CASE REPORT

Fatal measles pneumonitis during Hodgkin's lymphoma

Benjamin Wyplosz,¹ Marion Lafarge,² Lélia Escaut,¹ Jean-Baptiste Stern^{1,3}¹Assistance publique-hôpitaux de Paris, CHU Bicêtre, Service de Maladies Infectieuses et Tropicales, Le Kremlin-Bicêtre, France²Assistance publique-hôpitaux de Paris, CHU Bichat-Claude Bernard, Réanimation Médicale, Paris, France³Institut mutualiste Montsouris, Département Thoracique, Paris, France

Correspondence to

Dr Benjamin Wyplosz, benjamin.wyplosz@bct.aphp.fr

SUMMARY

The treatment of measles pneumonitis in immunocompromised adults is not established. We describe a patient with Hodgkin's lymphoma who developed acute pneumonia during a measles infection. On day 13, intravenous ribavirin and immunoglobulins were administered. On day 18, the patient developed acute respiratory failure. An examination of transbronchial pulmonary biopsies showed Warthin-Finkeldey giant cells that are pathognomonic of measles pneumonitis. The patient died despite aggressive supportive care. Our case and a review of literature show that measles pneumonitis is routinely fatal in patients with cancer. We suggest that antiviral drugs should be considered as soon as the diagnosis has been established.

BACKGROUND

From 2008 to 2011, more than 30 000 cases of measles were reported in Europe.¹ In 2012, the epidemics was still ongoing with 8230 cases reported to the European Center for Disease Control and Prevention (ECDC).¹ France, Italy, Romania, Spain and the UK accounted for 94% of the cases. In 2013, outbreaks have been reported in Sweden, Denmark, Germany, Italy, the UK (England and Wales), Lithuania and The Netherlands.²

In France, most cases occurred in children and young adults.³ Overall, about 4980 patients were hospitalised, including 1023 for severe pneumonia and 27 for encephalitis/myelitis, and 10 patients died.³

In adults with cancer, measles is frequently atypical and leads to progressive giant cell pneumonia, encephalitis and death.^{4 5} Two fatal cases of measles pneumonitis have been reported in adults with cancer but none of them received any antiviral drug. We report on a case of measles pneumonitis in a patient with Hodgkin's lymphoma who received ribavirin as well as immunoglobulins.

CASE PRESENTATION

A young man in his early 20s was admitted to our hospital for a suspected measles. He had no history of measles vaccination. Three months earlier, he had been diagnosed with stage IV Hodgkin's lymphoma with mediastinal lymph nodes and pulmonary excavation in the left apical lobe. Cultures of respiratory samples were negative for bacteria, mycobacteria and fungi and no respiratory viruses were detectable (influenza virus, parainfluenza virus, metapneumovirus, rhinovirus, coronavirus and adenovirus). After completion of a first

BEACOPP escalated (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone) chemotherapy cycle, the patient was discharged home.

Two days after starting the second cycle of chemotherapy, the patient experienced fever (38–39°C) with sore throat and conjunctivitis (day 1 of characteristic illness) (figure 1). An erythematous rash rapidly spread from the face to the trunk. No Koplik's spots were observed. A diagnosis of measles was considered and the patient was referred to the Infectious Diseases Unit.

INVESTIGATIONS

Serological studies were negative for IgG and IgM antibodies to measles. The measles virus (MVs/Villejuif.FRA/20.10(D4)) was detected from nasal swabs by real time reverse transcriptase (RT)-PCR. After sequencing 456 base-pairs of the nucleocapsid gene, the strain was indistinguishable from the genotype D4 (MVs/Montaignu.FRA/43.08) circulating in France.

On day 3, febrile neutropenia occurred with a nadir at 100/mm³. Piperacillin/tazobactam was started. On day 8, the neutrophil cell count increased to >500/mm³ and the patient experienced progressive shortness of breath. A chest-CT scan visualised a bilateral interstitial infiltrate. On day 10, a fiberoptic bronchoscopy showed bronchial inflammation. A microscopical examination of the bronchoalveolar lavage (BAL) fluid showed leucocytes at 150/mm³ (neutrophils 74%, lymphocytes 26%). On day 12, cultures of BAL were sterile. No respiratory viruses were detectable (influenza virus, parainfluenza virus, metapneumovirus, rhinovirus, coronavirus, adenovirus). Measles pneumonitis was considered because MV was detected by PCR in BAL and urine and no antibody to measles was detectable in the serum.

DIFFERENTIAL DIAGNOSIS

Possible differential diagnosis:

- ▶ Pneumocystosis
- ▶ Viral pneumonia (influenza)
- ▶ Severe acute cardiac failure
- ▶ Drug-induced pneumonitis (bleomycine)
- ▶ Acute respiratory distress syndrome associated with abdominal infections

TREATMENT

On day 13, the patient's respiratory condition was worsening. Intravenous ribavirin was started at 20 mg/kg/day in addition to immunoglobulins at 1 g/kg/day for 2 days.

To cite: Wyplosz B, Lafarge M, Escaut L, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200252

Figure 1 Clinical events, evolution of biological markers and treatments given to a patient with measles and advanced Hodgkin's lymphoma. The horizontal line shows an absolute neutrophil count of 500 cells/mL which is a major risk factor for invasive aspergillosis. BAL: bronchoalveolar lavage.

OUTCOME AND FOLLOW-UP

On day 18, the patient experienced acute respiratory failure. He was transferred to the intensive care unit and required mechanical ventilation. A second fiberoptic bronchoscopy was unremarkable. BAL cultures grew *Aspergillus fumigatus* and MV was still detected by RT-PCR. The histopathological examination of transbronchial biopsies showed numerous conidia of *A fumigatus* and Warthin-Finkeldey giant cells that are pathognomonic of measles pneumonia (syncytial giant cells containing intranuclear eosinophilic inclusion bodies) (figure 2). Intravenous liposomal amphotericin B and caspofungin were administered.

Because of worsening of the respiratory failure, the patient was ventilated in a prone position, received inhaled nitric oxide and finally required veno-venous extracorporeal membrane oxygenation (ECMO) on day 22. Ribavirin was stopped after 12 days of therapy because of its lack of efficacy on the course of the disease and the occurrence of haemolytic anaemia. On

day 31, a ventilated-associated pneumonia was suspected. Culture of BAL grew *P aeruginosa*; MV was still detectable by PCR amplification. Ceftazidime and amikacin were started. On day 41, the patient died from an unexplained refractory hypotension associated with renal failure and severe metabolic acidosis attributed to propofol (propofol-related infusion syndrome) used at high doses for sedation under ECMO.

DISCUSSION

We report on a case of measles pneumonitis during the treatment of an advanced-stage Hodgkin's lymphoma. Intravenous administration of ribavirin and immunoglobulins, 5 days after the onset of the pneumonitis, did not prevent a subsequent fatal outcome.

In severe immunocompromised adults, only five cases of measles pneumonitis have been reported, including four deaths (case death of 80%).^{4–8} The underlying diseases were advanced HIV infection (n=3), lymphoma (n=1) and chemotherapy-induced neutropenia for rhabdomyosarcoma (n=1). Factors predicting a poor outcome have not been examined in the literature. In our patient, the following conditions may have predisposed to a fatal outcome: (1) Hodgkin's lymphoma unresponsive to chemotherapy; (2) profound chemotherapy-induced neutropenia at the onset of the rash; and (3) sustained MV-induced immune suppression that was responsible for prolonged lymphocyte depletion (<250/mm³) for 24 days worsening the patient's immune status.

Our patient was unable to mount an adequate immune response, as shown by the negative serological tests on day 10. Therefore, measles were diagnosed using a real time RT-PCR validated to detect MV in clinical specimens but not for patient management.⁹ The shedding of the MV into the lungs of immunocompromised patients has not yet been reported.¹⁰ Although our RT-PCR was designed for diagnosis but not to quantify the viral load, the results of analyses suggest that the treatments lacked efficacy. Indeed, that viral shedding lasted for weeks at a significant concentration despite aggressive treatment.

Figure 2 Transbronchic biopsies showing multigiant cells with viral intranuclear eosinophilic inclusions (Warthin-Finkeldey giant cells) pathognomonic of measles pneumonia (H&E stain, ×40).

Our patient received ribavirin as well as intravenous immunoglobulins. None of the two previously reported patients with malignant diseases received any antiviral drugs. A patient with non-Hodgkin's lymphoma and a patient with rhabdomyosarcoma died from pneumonia.^{4 7} Conversely, all three HIV-infected patients were treated with ribavirin and/or immunoglobulins.^{6 8} One patient, who was treated with ribavirin before respiratory deterioration and immunoglobulins after endotracheal intubation, survived the disseminated measles,⁸ while the other two, who received ribavirin after mechanical ventilation, had fatal outcomes.⁶ These cases and ours suggest that ribavirin and immunoglobulins should be considered for use in patients with severely impaired cellular immunity as soon as the diagnosis of measles is established.

Vaccination is the best way to prevent measles, but the live-attenuated virus vaccine is contraindicated in immunocompromised patients, such as those with malignant tumours or receiving immunosuppressive therapies. Immunity to measles should probably be checked in patients with immune deficiency in the context of epidemics. Those without circulating neutralising antibodies should be advised to seek prompt medical attention if they suspect or have evidence of exposure to measles to receive post-exposure prophylactics with intravenous immunoglobulins. Although treatment efficiency of measles pneumonitis in severely immunocompromised patients has not been established, the high likelihood of a fatal outcome may justify early treatment.

Learning points

- ▶ Measles pneumonitis is frequently fatal in immunocompromised hosts.
- ▶ Given the mostly fatal outcomes when measles occur in immune compromised patients, treatment should be tried as soon as possible.
- ▶ Vaccination should be administered at least 4 weeks before the initiation of immunosuppressive therapy.

Acknowledgements The authors would like to thank Dr Claire Danel (Hôpital Bichat, AP-HP) for performing histological analyses and providing microscopic photography; Pr Daniel Vittecoq (hôpital Bicêtre) and Dr Lila Bouadma (Hôpital Bichat, AP-HP) for providing care to the patient; Dr Rémi Lefrançois (Hôpital Bicêtre, AP-HP) for providing care to the patient and for his assistance in writing the first draft; Dr François Freymuth and Astrid Vabret (CNR de la rougeole et des paramyxoviridae respiratoires, CHU Caen) for virological analyses. We are indebted to Véronique Necyporenko for critically reviewing the manuscript.

Contributors All authors have cared for the patient, help to collect data, wrote the draft and approved the published version.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 European Center for Disease Control. Epidemiological update on measles in EU and EEA/EFTA Member States. Measles—surveillance data. 2013. <http://ecdc.europa.eu/en/publications/Publications/measles-rubella-monitoring-may-2013.pdf>
- 2 European Center for Disease Control. *Communicable disease threats report*, 2013. Week 27, 30 Jun–6 July 2013. <http://ecdc.europa.eu/en/publications/Publications/Communicable-disease-threats-report-05-jul-2013.pdf>
- 3 Antona D, Levy-Bruhl D, Baudon C, *et al.* Measles elimination efforts and 2008–2011 outbreak, France. *Emerg Infect Dis* 2013;19:357–64.
- 4 Kaplan LJ, Daum RS, Smaron M, *et al.* Severe measles in immunocompromised patients. *JAMA* 1992;267:1237–41.
- 5 Permar SR, Griffin DE, Letvin NL. Immune containment and consequences of measles virus infection in healthy and immunocompromised individuals. *Clin Vaccine Immunol* 2006;13:437–43.
- 6 Forni AL, Schluger NW, Roberts RB. Severe measles pneumonitis in adults: evaluation of clinical characteristics and therapy with intravenous ribavirin. *Clin Infect Dis* 1994;19:454–62.
- 7 Klimkiewicz A, Muller-Schulz M, Gerigk C, *et al.* [Fatal course of measles infection in a patient with a low-grade malignant non-Hodgkin lymphoma]. *Dtsch Med Wochenschr* 1998;123:901–4.
- 8 Ross LA, Kim KS, Mason WH Jr., *et al.* Successful treatment of disseminated measles in a patient with acquired immunodeficiency syndrome: consideration of antiviral and passive immunotherapy. *Am J Med* 1990;88:313–14.
- 9 Hubschen JM, Kremer JR, De Landtsheer S, *et al.* A multiplex TaqMan PCR assay for the detection of measles and rubella virus. *J Virol Methods* 2008;149:246–50.
- 10 Hummel KB, Lowe L, Bellini WJ, *et al.* Development of quantitative gene-specific real-time RT-PCR assays for the detection of measles virus in clinical specimens. *J Virol Methods* 2006;132:166–73.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow