



Herpes simplex induced necrotizing tonsillitis in an immunocompromised patient with ulcerative colitis

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Abstract

We here present the case of a 22-year-old female of Suriname ethnicity with ulcerative colitis who received treatment with mercaptopurine and infliximab. She presented herself with a severe necrotizing tonsillitis due to herpes simplex virus type-1 (HSV-1). Combination therapy consisting of immunomodulators and anti-tumor necrosis factor (TNF) agents is increasingly being used. Anti-TNF therapy is associated with an increased risk of developing serious infections, and especially patients receiving combination treatment with thiopurines are at an increased risk. We here show that HSV infections can cause a severe tonsillitis in immunocompromised patients. Early recognition is essential when there is no improvement with initial antibiotic therapy within the first 24 to 72 h. HSV infections should be in the differential diagnosis of immunocompromised patients presenting with a necrotizing tonsillitis and can be confirmed by polymerase chain reaction. Early treatment with antiviral agents should be considered especially if antibiotic treatment fails in such patients.

Key words: Herpes simplex virus; Tonsillitis; Ulcerative colitis; Immunosuppression; Anti-tumor necrosis factor agents

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Core tip: Combination therapy that consists of immunomodulators and anti-tumor necrosis factor (TNF) agents is increasingly being used for patients with chronic inflammatory diseases, such as ulcerative colitis. Anti-

TNF therapy is associated with an increased risk of developing serious infections, and especially patients receiving combination treatment with thiopurines are at an increased risk. This is the first report of an acute severe tonsillitis caused by herpes simplex virus in an immunocompromised patient due combination treatment with a thiopurine and an anti-TNF agent.

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INTRODUCTION

Viral throat infections are a common problem and are generally self-limiting. Viral causes of a tonsillitis include: rhinovirus, respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), parainfluenza, influenza, Coxsackievirus, adenovirus, etc^[1]. There are two types of the herpes simplex virus (HSV): HSV-1 and HSV-2. HSV-1 can cause primary or recurrent infections, with the most common manifestation as vesicular lesions of the oral mucosa. HSV-2 is known as genital herpes simplex. However, both HSV types can cause herpes labialis as well as genital herpes^[2], which can extend into other organs, such as the hard palate, tonsils, liver, lungs and eyes. A primary HSV infection can result in an acute pharyngotonsillitis. The diagnosis of an HSV infection can usually be made based on the clinical picture. The diagnosis can be confirmed by polymerase chain reaction (PCR), which is considered as the gold standard, and with serology and/or histology.

CASE REPORT

A 22-year-old female of Suriname ethnicity with known beta thalassemia and ulcerative colitis presented herself to the family physician with a sore throat. She used infliximab, mercaptopurine, allopurinol and mesalamine enema's. Treatment with feneticillin was started (500 mg 3 times daily) under the suspicion of a bacterial tonsillitis. After 4 d, the patient presented herself to the emergency department of our hospital because of severe dysphagia for solid and liquid foods and intermittent fever up to 39.2 Celsius. An acutely ill patient was seen with a heart rate of 135 per minute and a blood pressure of 100/60 mmHg. Her neck was diffusely swollen and painful at palpation. Cervical lymphadenopathy was seen. Oral examination revealed severely enlarged tonsils that were covered with a grey-whitish exudate. No other lesions were observed and there was no trismus. Because of a symmetric pharynx arch there was no suspicion of a peritonsillar abscess at physical examination. Laboratory investigation showed an increased C-reactive protein of 137 mg/L, Hb 4.5

mmol/L, leucocyte count of $4.7 \times 10^9/L$ (leucocyte differentiation: Neutrophils 55%, eosinophils 1%, basophils 1%, lymphocytes 38%, monocytes 4%) and a thrombocyte count of $232 \times 10^9/L$. Cultures of throat and nasopharyngeal swabs as well as blood cultures were negative. Viral screening using PCR and plasma viral load measurements were negative for cytomegalovirus and EBV. A multiplex PCR analysis for respiratory viruses, including rhinovirus, adenovirus, RSV, parainfluenza and influenza was also negative. The patient was admitted and amoxicillin was started instead of feneticillin because of the immunocompromised status and the fact that she did not respond to feneticillin treatment. A computed tomography (CT)-scan showed bilateral heterogeneous contrast enhancement of both enlarged pharyngeal tonsils and arytenoids. Imaging did not reveal a peritonsillar or retropharyngeal abscess. At laryngoscopy a swollen nasopharynx was seen that was covered with grey-whitish exudate, and ulcerations of both arytenoids and in the aryepiglottic fold (see record). The patient deteriorated and became respiratory insufficient. Empirical treatment with valacyclovir was started (1000 mg 3 times daily) under the suspicion of an HSV infection. Treatment with mercaptopurine and allopurinol was stopped. The patient responded to the antiviral treatment within one day. The diagnosis of HSV type I was confirmed by PCR of the nose and throat swabs and by serology. The patient was seen at the outpatient clinic 10 d after discharge and was asymptomatic.

DISCUSSION

HSV can cause life-threatening infections in immunocompromised patients^[3-5]. We here describe a patient with ulcerative colitis who received treatment with infliximab and mercaptopurine. Therapeutic efficacy of combination therapy with anti-tumor necrosis factor (TNF) agents (such as infliximab) and immunomodulators (including mercaptopurine) should be balanced against the potential risks, such as infections^[6]. The use of anti-TNF therapy has been associated with serious infections and especially patients receiving combination treatment with thiopurines seem to be at an increased risk^[4,7-9]. Our patient developed a severe necrotizing tonsillitis due to an infection with HSV, which was confirmed by PCR and serology. She responded promptly to antiviral treatment which was empirically started after failure of antibiotic therapy. Mercaptopurine treatment was stopped and infliximab was continued. Histological findings were reported by Wat *et al*^[10] who described a patient with a herpes simplex infection that also caused an acute necrotizing tonsillitis. In contrast to our patient, this particular patient had a blanc medical history and was not immunocompromised. We here demonstrate that histology is not always required in order to accurately diagnose herpes simplex induced necrotizing tonsillitis.

To the best of our knowledge, this is the first report of an acute pharyngotonsillitis caused by HSV in an immunocompromised patient due combination

treatment with a thiopurine and an anti-TNF agent. Hence, HSV infections should be in the differential diagnosis when immunocompromised patients present with a severe necrotizing tonsillitis, and early treatment with antiviral agents should be considered especially if antibiotic treatment fails.

COMMENTS

Case characteristics

A 22-year-old female with known ulcerative colitis presented herself to the family physician with a sore throat.

Clinical diagnosis

Herpes simplex induced necrotizing tonsillitis in an immunocompromised patient.

Laboratory diagnosis

C-reactive protein of 137 mg/L, Hb 4.5 mmol/L, leucocyte count of $4.7 \times 10^9/L$ (leucocyte differentiation: Neutrophils 55%, eosinophils 1%, basophils 1%, lymphocytes 38%, monocytes 4%).

Imaging diagnosis

A computed tomography-scan showed bilateral heterogeneous contrast enhancement of both enlarged pharyngeal tonsils and arytenoids. At laryngoscopy a swollen nasopharynx was seen that was covered with grey-whitish exudate, and ulcerations of both arytenoids and in the aryepiglottic fold.

Treatment

Valacyclovir (1000 mg 3 times daily).

Experiences and lessons

Herpes simplex virus infections should be in the differential diagnosis when immunocompromised patients present with a severe necrotizing tonsillitis, and early treatment with antiviral agents should be considered especially if antibiotic treatment fails.

Peer-review

An highly interesting case report.

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