Alice in Wonderland syndrome and upper airway obstruction in infectious mononucleosis

P. Piessens, F. Indesteege and P. Lemkens
Department of Otorhinolaryngology and Head and Neck Surgery, Ziekenhuis Oost Limburg, Genk, Belgium

Key-words. Alice in Wonderland syndrome; upper airway obstruction; infectious mononucleosis

Abstract. Alice in Wonderland syndrome and upper airway obstruction in infectious mononucleosis. The Alice in Wonderland syndrome is a rare clinical feature characterised by perceptual disturbances including visual disturbances and distortion of the body image. This uncommon – but often easy to recognise – syndrome, to which children seem particularly susceptible, can be defined in patients with Epstein Barr Virus (EBV) infection. This report describes a 10-year-old child with a mild upper airway obstruction and manifestations of the Alice in Wonderland syndrome resulting from an acute EBV infection. Because meningo-encephalitis was considered in the differential diagnosis, an MRI examination was performed under midazolam sedation, leading to a severe life-threatening upper airway obstruction.

Introduction

Infectious mononucleosis (IM) – first described as a clinical entity in 1920 – results from acute infection with the Epstein Barr virus, a member of the Herpes-virus family.\(^1\) Transmission mostly occurs through the passage of infected saliva. Contact with oropharyngeal epithelial cells and lymphoid tissue allows replication of the virus. Infection of the B and T cells is also responsible for the dissemination of the infection. The incubation period prior to the development of symptoms averages four to eight weeks.\(^2\)

Although the clinical course is usually benign and self-limiting, uncommon and even potentially life-threatening complications can occur. This case involved a child with acute EBV tonsillitis presenting at the paediatric emergency department with mild airway obstruction and manifestations of the “Alice in Wonderland” syndrome, a clinical feature that is uncommon but easy to recognise when kept in mind. However, the possibility was not recognised in this case and so clinical management led to a severe life-threatening upper airway obstruction. The clinical course and both clinical features will be discussed.

Case report

A 10-year-old male presented at the paediatric emergency department with a three-day history of a sore throat and odynophagia, accompanied by nasal obstruction and abdominal discomfort. For the past day, he had complained about seeing objects in unusual colours and shapes in association with anxiety. These episodes recurred several times a day. He had been treated with amoxicillin (Clamoxyl®) and analgesics for two days. The patient had no relevant personal medical or family history.

Physical examination revealed a pale, absent and afebrile patient with a mild, low-pitched, inspiratory stridor without evidence of respiratory distress. Bilateral tender cervical lymphadenopathies were palpated and enlarged, and the tonsils were congested, with exudates. Further thoracoabdominal and neurological examination were normal. Body weight was 31 kg for 140 cm.

Laboratory tests revealed mild leukocytosis (14 300/mm\(^3\)) with a large number of atypical lymphocytes and C-reactive protein elevation (4.8 mg/dl). The erythrocyte sedimentation rate was elevated at 42 mm/h. Liver enzymes were not elevated. Paul-Bunnell test and EBV IgM titres were both positive. Blood culture was sterile. Cerebrospinal fluid showed a normal cell count, normal protein and glucose, and no organisms on gram stain and bacterial culture.

The patient was administered intravenous analgesics and cefotaxime (Claforan®, a third generation cefalosporin), which was stopped later after serological confirmation of EBV infection.

The following day, there were visual disturbances with more
severe anxiety. Because meningoencephalitis was considered in the differential diagnosis, aciclovir (Zovirax®) was given and an MRI examination was performed. During sedation with midazolam 10 mg (Dormicum®), respiratory distress with severe inspiratory stridor occurred. Arterial oxygen saturation fell to 74% and urgent intubation was needed. In the days that followed, the patient was monitored and managed at the intensive care unit with oxygen, intravenous penicillin and high-dose steroids. MRI examination did not reveal any relevant abnormalities. Four days later – after three failed extubation attempts – the ENT surgeon was consulted. The patient underwent a bilateral palatine tonsillectomy with adenotonsillitis (70%), but virtually any other organ system can be affected with symptoms suggestive of second- ary bacterial infection.1-3 The pathophysiology is unknown; however, it is thought that focal inflammation resulting from viral infections causes focal brain parenchymal edema and dysfunction as well as concomitant decrease in regional cerebral blood flow. Computed tomography and MRI are unable to demonstrate any specifically involved brain areas. EEG can only sometimes show electrophysio-logically abnormal lesions. Scintigraphic studies (SPECT) show hypoperfusion near the visual pathway, especially at the temporal lobe, occipital lobe and perisylvian area.4,5 The symptoms are – when kept in mind – easy to recognise in a patient with full-blown features of IM but this is not so if the visual disturbances precede the classic symptoms of IM or if IM follows a subclinical course. Specific therapy is not indicated, as all patients recover completely.4,5,7

Upper airway obstruction is an uncommon (1-3.5% of IM cases) but potentially fatal complication of IM due to massive lymphoid hyperplasia and tissue oedema in Waldeyer’s ring. Peritonsillar abscesses occur in approximately 1% of patients and may further obstruct the airway.2 Mild airway obstruction – presenting as a soft stridor – is a common clinical sign in IM that can generally be successfully managed conservatively. Patients should be observed closely and oral or systemic corticosteroids are often administered to shrink lymphoid tissue. However, the use of steroids also mandates careful monitoring for signs or symptoms suggestive of secondary bacterial infection.3,4,10,11 Moderate airway obstruction in IM is characterised by nasal flaring, suprasternal retraction and low-pitched, inspiratory stridor. Maintaining airway passage patency by passing a nasopharyngeal tube can be used as a temporary measure.10,11 When medical management – including systemic steroid therapy – fails or symptoms progress to a severe airway obstruction with worsening stridor, tachypnoea, tachycardia and hypoxia, surgical intervention will usually be required.2,10 Both tracheotomy and “hot” tonsillectomy

Discussion

Infectious mononucleosis (IM) is a clinical entity that results from infection with the Epstein Barr virus (EBV). Clinical manifestations vary widely, but infection is clinically silent in most infants and young children. Most patients present with a clinical triade of fever (95%) with cervical adenopathy (94%) and pharyngotonsillitis (70%), but virtually any other organ system can be affected by the virus. Neurological syndromes can include Guillain-Barré syndrome, facial nerve palsy, aseptic meningitis, meningoencephalitis and transverse myelitis.1,3 The remarkable perceptual disturbances from which our patient suffered are known as the Alice in Wonderland syndrome.4,7 This uncommon form of visual metamorphopsia was first described in 1955 as “a singular group of symptoms intimately associated with migraine and epilepsy”. Its name is derived from the book “Alice’s adventures in Wonderland” due to the similarity with Alice’s dreams.4 The symptoms are also defined in patients with viral infections (especially after EBV infection), intoxication due to hallucinogenic drugs, schizophrenia, hyperpyrexia and cerebral lesions. Various types of illusions have been described including visual distortion of form, size, movement or colour, distortion of the body image (having a sensation that particular body parts are too small or too big) and a sense of time speeding up or slowing down. Unlike visual hallucinations patients are keenly aware that the distortions are not real. Patients with “Alice in Wonderland syndrome” may be of any age, though the syndrome is more common in young people. Children seem to be particularly susceptible.4,7 The pathophysiology is unknown; however, it is thought that focal inflation in regional cerebral blood flow. Computed tomography and MRI are unable to demonstrate any specifically involved brain areas. EEG can only sometimes show electrophysio-logically abnormal lesions.
Alice in Wonderland syndrome have been reported as surgical options, the latter having emerged as the preferred treatment. Palatine tonsillectomy under general anaesthesia appears to be a safe and well tolerated operation in IM. The usual cause of the obstruction is therefore directly and rapidly relieved. In our case, medical treatment was not effective and tonsillectomy was required after several failed attempted extubations. Tracheotomy on the other hand does not directly relieve the cause of respiratory distress and is also a difficult procedure to perform hastily under local anaesthesia in a hypoxic and agitated patient. It should be reserved for those patients with the Guillain-Barré syndrome who develop progressive alveolar hypventilation and bulbar paralysis and require prolonged airway support.

Another point our case highlights is that patients with an upper airway obstruction are extremely vulnerable during anaesthesia and sedation. Sedation results in loss of muscle tone and arousal responses, so upper airway patency may be even more compromised. Serious precautions should be taken if sedation is needed because intubation in these patients is also more difficult. Furthermore, during extubation, appropriate personnel and equipment should be immediately available in case of recurrent respiratory distress.

Conclusion

Alice in Wonderland syndrome is an uncommon but – when kept in mind – easily recognisable neurological manifestation of acute EBV infection, characterised by perceptual disturbances including visual disturbances and distortion of the body image. This feature could be easily confused with meningo-encephalitis by a clinician who is not aware of the existence of the syndrome and the link with IM.

As mild upper airway obstruction is a much more common clinical feature in infectious mononucleosis, it remains important to emphasise that patients with decreased airway patency – especially children – are extremely vulnerable during anaesthesia and sedation. Serious precautions should be taken to avoid a possible evolution to severe, life-threatening airway obstruction.

References

