CASE REPORT

Atypical measles syndrome in adults: still around

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SUMMARY

Measles, a vaccine-preventable disease, is currently responsible for worldwide outbreaks mainly due to the failure to maintain high coverage of childhood immunisation. Atypical measles syndrome was first described in the 1960s in association with the inactivated measles vaccine. We report a case of atypical measles syndrome in a 29-year-old man without previous measles immunisation. He presented with fever, shortness of breath and a purpuric rash. Radiological investigations allowed the diagnosis of severe nodular pneumonia. Positive PCR in nasal and pharyngeal samples, and positive serology for a primary infection confirmed measles diagnosis. Both clinical symptoms and pulmonary nodules regressed spontaneously, whereas mediastinal lymph nodes increased and persisted up to 3 months after the primary infection. Physicians should be aware of the atypical measles syndrome presentation in order to limit the delay of diagnosis, to avoid unnecessary investigations and to prevent the potential spread of this infectious disease.

BACKGROUND

Measles remains a major public health concern with around 147 000 deaths reported worldwide in 2013.¹ It can be easily prevented by vaccination. Indeed, as the worldwide coverage of the first dose of measles vaccine reached 82% in 2007, the estimated number of deaths from measles dropped from 750 000 to 197 000 between 2000 and 2007.² To date, a two-dose schedule of live-attenuated vaccine achieves 97% efficacy.³ In countries where vaccination has substantially reduced the incidence of measles, clustering of unvaccinated persons and failure to maintain high coverage of childhood immunisation in all districts have resulted in a resurgence of measles.^{2–4} Thus, a re-emergence has recently been reported throughout Europe and North America.⁵ In 2014, 23 outbreaks have been identified in the USA and 3616 cases of measles have been notified in Europe,⁶ with severe cases of measles described in young adults.^{7–8}

We report a case of atypical measles syndrome characterised by fever, hilar lymphadenitis and severe pneumonia along with a polymorphic rash beginning on the hands.

The authors have obtained informed written consent for print and electronic publication of this case report.

CASE PRESENTATION

A 29-year-old Frenchman presented to our University hospital with fever and shortness of breath. He had no known allergies or significant

medical history, except for tobacco addiction. He reported no history of insect bites or recent travel and worked as a merchant. On admission, he had chest pain and shortness of breath. He was febrile (39°C) and his oxygen saturation was 90% at room air. Chest auscultation was normal and diffuse lymphadenitis was present on palpation (cervical, inguinal and axillary). Four days later, a skin rash progressed as purpuric exanthema affecting the trunk, neck, arms, legs and palms ([figure 1](#)).

INVESTIGATIONS

The arterial blood gas demonstrated a respiratory failure with partial pressure of oxygen (pO₂) = 57 mm Hg, and partial pressure of carbon dioxide (pCO₂) = 37 mm Hg, pH = 7.44 at room air. Thrombocytopenia (100 G/L), lymphopenia (0.34 G/L) and C reactive protein elevated at 62 mg/L were noted. Blood chemistry analysis showed elevated liver enzymes: aspartate transaminase (105 UI/L), alanine transaminase (147 UI/L), γ-glutamyl transpeptidase (762 UI/L) and alkaline phosphatase (250 UI/L). CT scan revealed bilateral pulmonary nodules from 4 to 14 mm with mediastinal lymph nodes. Blood cultures, legionella urinary antigen and pharyngeal aspirations tested for influenza were negative.

F¹⁸ fluorodeoxyglucose positron emission tomography (FDG PET scan) imaging showed areas of increased uptake: mediastinal cervical and coeliac lymphadenopathy, pulmonary bilateral nodules ([figure 2](#)) and areas of homogeneous increased uptake in the spleen.

DIFFERENTIAL DIAGNOSIS

The serum protein electrophoresis and primed lymphocyte typing showed normal results; HIV and human T-lymphotropic virus type 1 serology were

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Figure 1 (A) Maculopapular and purpuric rash affecting the trunk, neck, arms and legs; (B) purpuric exanthema affecting the palm and soles.

Figure 2 Positron emission tomography: mediastinal, cervical and coeliac lymphadenopathy uptake, pulmonary bilateral nodules and areas of homogeneous increased uptake in the spleen.

negative. Microbiological investigations were positive for measles: positive PCR in nasal and pharyngeal samples, and positive serology for a primary infection. Seroconversion appeared 3 months later. These results confirm the diagnosis of primary measles infection in an immunocompetent patient.

TREATMENT

Initial treatment with oral amoxicillin 1 g three times a day was interrupted at day 5. Symptomatic treatments with

oxygen therapy and paracetamol (1 g three times a day) were administered.

OUTCOME AND FOLLOW-UP

Fever persisted for 1 week despite treatment with amoxicillin. The purpuric rash and pulmonary symptoms regressed progressively after 10 days. Hepatic cytolysis regressed spontaneously as did the blood count anomalies initially observed. The patient did not present any neurological symptoms. He recovered without specific treatment, such as immunoglobulin therapy.

Figure 3 Control fluorodeoxyglucose positron emission tomography CT (FDG PET-CT) scan at 3 months: regression of cervical, coeliac lymph nodes and spleen uptake but a highly FDG uptake in enlarged mediastinal lymph nodes. Pulmonary nodules showed faint uptake and wound glass aspect.

Figure 4 Comparison of Maximum Intensity Projection (MIP) at diagnosis, and follow-up at 3 months and 15 months.

However, the radiological lung lesions persisted and required close monitoring by a pneumologist and infectious diseases specialists.

At 3 months follow-up, the FDG PET scan showed regression of cervical and coeliac lymph nodes and spleen uptake but a high FDG uptake in the enlarged mediastinal lymph nodes, suggesting a malignancy (figure 3), whereas pulmonary nodules showed only faint uptake and ground glass aspect. The patient reported of fatigue but had neither weight loss nor fever. Transbronchial biopsy of the lymph nodes revealed a granulomatous non-specific reaction and the PCR for paramyxovirus was negative. At 1-year follow-up, the patient was asymptomatic and the CT scan at 15 months showed regression of pulmonary nodules and lymph nodes (figure 4).

DISCUSSION

We present here a case of severe atypical measles in an immunocompetent patient without previous measles immunisation. The entity of atypical measles syndrome was well described in the 1970–1980s^{9 10} before the vaccination schedule, and has been mostly related to the use of the inactivated measles vaccine.^{11 12} To the best of our knowledge, since 80', no case of atypical measles syndrome has been reported in the literature. In contrast, non-classical measles that is characterised by a mild clinical presentation has been reported during outbreaks as a diagnosis challenge, mostly in vaccinated patients.^{13 14} Currently, the live-attenuated and combined measles-mumps-rubella (MMR) vaccine is used and recommended since 1985 in Europe and the USA.^{1 3} Our patient did not receive any previous measles vaccine. Moreover, no immunodeficiency was diagnosed, so he did not fulfil the criteria for immunoglobulin therapy.⁴

This syndrome is characterised by pneumonia with lobular or segmental infiltrations, hilar lymphadenopathy and pleural effusion. The pulmonary presentation can be severe and is associated with a maculopapular rash that progresses to vesicular, petechial or purpuric lesions.^{11 12 15} Other infectious microorganisms that could be evoked when confronted with this condition include *Streptococcus pyogenes*, *Staphylococcus aureus* (toxic rash), *Neisseria gonorrhoeae*, rickettsioses, *Treponema pallidum*, Epstein-Barr virus (EBV), cytomegalovirus, rubella, enteroviruses, herpes simplex virus, varicella-zoster virus, human herpesvirus6 and the haemorrhagic fever group of viruses. Atypical measles has also been associated with nodular pulmonary lesions that can persist as long as 2 years after the primary infection.^{12 16} Despite the fact that patients may appear severely ill during the acute illness, a spontaneous recovery is

expected in patients with atypical measles.¹² Invasive methods of explorations may therefore be avoided with a close follow-up. Here, we were alerted by the secondary lymph node enlargement in a young adult. In fact, viral and bacterial infectious diseases such as EBV, HIV, *Helicobacter pylori*, *Campylobacter jejuni*, *Chlamydia psittaci* and *Borrelia burgdorferi* have been described in association with lymphoma.^{17 18} An association between Hodgkin's lymphoma and measles has also been described.¹⁹ We therefore performed a transbronchial lymph node biopsy that revealed a granulomatous reaction without specific lesion.

The clinical presentation of atypical measles syndrome is so unlike that of typical measles that the diagnosis may be elusive. We placed our patient under airborne precautions as recommended for typical measles with no case of secondary transmission. Although this condition has not been reported to be contagious with no cases of secondary transmission,¹² further studies are needed to confirm this statement.

Learning points

- ▶ While circumventing the need for a more invasive diagnostic workup, physicians should be aware of the presentation of atypical measles syndrome.
- ▶ To date, no case of secondary transmission has yet been reported but the high contagiousness of typical measles merits caution.
- ▶ Further studies are required in order to fully elucidate the pathophysiology of atypical measles syndrome as it could occur without previous immunisation.

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Contributors CM and NC wrote the article. LT performed the PET scan. PB supervised the work.

Competing interests None declared.

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