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Measles-induced Acute Disseminated Encephalomyelitis in a Non-vaccinated Patient

Deeba Ali[1], Arnaud Detroz[1], Yilmaz Gorur[2], Lionel Bosquee[3], Noel Lorenzo Villalba[4], Benoît Cardos[5]

[1]University of Liège, CHU Liège, Liège, Belgium

[2]Service de Radiologie, Clinique André Renard, Herstal, Belgium

[3]Service de Pneumologie, Clinique André Renard, Herstal, Belgium

[4]Service de Médecine Interne, Diabète et Maladies Métaboliques, Hôpitaux Universitaires de Strasbourg, Strasbourg, France

[5]Service des Urgences, Clinique André Renard, Herstal, Belgium

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ABSTRACT

We reported a case of measles-induced acute disseminated encephalomyelitis (ADEM) in a 40-year-old immunocompetent adult. The patient presented a week after the development of respiratory symptoms and a cutaneous rash, and was admitted to hospital for altered mental status. Blood tests showed hyperleukocytosis, thrombopenia and cytolysis. A lumbar puncture was consistent with acute meningitis and the patient was initially treated with antiviral and wide broad-spectrum antibiotics. Serology and PCR for measles came back positive.

LEARNING POINTS

- Acute disseminated encephalomyelitis (ADEM) associated with measles infection is not uncommon.
- Clinical suspicion must be based on the presence of measles infection or recent vaccination.
- A normal CT scan does not rule out the disease but magnetic resonance imaging (MRI) is not required to confirm the diagnosis.

KEYWORDS

Measles, acute disseminated encephalomyelitis, magnetic resonance imaging

INTRODUCTION

Measles is highly contagious but can be avoided with adequate vaccination.

The disease may cause severe respiratory and neurological complications. Approximately 1/1,000 patients develop acute disseminated encephalomyelitis a few days after the appearance of a cutaneous rash. Measles elimination in the European Union is an urgent public health goal, yet despite the efforts of member states, there are vaccination gaps and outbreaks do occur. Between 1 July 2015 and 30 June 2016, some 1,818 measles cases were reported in the European Economic Area (EU/EEA), 309 of which occurred in Germany, a country where vaccination is not mandatory[1]. Mandatory vaccination has always been controversial and gives rise to opposition and debate. Inflammation and demyelinating lesions of the central nervous system can be induced by measles vaccination or infection. The diagnosis must be confirmed by serology or polymerase chain reaction (PCR). Morbidity and mortality can be high even in patients who have shown clinical improvement following administration of intravenous corticosteroids or immunoglobulins.

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CASE PRESENTATION

A 40-year-old woman without a relevant medical history was admitted to the emergency department for changed mental status and walking disturbance during the previous 24 hours. One week previously, she had experienced fever, headache, rhinorrhoea and an extensive cutaneous rash. The cutaneous rash had started on the ears and face, subsequently extending to the entire trunk. The rash disappeared after 8 days.

Of note, her son had been admitted the previous week for dyspnoea associated with a cutaneous rash and fever, which was diagnosed as measles; he had never been vaccinated against measles. Her grandson had not been vaccinated against measles either and was also diagnosed with the disease. The patient's granddaughter also developed a cutaneous rash and fever.

No history of previous vaccination for measles or measles during childhood was reported by the patient.

Upon admission, the patient was unable to talk, somnolent and disorientated. She was febrile, her blood pressure was 120/70 mmHg, her heart rate was 85 bpm, and she was saturating well on room air. The neurological examination was consistent with axial ataxia (cerebellar syndrome). Global hypotonia and absent rotular reflexes were noted, but reflexes were normal in the upper extremities. The rest of the clinical examination was normal. Vital signs were normal except for body temperature (39.1°C).

Blood tests showed hyperleukocytosis (11,600/mm^3) with lymphocytosis, thrombopenia (78,000/mm^3) and elevated C-reactive protein (215 mg/l). A liver panel showed slight cytolysis, an aspartate aminotransferase (ASAT) level of 76 U/l, an alanine aminotransferase (ALAT) level of 99 U/l, and elevated lactate dehydrogenase (1,048 U/l). Renal function tests, coagulation and electrolytes were within the normal range.

The patient was initially sent for a brain scan which came back normal. A lumbar puncture was performed: the liquid was clear and showed 12,680/mm^3 white cells predominantly neutrophils (80%), proteins (1400 mg/l) and normal glycorrhachia. In the setting of suspected acute meningitis, empiric treatment with acyclovir, ceftriaxone and ampicillin was initiated. The patient was then transferred to the intensive care unit (ICU).

The diagnosis should have been confirmed with a cerebral MRI, but this was contraindicated by the fact that the patient had a metallic implant. Polymerase chain reaction (PCR) tests for herpes simplex virus (HSV), varicella zoster virus (VZV), cytomegalovirus (CMV), adenovirus, enterovirus and Epstein-Barr virus (EBV) in the cerebrospinal fluid (CSF) were all negative. Serology for rubella, *Borrelia*, *Listeri*a, CMV, herpes, VZV and EBV was also negative, but was positive for measles. PCR for measles on a nasopharyngeal sample also came back positive

In light of these biological and imaging results and the clinical context, a diagnosis of acute disseminated encephalomyelitis (ADEM) following measles infection was made.

Acyclovir and antibiotics were discontinued and replaced by high doses of corticosteroids (30 mg/kg/day for 5 days), together with ribavirin (600 mg twice a day for 2 weeks) and vitamin A (20,000 IU/day)

After 2 weeks of treatment and supportive care, the patient was discharged from hospital. She received physical therapy and the neurological examination at 1 month showed no neurological sequelae.

DISCUSSION

Transmission of infectious diseases can be reduced by achieving and maintaining a high level of vaccination coverage. The WHO has set specific targets for the control, elimination or eradication of different infectious diseases (measles and polio), which are periodically updated. Vaccinations are an important tool of primary prevention. Lack of information and fake news are significant factors contributing to low immunization coverage. In particular, the increasing incidence of vaccine-preventable disease and the decreasing vaccine coverage may be related to vaccine hesitancy. Anti-vaccination campaigns have had a damaging impact on vaccine uptake.

Measles is a preventable infectious diseases. It is highly contagious and one of the most important causes of morbidity and mortality worldwide. It can cause serious respiratory and neurological complications[2], including encephalitis, which is the most common neurological sequela associated with measles. Three types of encephalitis have been described: acute disseminated encephalomyelitis or acute demyelinating encephalomyelitis (ADEM), subacute sclerosing panencephalitis (SSPE) and measles inclusion body encephalitis (MIBE)[3].

We have described a case of ADEM following measles infection in an immunocompetent adult. ADEM is an inflammatory demyelinating disease of the central nervous system (CNS). It is described more often in adolescents and young adults, typically presenting after acute infection or vaccination and 3–10 days after a cutaneous rash[3]. The incidence of ADEM associated with measles infection is higher (1 per thousand) than ADEM associated with live measles vaccination (1 per million)[4].

Other causes of ADEM include viruses (rubella, chickenpox, cytomegalovirus, herpes simplex), bacteria (*Campylobacter*, *Chlamydia*, *Legionella*), and, less frequently, parasites (*Plasmodium*, *Toxoplasma*)[5].

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The pathogenic mechanism depends on direct mimicry of a molecule which enables a viral protein to bind directly to a normal substrate as a substitute for the homologous normal ligand (myelin). Its clinical presentation is abrupt with fever, convulsions, and cerebellar, pyramidal or medullar signs.

Blood tests are usually normal except for the presence of hyperleukocytosis and C-reactive protein. In addition, CSF may show pleocytosis, increased protein concentration and normal glycorrhachia.

As a CT scan is usually normal, MRI is the gold standard for diagnosis and may show lesions appearing as hypersignals on T2 and FLAIR sequences. The lesions are typically numerous and disseminated and predominantly on the white matter of the brain [6].

In this case, the clinical presentation (fever, cutaneous rash the previous week and conjunctivitis) and the anamnesis (contact with a measles patient with pneumonia) made us suspect this entity. The suspicion of measles was confirmed by the results of serology and PCR of a nasopharyngeal sample.

In such a situation, it is very important to rule out other possible diagnoses, as the classic therapy for ADEM (high-dose corticotherapy) should not be prescribed unduly. Consequently, the priority is to rule out a CNS infection by performing a lumbar puncture. The differential diagnosis includes other demyelinating inflammatory diseases of the CNS, such as multiple sclerosis and leukoencephalopathy (neurosarcoidosis, lupus) induced by systemic disease. In addition to physical therapy and supportive care, high doses of vitamin A reduce mortality and ocular lesions [5].

The role of corticosteroid therapy in measles-induced ADEM is unclear. Fox described the results in a cohort of 15 patients treated successfully with corticosteroids, but there are no randomized studies evaluating the optimal treatment (dose and duration) of measles-related ADEM. Treatment is therefore empirical, with high doses (30 mg/kg) of intravenous corticosteroids administered for 3–5 days [6]. In case of non-response or contraindications, second-line therapy consists of intravenous immunoglobulin (0.4 g/kg/day) with plasmapheresis used as third-line therapy. Antiviral treatment is sometimes given in severe forms of measles, for instance in immunosuppressed patients, but its effectiveness is uncertain.

Evolution of the disease is unpredictable as it can resolve in a few days or take several weeks. Mortality ranges from 10 to 25% and neurological sequelae (hearing loss, visual impairment, paraplegia, epilepsy and intellectual or psychological disability) occur in 10–45% of patients[6]. As measles-induced ADEM is a rare and life-threatening condition, it is not easy to establish recommendations concerning the use of corticosteroids and immunoglobulins in the management of these patients.

However, in the case presented here, the clinical response to high-dose corticosteroids was excellent and full recovery was achieved after 4 weeks.

CONCLUSION

Measles-induced ADEM is an uncommon but severe complication of measles infection. Corticosteroid therapy must be considered even in the absence of current established treatment recommendations. Preventive treatment such as vaccination or immunoglobulins should be considered in individuals previously in contact with a confirmed case.

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