocele, and testicular tenderness). US of these 4 cases showed inflammatory imaging hallmarks such as the thickened fibrous covering of the testis (tunica albuginea), mild hydrocele, and scrotal skin edema in one or both testes (Fig. 1, 2). In 2 of these four patient, the epididymal head was heterogenous and enlarged (Fig. 3), which means epididymitis. The echo structure of the testes in one of these 2 cases was mostly homogenous, and the other showed mild hypogenicity (Fig. 2). On Colour Doppler US, there was an increased flow signal in the 4 cases.

On follow-up, three days after the first visit, testicular pain and local signs, scrotal edema, hydrocele, and local tenderness started to subside. The US showed some improvement in the testicular covering tissues and scrotal skin, and the secondary hydrocele improved. After ten days, the local signs and US findings were almost normal.

Table 1: Results related to the history of urological complaints in both groups.

Parameter	Group A (n=69)	Group B (n=7)	P-Value
Age (years) Mean±SD Median	9.24±2.76 10.0	10.92±2.48 11.0	0.126
Duration of infection (days)	11.25±1.95	12.38±2.14	0.151
History of Urinary Tract Infection (UTI)	4 (5.79%)	0 (0%)	0.513
History of urological or testicular problems	8 (11.59%)	0 (0%)	0.341
History of congenital hydrocele	6 (8.69%)	1 (14.28%)	0.626
History of urological or testicular surgery	4 (5.79%)	0 (0%)	0.513

Table 2: Results of laboratory investigations in both groups.

Lab. Test	Group A (n=69)	Group B (n=7)	P-value
Neutrophil count ($10^3/mm^3$)	3.8±1.2	4.2±0.92	0.395
Lymphocyte count ($10^3/mm^3$)	1.7±0.14	1.8±0.41	0.160
Neutrophil-lymphocyte ratio (NLR)	2.16±0.24	2.22±0.34	0.546
C-reactive protein (mg/L)	4.2±1.75	3.1±0.20	0.102
Urine analysis Urinary Tract infection	2 (2.89%)	0 (0%)	0.648

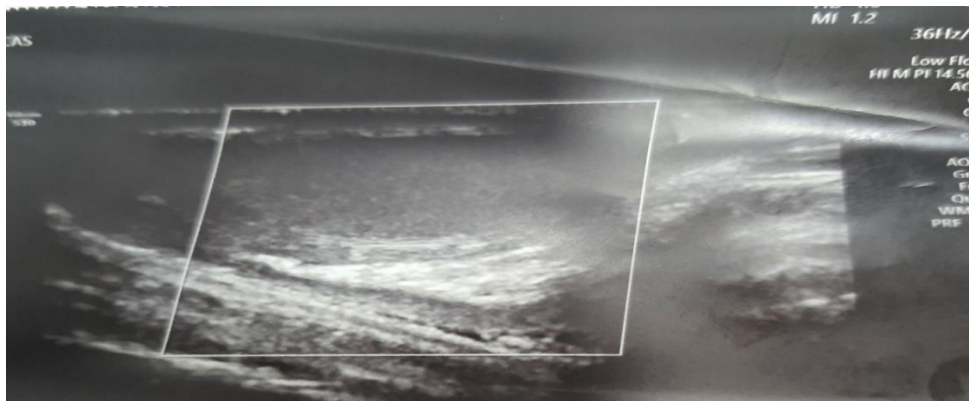


Figure 1: US showing thickened testicular coverings, tunica albuginea, Dartos, and scrotal skin

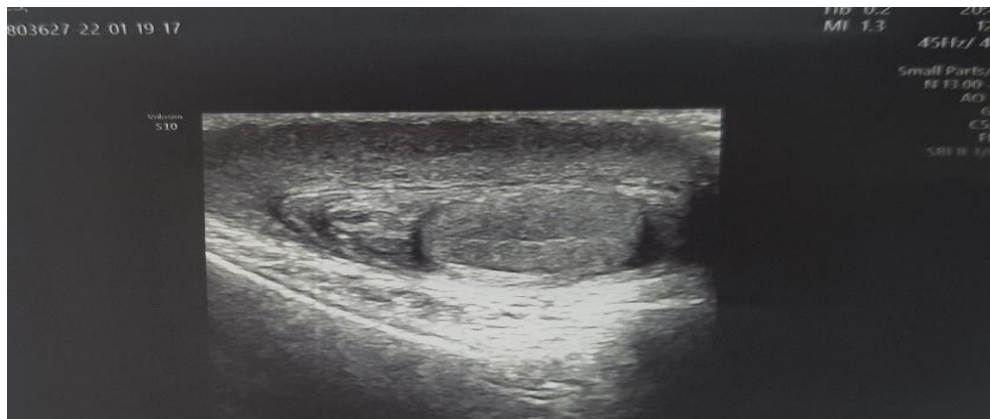


Figure 2: US showing mild reduced testicular echogenicity, mild rim of hydrocele, and relatively thickened tunica albuginea

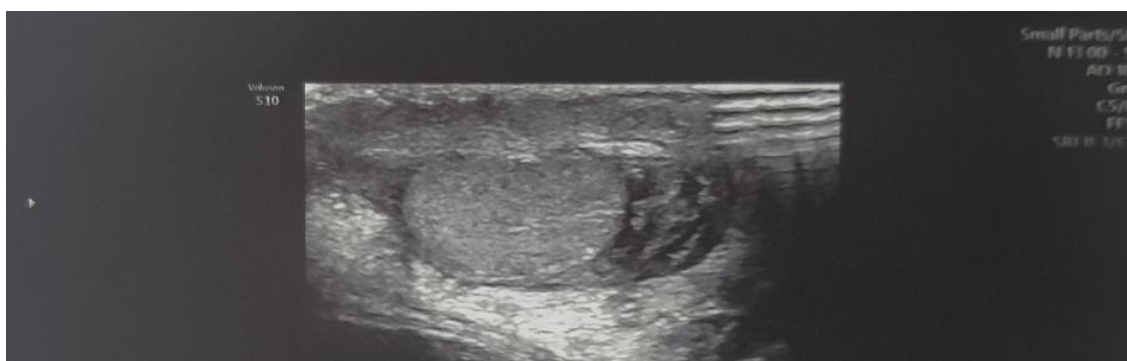


Figure 3: US showing swollen epididymal head with mild heterogeneity, picture of epididymitis

DISCUSSION

COVID-19 was first reported in January 2020 as a result of investigations of pneumonia cases of unknown etiology in Wuhan, China [11]. In November 2021, the World Health Organization (WHO) designated variant B.1.1.529 a variant of concern named Omicron [12]. Omicron is much more transmissible than the previous variants, leading to many more children being exposed to and infected with it. Early surveillance data from South Africa showed that children and teens under 20 represented 17% of all hospital admissions during the Omicron wave [10]. Although COVID-19 viral infection mainly affects the respiratory tract, many authors report it may also cause testicular pain and epididymal-orchitis [4,7-9,11,13-14]. The first case of epididymal orchitis in a boy with COVID-19 was reported by *Gagliardi et al.* in Italy in May 2020 [8]. The mechanism of COVID-19 infection by binding to Angiotensin-converting enzyme2 (ACE2) is the main pathway of influencing host cells [2,3]. ACE2 is expressed in many tissues, including kidney, bladder, and testicular cells, and therefore, the virus may affect testicular tissue and cause inflammation [13,14].

During the Omicron outbreak, we reviewed seven boys with testicular pain and acute scrotum out of 96 boys who proved to have Omicron infection. These boys with testicular pain were evaluated and followed up by clinical and scrotal US examination.

We tried to search for any predisposing factor for epididymal in these cases by comparing these patients with other patients having Omicron infection without testicular pain regarding age, duration of infection, and history of previous urological problems or urological surgery. However, we didn't find any significant difference between the two groups.

The symptoms, clinical pictures, and US findings were milder than mumps epididymal-orchitis in these cases. The course was also smooth, with rapid recovery in a few days. It was proven that the mumps virus could attack and enter the testis causing viral orchitis, which may cause testicular atrophy [5], which may result in male infertility and testicular tumors [15]. Several studies demonstrated the relationship between coronavirus family and orchitis during the past SARS virus epidemic. Even if the Coronavirus has not been detected in testicular tissues [16], testicular damage and germ cell destruction were clearly observed in these cases [17]. The genital involvement and the testicular pain in these cases may occur by vascular mechanisms and not by direct attack of testicular tissues, as in cases of mumps [18]. This may explain why the clinical pictures and US findings are milder than the mumps orchitis. However, further studies are necessary to study the pathological effect of the Coronavirus on the male reproductive system and to ensure future fertility and proper andrological follow-up [9].

CONCLUSION

The Omicron variant of Coronavirus is one of the causes of viral epididymal orchitis in children. Further clinical and pathological studies are recommended to assess the extent of testicular tissue damage that may occur in these cases, which may affect future fertility.

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