Epididymitis caused by coxsackievirus A6 in association of hand, foot and mouth disease

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Coxsackievirus A6 (CV-A6) caused hand, foot and mouth disease (HFMD) with unique manifestation of epididymitis. The patient underwent operation due to suspicion of testicular torsion. Epididymitis was diagnosed by ultrasound examination. Enterovirus was detected from epididymal fluid by PCR and typed by partial sequencing of viral protein 1 as CV-A6.
39  CASE REPORT

40  The case patient was 17 y.o. male, who was previously in good health. He was not on any regular
41  medication. He sought medical care at the emergency department of the university hospital due to
42  an intense pain in his left testis. He was admitted to the surgical ward as a suspicion of a testicular
torsion. On admission his general condition was good. He had mild fever, swelling in the left side
43  of scrotum and this area was painful in palpation. Vesicular exanthema had appeared on palms
during the week before admission to hospital.

44  Due to the suspicion of testicular torsion an ultrasound examination was performed, which revealed
45  epididymo-orchitis. The right testicle was normal when examined by ultrasound. Because torsion
46  could not be excluded an explorative operation was performed. Left testis and epididymis were
47  found to be swelling and irritated. There was no pus in the scrotal area, but under the tunica
vaginalis there was a small amount of fluid, which was aspirated and sent for the microbiological
analysis. Antimicrobial treatment was started with cefuroxime and ciprofloxacin. After operation
the patient remained on the ward for three days and on discharge he was recovering; he was afebrile
and did not have any pain or swollenness in the scrotal area.

48  Laboratory analysis showed increased blood C-reactive protein level 105 mg/ml (normal level
49  < 10mg/l). On discharge CRP was 30 mg/ml. White blood cell count was normal (6.2-7.8 x 10\(^9\)/l).
50  Bacterial culture from the epididymal fluid was negative, as well as was urine culture. Chlamydia
trachomatis and Neisseria gonorrhoea PCR tests from epididymal fluid were negative.

51  The patient had mild fever and small vesicles on palms before the admission to the hospital, which
52  led the clinician to suspect a viral etiology. Therefore enterovirus PCR was performed from
epididymal fluid sample. An in-house RT-PCR with primers derived from the 5'–non-coding region of enterovirus genome was used (1). The PCR test gave a positive result. Because CV-A6 had been circulating in Finland causing HFMD, also PCR with CV-A6 specific primers (1) was run, which was positive. For typing the enterovirus, RT-PCR with primers specific for a partial sequence of viral protein 1 was performed (2). The amplicons were sequenced and run in the BLAST search confirming the sequence as CV-A6 (http://www.ncbi.nlm.nih.gov/nucleotide, GenBank accession number: KF 687973) Enterovirus IgG antibodies from the sera were slightly elevated, 82 EIU (enzyme immunoassay units; cut-off value for positive enterovirus IgG is 10 EIU), and also enterovirus IgM antibodies were detected confirming a recent enteroviral infection.

Coxsackievirus A6 (CV-A6) is a member of human enterovirus Species A in the genus Enterovirus in the family of Picornaviridae. The most common clinical manifestation of CV-A6 infection is herpangina, a febrile illness with vesicular lesions on oral mucosa mainly affecting children. Other clinical manifestations include central nervous system infections.

In 2008 the virus emerged as a cause of HFMD (3), which is a childhood febrile illness with vesicular exanthema on hands, feet and oral mucosa caused mainly by coxsackievirus A 16 and enterovirus 71. Since then CV-A6 has been associated with global HFMD outbreaks. The features of CV-A6 HFMD have been atypical and more severe than in the classic disease and also adults have been affected (3-6).

In a large CV-A6 outbreak in Singapore and in France patients mainly had herpangina (7,8), whereas in an outbreak in Taiwan CVA6 infections occurred as macular or vesicular lesion on
palms, soles and oral mucosa (9). Atypical HFMD presenting with onychomadesis, nail shedding, caused by CV-A6 was first reported from Finland and Spain (3,10). Unusual lesions on scalp (11) and perioral and perirectal papules, as well as vesicles on the dorsum of the hands (12) have been shown. Recently, atypical HFMD cases with exanthema resembling chickenpox or eczema herpeticum was reported from United Kingdom (4).

The patient presented in this paper had a unique manifestation of CV-A6 infection as an epididymitis. On admission the patient gave history of previous febrile illness with vesicular rash on palms and soles and also his sister had same symptoms, which suggested a contagious disease as an etiology. Within the previous three months there were also two other young males with similar testicular symptoms who were exploratively operated by the same urological team due to suspicion of testis torsion. However, this could not be confirmed in the operation. Atypical clinical features as well as admission and operation of the third patient within a quite a short period of time led to the suspicion of a contagious viral disease. Vesicular exanthema on palms suggested enterovirus as a possible etiologic agent. Because infection could not be suspected in the first two surgical cases, no samples for microbiological detection were taken and thus a possible common exposure between the cases could not be confirmed. However, anamnesis showed that before the admission to the hospital, the patients had had symptoms of a viral infection, such as mild fever. Anyway, this implies that epididymitis of viral origin might have been more common than could be suspected.

There are several enterovirus types circulating during epidemics, therefore we can’t speculate about the virus specific tropism of CV-A6 to epididymal tissue based on a single case.

Bacteria are the most common cause of epididymitis in adults, while orchitis is the classic complication of viral infection (mumps) (13). A bacterial etiology is defined in 64 % of the cases and they cause infections in young men under 35 years as common as in older men (14).
Epididymitis in boys under 14 years is considered to be mainly a post-infectious inflammatory process (15).

Outcome of epididymitis is usually self-limiting and favourable, but mumps orchitis may lead to testis atrophy and influence for infertility (13). Recently significant changes in sperm protein composition have been found to occur following epididymitis (16).

This is the first report to show that enteroviruses can be detected from epididymal fluid indicating virus replication in the tissue. Epididymitis in young boys has been thought to be post-infectious inflammatory phenomenon, which is based on the findings that the patients have had symptoms of upper respiratory infections preceding scrotal symptoms (15). Also viruses have been detected from nasopharyngeal specimens or stool samples and the patients have had higher virus antibody levels in sera than controls (15).

The patient described here underwent first surgery due to suspicion of testicular torsion. However, the final diagnosis was epididymitis caused by an enterovirus. Clinical heed is important to recognize unusual clinical presentation of HFMD and atypical etiology of epididymitis in order to avoid unnecessary invasive procedures as well as inappropriate antibiotic treatments. Our experience suggests that viral epididymitis should be suspected in young men with recent HFMD, who present with testicular pain.
References


