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CASE REPORT

Necrotizing appendicitis as complication of varicella disease: case report and literature Review

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Varicella zoster virus infection, Appendicitis, Child.

Abstract

In immunocompetent children, complications of varicella are rare. Acute appendicitis (AA) is one of the most exceptional complications of chickenpox. In this report we describe a case of a 6-year-old girl with a perforated AA in the course of varicella. We intend with this clinical case to remember an extremely rare complication of varicella, which is at the same time the most common cause of abdominal surgery in children.

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INTRODUCTION

Varicella or chickenpox is an acute infectious disease primarily affecting children caused by the varicella-zoster virus (VZV)[1]. VZV infects susceptible individuals via the conjunctivae or respiratory tract and replicates in the nasopharynx and upper respiratory tract[2]. It disseminates by a primary viremia and infects regional lymph nodes, the liver, the spleen, and other organs[2]. A secondary viremia follows, resulting in a cutaneous infection with the typical vesicular rash[2]. Varicella is usually a benign, self-limited disease, but it can cause considerable morbidity and on rare occasions even mortality in healthy children[3]. In immunocompetent children, complications of varicella are rare. The most common complications are bacterial skin infections, by sthaphylococci or streptococci, from scratching[4]. Encephalitis, cerebellar ataxia, pneumonia, hepatitis, myocarditis, enteritis, thrombocytopenia, Henoch-Schönlein purpura, arthritis, osteomyelitis and optic neuritis may complicate varicella[5,6].

Acute appendicitis (AA) is an extremely rare complication of varicella and is rarely reported[1,3,4]. Although AA is the most common cause of abdominal surgery in children, it`s etiology is not yet quite clear[1,3,4,7,8]. Luminal obstruction of the appendiceal lymphoid follicle is generally accepted as the primary cause of appendicitis. This obstruction is mostly caused by lymphoid hyperplasia, fecaliths, carcinoid tumours or foreign bodies[1,3,4]. Bacterial (*Escherichia coli, Bacteriodes fragilis, Yersinia, Salmonella* or *Shigella*), parasitic (*Entamoeba histolytica*) and viral (*Epstein-Barr virus* (EBV)*, Measles virus, Adenovirus* and *Cytomegalovirus* (CMV)) infections can cause lymphoid hyperplasia[1,3,4,7,8].

In this report we describe a case of a child with an AA in the course of varicella. Our case report includes a narrative literature review and given the small number of publications about AA as a complication of varicella the cited articles were all read in full. The literature review process was carried out by two of the authors. The cited articles were searched in the PubMed database.

CASE REPORT

A previously healthy six-year-old girl with active phase of previously diagnosed varicella was admitted to a Pediatric surgery emergency department with six-hour complaints of abdominal pain and vomiting. She was being treated with acyclovir since the day before. On admission, she was febrile (38.3ºC) and her skin was covered with a generalized rash consisting of lesions in different stages (macular, papular and vesicular lesions). Her abdomen was sensitive especially in the right lower quadrant. Neither liver or spleen were palpable and peristalsis was normally heard. Laboratory findings showed normal haemoglobin concentration (13.9g/dL) and platelet count (337 x 10^9/L). The patient's white blood cell count was 19.2 × 10^9/L (normal age-adjusted range 5-14.5 x 10^9/L) with 88.3% neutrophils, 7.1% lymphocytes and 3.9% monocytes. C reactive protein was 33mg/L (normal age-adjusted range <20mg/L). All other laboratory studies showed normal values. An acute abdomen was suspected and an abdominal ultrasonography revealed a perforated acute appendicitis. The girl underwent laparoscopic appendectomy. A perforated appendix with localized peritonitis was found. She was given a five day intravenous antibiotic treatment with ceftriaxone and metronidazole and completed five days of acyclovir *per os*. A polymerase chain reaction (PCR) assay detecting VZV DNA was performed and there was no PCR evidence of VZV in the appendix tissue. The girl made a rapid recovery and was discharged on the fifth postoperative day. Antibiotic treatment was completed with oral amoxycilin/clavulanic acid and metronidazole for five days after discharge.

DISCUSSION

In immunocompetent children, complications of varicella are rare. AA is one of the most exceptional complications of varicella. However, the number of cases of varicella related appendicitis is probably undervalued, since it is often difficult to establish a causal relationship between these two diseases, especially in cases where the varicella rash is not very clear. We have found a few reports on AA as a complication of primary VZV infection, and we only found two case reports where VZV DNA was verified by PCR in the appendix tissue[3,4]. At 1950 Camens[9] reported a case of varicella encephalitis complicated by AA and peritonitis. Forty years later, Harvanek et al. (1990)[10] reported a group of four children with varicella and acute perforated appendicitis and peritonitis. Lukšić B et al. (2012)[1] describes three cases of AA in the course of varicella diagnosed in Clinical Department of Infectious Diseases at Split University Hospital, Croatia, between 1998 and 2010. Varicella was diagnosed clinically and in two cases confirmed by positive serological tests for VZV[1]. Košćak[11] at 2002 reported a case of a nine-year-old girl with an acute perforated appendicitis, which developed as a complication of varicella. However, the first case of varicella related appendicitis with PCR evidence of VZV in the appendix was only described at 2012 by Pogorelic et al. (2012)[4], on a eleven-year-old boy. At 2017 Smedegaard et al. (2017)[3] describe the second case with PCR evidence of VZV DNA from the appendix in a child with DiGeorge Syndrome who developed a perforated appendix and an intraperitoneal abscess during a prolonged primary VZV infection.

In our case the PCR analysis of appendix tissue was negative for VZV DNA, probably because the appendectomy specimen was fixed at the formalin solution routinely used. In fact, some authors suggest that fixation of human tissue with formaldehyde can cause disintegration of DNA. Furthermore, no serological tests for VZV were performed, so varicella was diagnosed only based on clinical presentation. This would have been important to do because testing for viral antigens or DNA in the appendix, omentum and

peripheral blood would be useful to clearly establish the role of VZV at etiopathogenesis of AA. As in most cases of AA, our child had leukocytosis. However, it is important to remember that since varicella is characterized by moderate leukopenia when AA appears as a complication of varicella it often result in the absence of leukocytosis probably because the modulation of immune response.

Regarding acyclovir use, when this child came to us, she was already medicated with acyclovir since the day before. In fact, since it is an healthy and immunocompetent six-year-old child, who doesn't take any medication (namely intermittent oral or inhaled steroid therapy and chronic salicylates) and that is the first case of varicella in household contacts, there was no formal reason to be treated with acyclovir. However, we know that although antiviral therapy is not recommended for healthy children ≤12 years, since varicella is typically a self-limited disease in this population, acyclovir can modestly reduce the duration and severity of symptoms[12].

VZV belongs to the greater Herpes viruses family, which are ubiquitous pathogens in children and remain quiescent after an active infection. The relation between herpes viruses and AA is still not entirely clear, but the hypothesis is that they are latent in the appendix and could be occasionally reactivated by certain triggers, such as stress or individual immune status. This may cause an acute viral infection, leading to lymphoid hyperplasia that can produce an acute obstruction of the appendix causing AA. A historical study from United Kingdom[13] determinated the association between outbreaks of each of six common acute childhood infections (varicella, measles, mumps, rubella, scarlet fever and whooping cough) and the recorded incidence of AA in twenty seven English public boarding schools, in the inter-war period (1930-1934). Nevertheless they only found a significant association between appendicitis and mumps. The first study documenting the presence of herpes virus DNA was performed by Katzoli et al. (2009)[7] and showed viral DNA of CMV (21%), human herpes virus 6 (HHV-6) (7.9%), EBV and herpes simplex virus type 1 (HSV-1) viruses in the appendectomy specimens of thirty eight children with AA. However in their study no specimen were positive for VZV, herpes simplex virus type 2 (HSV-2) and human herpes virus 7 (HHV-7).

CONCLUSION

Abdominal pain is one of the main reasons of children brought to the emergency department. In those with acute viral disease it can be a real challenge and paediatricians should not forget the possibility, although rare, of AA arising as a complication of acute viral infections in children. Although varicella is an infectious disease with a generally benign course in healthy children, it rarely can cause surgery requiring complications, such as AA. Therefore, the presence of abdominal pain in a children with varicella should make us think of the possibility of AA as a varicella complication, which requires urgent surgical intervention.

Further studies are necessary to determinate the exact role of VZV in the pathogenesis of AA.

This case report was authorised by the ethics committees of the institution where it was carried out, as defined by the current legislation.

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