CASE REPORT

Severe acute measles pneumonitis: virus isolation in bronchoalveolar lavage fluid

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SUMMARY

In the past few years, several endemic outbreaks of measles have been recognised, not only in children but also in adults, with severe and, occasionally, even fatal complications, possibly due to delayed diagnosis of the disease in adult medicine and decreasing vaccination rates. Furthermore, the treatment consists of supportive measures only. We present a case of severe measles pneumonitis in a 42-year-old man, a travel returnee, proven by direct virus isolation with PCR from bronchoalveolar lavage fluid. CT findings and pulmonary function testing revealed features of obstructive bronchiolitis; the patient was successfully treated with corticosteroids. He fully recovered, and lung function measurement returned to normal values. We conclude that acute measles can present as obstructive bronchiolitis and may be successfully treated with corticosteroids.

BACKGROUND

Measles are an important differential diagnosis in adults presenting with symptoms of an airway infection. Because it is primarily known, in the Western hemisphere, as a paediatric disease, leads to significant delays in diagnosing, isolating and treating the patient. Furthermore, there may be severe respiratory complications—as in our patient—which can be successfully treated with corticosteroids.

CASE PRESENTATION

A previously healthy 42-year-old man presented to the emergency department because of asthenia, fever, watery and bloody diarrhoea, myalgia, headache and cough, 10 days after returning from a trip to Thailand. On clinical examination, the patient was febrile (40°C), tachycardic (116/min), hypertensive (149/88 mm Hg) and in mild respiratory distress (respiratory rate 30/min), with oxygen saturation between 89% and 94% while breathing ambient air. Unilateral pulmonary crackles, a maculated exanthema over the chest, erosions of the enoral mucosa, and conjunctivitis, were present. No enlarged lymph nodes were noted and no palpable spleen tip was found.

INVESTIGATIONS

Laboratory tests revealed a normal leucocyte count, moderately elevated C reactive protein (45 mg/L; normal value <5 mg/L) and normal liver enzymes (alanine aminotransferase (40 U/L) and creatinine (102 µmol/L).

There was no apparent infiltration on chest radiograph, however, there were condensed

perihilar structures. Blood cultures and urinary legionella antigen remained negative.

Within 48 h of initial treatment with clarithromycin 500 mg twice daily, the patient developed progressive respiratory distress with marked hypoxaemia in the arterial blood gas analysis (pO₂ 5.2 kPa on ambient air with elevated alveolar-arterial gradient of 10.1 kPa, normal value <1.5 kPa). Pulmonary embolism was excluded by CT, but radiological signs suggestive of small airway disease with centrilobular micronodules and tree-in-bud pattern were detected (figure 1). Ceftriaxone (intravenously, 2 g once daily) was added, but the patient's respiratory symptoms worsened during the subsequent 2 days, and his C reactive protein increased to 223 mg/L (normal value <5 mg/L). Meanwhile, the exanthema had spread to the limbs and the patient eventually developed erythrodermia.

After exclusion of common causes of fever in the returning traveller (malaria, HIV primoinfection, hepatitis A, B and C), a flexible bronchoscopy with bronchoalveolar lavage (BAL) was performed under the local standard precautions when confronted with an unclear, possibly infectious case, such as tuberculosis masks, gloves and a water-repellent coat.

The BAL revealed a predominantly lymphocytic alveolitis (complete cell count 790/µL, lymphocytes 30%, macrophages/monocytes 58%, neutrophils 1%). None of the microbiology samples showed evidence of common bacterial, viral or fungal infection (BAL fluid with negative Gram smear, negative PCR for *Mycoplasma pneumoniae*, *Mycobacterium tuberculosis* complex, influenza virus, parainfluenza virus, adenovirus and rhinovirus, no fungi detected).

Figure 1 A 1 mm axial CT scan showing bilateral signs of a bronchiolar disease with tree-in-bud sign and diffuse centrilobular nodules in both upper lobes.

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with direct microscopy or culture; sputum negative for *Mycoplasma pneumoniae* and *Chlamydothila pneumoniae* (PCR), and urine negative for *Legionella pneumophila* antigen). However, the measles virus was isolated with PCR from the BAL fluid. Accordingly, the blood serology for measles IgM and IgG antibodies tested positive.

DIFFERENTIAL DIAGNOSIS

As the patient had returned from travelling abroad, there was a wide differential diagnosis including HIV, viral and bacterial respiratory infections, and tuberculosis. However, in patients with incomplete vaccination status, other respiratory pathogens must be considered. Concerning the radiological presentation of the disease, an infection with *Mycoplasma pneumoniae* or influenza would be suggestive.

TREATMENT

Initially, a pneumonia with bacterial pathogens was considered, and clarithromycin (orally, 500 mg twice daily) was started.

After respiratory deterioration and diagnosis of an acute measles pneumonitis presenting as obliterative bronchiolitis was diagnosed, corticosteroid treatment was initiated (day 1:80 mg methylprednisolone intravenously, day 2–7:50 mg prednisolone orally with continuous tapering thereafter).

Before the diagnosis of an acute measles pneumonitis was established, the patient had stayed in a hospital room shared with others. However, since contagiousness of measles lasts until 4 days after exanthema eruption, the patient himself was not isolated after diagnosis. Also, the other patients who shared the room with him were not isolated, because all were tested positive for measles IgG and negative for IgM. Exposed hospital staff personnel were evaluated by the infectious diseases specialists.

OUTCOME AND FOLLOW-UP

Within 24 h after initiation of corticosteroids, the patient's condition and respiratory distress rapidly improved, oxygenation returned to normal and the patient was discharged 10 days after admission. The lung function test initially showed a restrictive pattern with a forced expiratory volume in 1 s (FEV1) of 2.45 L (70% predicted) and a slightly diminished diffusion capacity of 73%. Within 1 month of initiation of corticosteroids, lung function returned to normal (FEV1 3.51 L (100% predicted) and diffusion capacity of 98% predicted). After 2 months, the corticosteroid therapy was stopped.

Since measles vaccination was introduced to Switzerland only in 1976, the patient most likely was never vaccinated.

DISCUSSION

The measles virus is an RNA virus belonging to the Paramyxoviridae family. After an incubation period of 10–12 days, acute measles initially presents as a common upper respiratory tract infection lasting for 2–4 days, followed by pathognomonic Koplik spots and a characteristic maculopapular rash beginning on the head, then spreading to the trunk and limbs.^{1 2} Measles is highly contagious, with a transmission rate of at least 90%.^{3 4} Infected patients are contagious for 4 days after the onset of the rash. In populations with high vaccination rates, acute cases of measles are most often caused by infections acquired abroad.⁵ In 2010, a measles outbreak appeared in 13 unvaccinated people returning from a mass gathering in France.⁶

The diagnosis of measles pneumonitis is challenging, since up to 77% of these patients have a normal pulmonary auscultation,

and up to 79%, a normal chest radiograph. Moreover, 21% of measles-infected patients with respiratory insufficiency have a normal chest radiograph on admission.^{7 8} Therefore, laboratory confirmation of clinical suspicion of acute measles infection is highly recommended. PCR from pharyngeal swabs is, nowadays, considered equivalent to serological testing and, therefore, can be implied in the daily routine.⁹ Since our patient's oxygenation was markedly deteriorating, a rapid diagnosis was crucial. Successful direct virus isolation with PCR from either BAL fluid or blood, urine and throat swabs has previously been described.^{10 11} The PCR results—in contrast to serological testing—are rapidly available, which is crucial for therapeutic and epidemiological decision-making.

Complications typically occur in children below the age of 5 years and in adults over 20 years of age. Pneumonia—caused by the virus itself or a bacterial or viral co-infection—is the most common complication, with a prevalence of up to 6%. The most common pathogen is *Streptococcus pneumoniae*.¹² In our patient, a community-acquired pneumonia (CAP) with atypical bacterial pathogens was initially postulated, and treatment with clarithromycin, with the subsequent addition of ceftriaxone, was initiated. Retrospectively, it is uncertain whether a bacterial co-infection was present at the time, since BAL was performed after initiating the antibiotic treatment.

Measles pneumonitis presenting as obliterative bronchiolitis is a rare event, and knowledge on the course of radiological changes and pulmonary function is sparse.

In 1993, a case of measles pneumonitis successfully treated with corticosteroids and vitamin A was published.¹³ A recently published retrospective study documented the clinical course of 36 patients with acute measles admitted to the intensive care unit. Eight of the patients were treated with measles-directed therapy consisting of vitamin A, intravenous immunoglobulin supplementation, plasma exchange and corticosteroids or ribavirin,⁷ the corticosteroids having shown to inhibit measles virus replication in vitro. Despite these measures five patients died. In our patient, the corticosteroid treatment led to rapid recovery from respiratory distress and normalisation of oxygenation and lung function parameters over time. Based on this observation, we recommend corticosteroid treatment in patients with measles pneumonitis presenting as obliterative bronchiolitis.

First and foremost, a strict vaccination policy is mandatory to eliminate the disease in the long term, and every physician must be aware of the disease to prevent further infections through index patients.³

Patient's perspective

- ▶ Returning from Thailand, I initially thought I might be dealing with an acute flu. Then I was concerned, as infections such as HIV were discussed. I was not aware that I had never been vaccinated against measles, so at first I could not imagine I had a measles infection, especially since I thought only children could be affected.
- ▶ I was very concerned when my breathing deteriorated, and was glad that the treatment was so efficient and a transfer to the intensive care unit was unnecessary. After leaving the hospital, I made sure that my brother presented to his doctor for a measles vaccination, since he had never been vaccinated either.

Learning points

- ▶ Measles must be considered a differential diagnosis in an adult presenting with upper airway symptoms, particularly when an incomplete vaccination status is suspected.
- ▶ Virus isolation in the bronchoalveolar fluid may help to narrow the differential diagnosis down and is technically feasible in the clinical setting.
- ▶ Respiratory complications of measles can be severe and present as an obliterative pneumonitis, which can be successfully treated with corticosteroids.

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Competing interests None declared.

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