Fever and Rash: Revisiting Measles

Febre e Exantema: Recordar o Sarampo

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ABSTRACT

Fever and rash are a common combination of symptoms in the young adult patient. The etiologic investigation is usually oriented towards the most common diseases, but atypical presentations of less frequent conditions should also be recalled. We describe the case of a 44 year-old Portuguese woman who presented with fever, conjunctivitis, cough and rash, rapidly evolving to hepatitis and extensive pneumonia with respiratory failure. Although she claimed to be vaccinated according to the national immunisation schedule, a final diagnosis of primary measles pneumonia was clinically made and confirmed by serology. However, some less typical features mislead us initially. Although the rare form of primary measles pneumonia is more prevalent among immunosuppressed patients, our patient was immunocompetent. Moreover, absence of contagiousness, as was the case, occurs more frequently in atypical measles. This case highlights the need to always confirm the alleged vaccination status in adults and raises attention to some unusual features of typical measles.

Keywords: Exanthema; Fever; Measles

RESUMO

Febre e exantema são uma combinação comum de sintomas no jovem adulto. A investigação etiológica é geralmente direcionada para as doenças mais frequentes, mas apresentações atípicas de condições menos frequentes também devem ser recordadas. Apresentamos o caso clínico de uma mulher portuguesa de 44 anos que apresentou quadro caracterizado por febre, conjuntivite, tosse e exantema, evoluindo rapidamente para hepatite e pneumonia extensa com insuficiência respiratória. Embora afirmasse ter o programa nacional de vacinação actualizado, os achados clínicos e o resultado serológico foram conclusivos de pneumonia primária a sarampo típico. Contudo, algumas manifestações menos típicas tornaram o diagnóstico menos óbvio. Embora a forma rara de pneumonia primária a sarampo seja mais frequente nos doentes imunodeprimidos, a nossa doente era imunocompetente. A ausência de contágio, tal como neste caso, ocorre mais frequente no sarampo atípico. Este caso clínico pretende mostrar a importância da confirmação do estado vacinal nos adultos, sublinhando ainda algumas apresentações atípicas de sarampo típico.

Palavras-chave: Exantema; Febre; Sarampo

INTRODUCTION

Fever and rash are a common combination of illness presenting symptoms in the adult patient. Etiologic investigation is usually oriented towards the most common diseases within the infectious, autoimmune or drug-related categories. However, less frequent entities should be kept in mind until properly ruled out. Furthermore, both rare and common entities can often be more challenging due to atypical presentations.

CLINICAL CASE

A 44-year-old Caucasian woman presented to the emergency department with fever, odynophagia and rash with caudal extension, accompanied by worsening dyspnoea, dry cough, myalgia, vomiting and diarrhoea over the week before (Fig. 1). The diagnosis of tonsillitis was assumed by her General Practitioner three days after fever onset and she was prescribed amoxicillin/clavulanic acid and nimesulide. She had a prior history of epilepsy (treated with topiramate for several years) and occasional smoking habits. She worked in an elderly care facility in a rural setting. She was exposed to cats but had no history of recent travelling, drug allergies, drug abuse or contact with other ill people. She claimed to have an updated vaccination schedule. Upon examination, a tympanic temperature of 37.7ºC, bilateral conjunctival hyperaemia and cervical lymphadenopathy were documented. A generalized maculopapular skin rash including face but sparing the perioral skin and acral region was also seen (Fig. 2). The remaining physical examination was unremarkable, namely without Pastia lines, raspberry tongue, epidermolysis lesions or Koplik spots. The initial laboratory work documented a relative neutrophilia and lymphocytopenia with C-reactive protein elevation, a mixed hepatocellular and cholestatic pattern (Table 1) and a negative rapid strep test. The baseline chest radiography (CXR) had no pathological findings (Fig. 3). After admission, clindamycin and doxycycline were started empirically. On day two, her clinical condition deteriorated with severe odynophagia, new-onset dysphonia, right upper quadrant abdominal pain and worsening partial respiratory failure. CXR at that time revealed a diffuse reticular pattern (Fig. 3). Chest computed tomography (CT) documented several mediastinal and bilateral hilar ganglia; multifocal ground-glass opacities, septal thickening and micronodulation of the lung parenchyma; and homogeneous hepatomegaly

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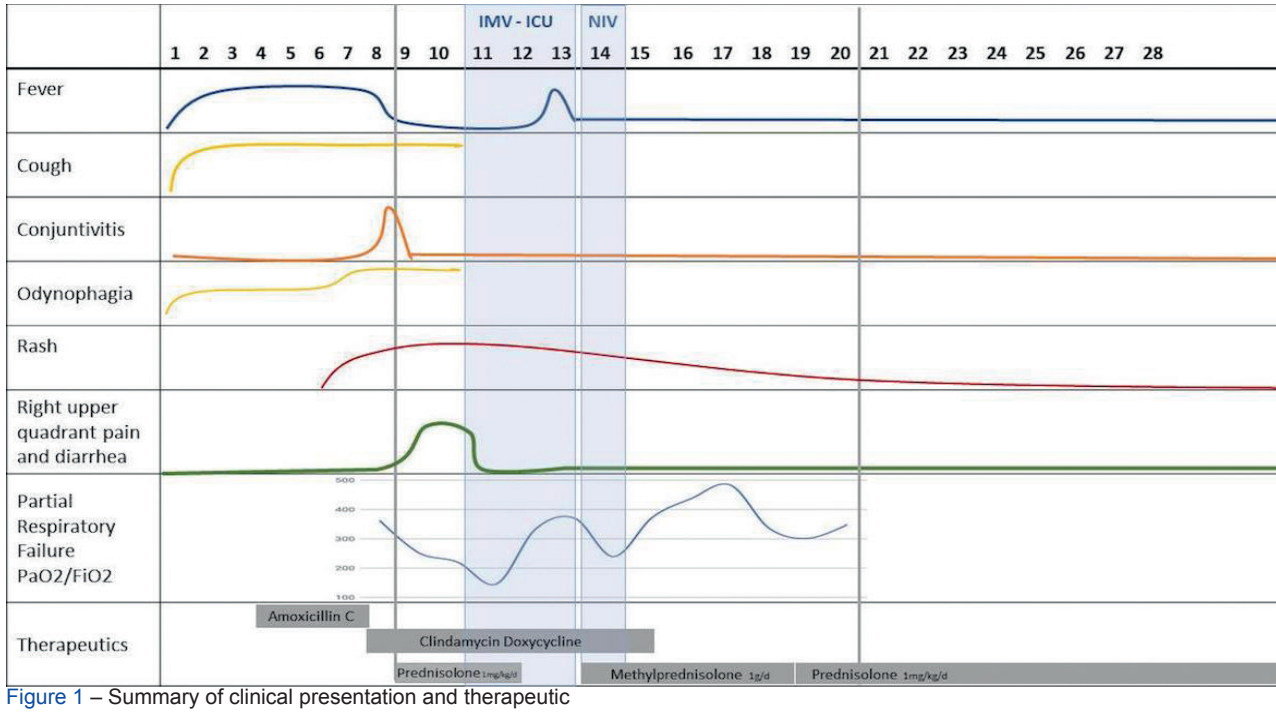

Figure 1 – Summary of clinical presentation and therapeutic

(Fig. 4).

Due to the worsening respiratory failure and rash progression, at that time with petechial areas, prednisolone was started assuming a possible DRESS syndrome (RegiSCAR score of 4) and she was admitted to the Intensive Care Unit for invasive mechanical ventilation. Bronchofibroscopy documented a lymphocytic alveolitis (45% lymphocytes; CD4/CD8 ratio of 0.1; 2% eosinophils). Extubation was possible on day three. Skin biopsy was suggestive of viral exanthem, leading to steroid discontinuation. However, two days later, there was a respiratory failure relapse with increasing eosinophilia requiring non-invasive ventilation. Improvement was observed after steroid resumption and she returned to the internal medicine ward. After assessing her vaccination bulletin, it became clear that she had not been previously vaccinated against measles. Measles serology was in favour of acute infection. Cultural, other serologies and autoimmune studies were all negative, as were the results for HHV 6. A definitive diagnosis of typical measles

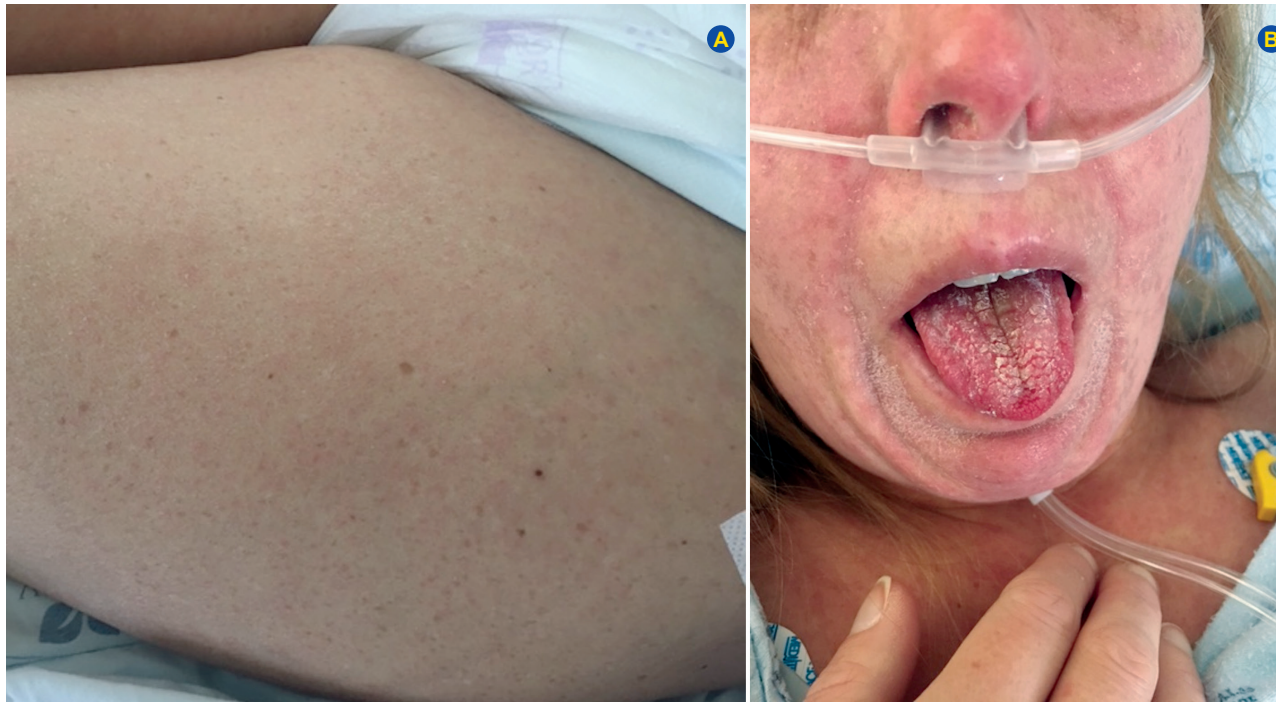

Figure 2 – Generalized maculopapular skin rash (A), including face and sparing perioral skin; edema, enanthema and flaking of the tongue (B)

Table 1 – Laboratory data and diagnostic workup

Laboratory data	Hospital admission	Hospital day 1	On discharge	Reference Range, Adults
Hemoglobin (g/dL)	15.5	13.9	12.2	12.0 - 15.3
White-cell count (x10^9/L)	9.270	7.700	**13.330**	4.0 - 11.0
Neutrophils	**92.6% / 8.58**	91.6% / 7.05	**79.1%/ 10.55**	1.9 - 7.5
Lymphocytes	**4.6% / 0.43**	**5.9% / 0.45**	12.5%/ 1.67	1.0 - 4.8
Eosinophils	0.2% / 0.02	0.7% / 0.05	0.1% / 0.01	0.0 - 0.5
Basophils	0.5% / 0.05	0.2% / 0.02	0.1% / 0.01	0.0 - 0.2
Monocytes	2.1% / 0.19	1.6% / 0.12	8.2% / 1.09	0.1 - 1.0
Platelet count (x10^9/L)	227	196	**675**	150 - 450
Aspartate aminotransferase (U/L)	**97**	**97**	14	0 - 32
Alanine aminotransferase(U/L)	**100**	**81**	26	0 - 33
Y-Glutamyltransferase (UI/L)	**150**	**141**	**110**	0 - 40
Total bilirubin (mg/dL)	**2.0**	**1.95**	0.49	< 1.2
Alkaline phosphatase (U/L)		**205**	**107**	35 -105
Amylase (U/L)		**55**	**496**	13 - 53
Lactate dehydrogenase (U/L)		**641**		100 - 250
Albumin (g/dL)		**2.8**		3.5 - 5.2
Sodium (mmol/L)	**132**	138	139	135 - 154
Potassium (mmol/L)		**3.1**	3.9	3.5 - 5.1
C-reactive protein (mg/dL)	**9.82**	**11.9**	0.240	< 0.5
Erythrocyte sedimentation rate (mm)		**33**		≤ 12

complicated by primary measles virus pneumonia and hepatitis was made. None of her relatives or friends had been infected. She was discharged with oral steroids and a complete clinical resolution was attained at follow-up.

DISCUSSION

Measles is a highly contagious disease caused by a RNA virus of the *Paramyxoviridae* family.[1] Pneumonia is the most common severe complication and accounts for most measles-associated morbidity and mortality, presenting in two main forms: primary measles virus pneumonia and secondary bacterial/viral pneumonia, which is associated with the immunosuppression caused by the virus.[1-3] Primary measles pneumonia, known as Hecht's giant cell pneumonia, is caused by measles virus inclusions and only occurs in 3% - 4% of infected individuals, mainly immunosuppressed.[2,4] It occurs early in the disease course and is associated with mixed reticular opacities, air-space consolidation and lymph node enlargement on CXR.[2] CT findings include ground-glass attenuation, air-space consolidation and small centrilobular nodules.[2] Secondary pneumonia is mainly caused by bacterial infection, but viral infection is also possible, most frequently by adenovirus.[1,3,5] It has a later onset and is characterized by a sudden exacerbation with symptoms and signs that usually begin 5 to 10 days after the rash, neutrophilic leukocytosis and lobar consolidation in the CXR.[6,7]

Despite its potential for eradication, measles and its complications are still observed worldwide, with periodic outbreaks in Europe.[8,9] Remarkably, our patient was

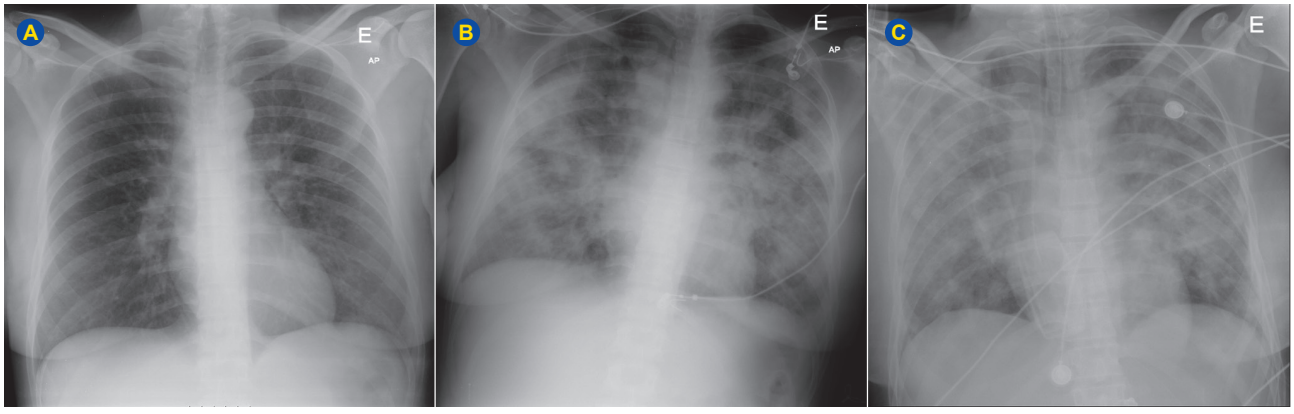

Figure 3 – Radiological progression of the interstitial pulmonary infiltrate (A) First day after admission; (B) and (C) day 3 after admission (with a difference of 9 hours)

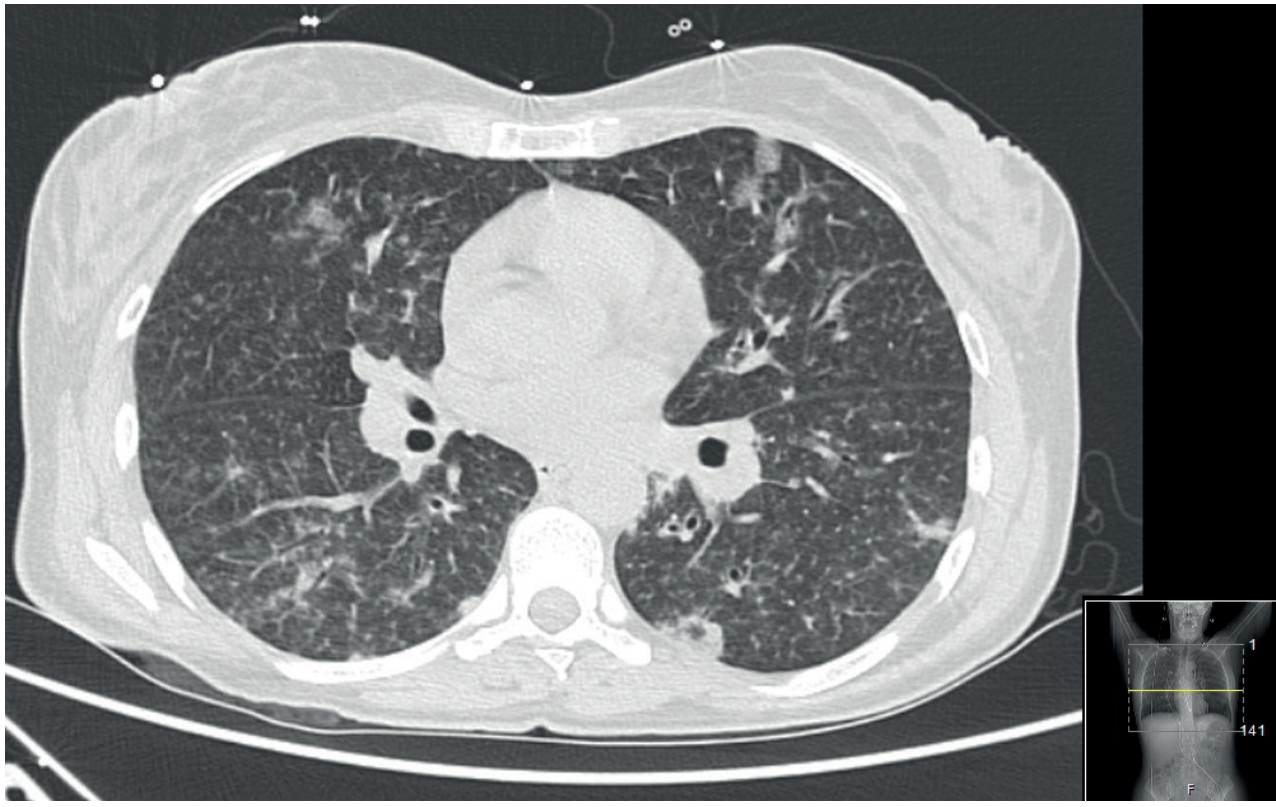

Figure 4 – Chest CT showing scattered and multifocal ground glass opacities and densities, septal thickening and micronodulation (day 1)

admitted right at the beginning of the last reported outbreak in Portugal (February - May 2017). There were 28 confirmed cases during the epidemic, of which 16 were unvaccinated and 19 were adults.[10]

In Portugal, no endemic transmission had been reported since 2005 and the rate of immune individuals is estimated at 93.4%.[10] The latter can be explained by the fact that measles vaccine was introduced in the Portuguese mandatory immunisation schedule for all children aged 12 - 15 months in 1974.[10] Therefore, the high levels of vaccination coverage and immunity in Portugal led us to initially pursue other diagnostic hypotheses, including DRESS syndrome, given the recent drug exposure, eosinophilia, lymphadenopathy, rash, and hepatic and pulmonary involvement, even prompting us to start corticosteroids. However, our patient was not vaccinated for measles, as she was born in 1972 and was not a candidate for mandatory vaccination at the time. In addition, there were some less common features in the typical measles setting which also mislead us at the beginning. Although the rare form of primary measles pneumonia is more prevalent among immunosuppressed patients, our patient was immunocompetent. Moreover, the absence of contagiousness occurs more frequently in atypical measles.[11] The fact that our patient did not infect any of her peers demonstrates the high levels of vaccination coverage in the Portuguese society. In this case, corticosteroids improved the final outcome since treatment with steroids has been reported as beneficial in severe measles.[12] Currently, the recommended schedule for adults born on or after 1970 without previous measles history is one single dose.[10]

To summarize, our unvaccinated immunocompetent patient presented typical symptoms of measles that evolved rapidly to a rare complication, highlighting the need to promptly diagnose measles in adults even in low incidence regions and to collect a thorough vaccination history.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

CONFLICTS OF INTEREST

All authors report no conflict of interest.

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