CASE REPORT

Rare extrapulmonary complications of *Mycoplasma pneumoniae* infection

Kiran Dhaliwal, Kevin Enright

St Georges NHS Trust, London, UK

Correspondence to

Dr Kiran Dhaliwal,
kirandhaliwal50@gmail.com

Accepted 22 January 2016

SUMMARY

Stevens-Johnsons syndrome (SJS) is a rare extra-pulmonary complication of *Mycoplasma pneumoniae* infection. We present the case of a 26-year-old man with fever, cough, extensive oral mucosal ulceration and a widespread truncal rash. He was diagnosed with *M. pneumoniae*-induced SJS. He responded well to antibiotics and steroids initially, but went on to develop pseudomembranous conjunctivitis requiring bilateral amniotic membrane grafting.

SJS is most commonly drug-induced, however, *M. pneumoniae* is the commonest infectious cause and should be considered in the differential diagnosis. It is also important to get specialist care involved early to minimise the long-term effects of any complications.

BACKGROUND

Mycoplasma pneumoniae is a common cause of atypical pneumonia in children and young adults, causing up to 30% of cases.¹ Extra pulmonary manifestations are rare, occurring in less than 10% of cases. They include haemolytic anaemia, arthritis, encephalitis and Stevens-Johnson syndrome (SJS).²

SJS is an acute disease, classically involving targetoid skin rash and the inflammation of two or more mucous membranes. The most commonly involved areas include the oral mucosa, genitals and conjunctivae.³ The most common cause of SJS is drug-induced. However, in children, the most common cause is infection.⁴

This case highlights the importance of identifying an underlying cause of SJS and getting specialist care involved early.

CASE PRESENTATION

A 26-year-old man presented with a 1-day history of extensive, painful oral ulceration. This was associated with fever and a 3-day history of cough productive of yellow sputum.

The patient had no previous medical history. He had returned from Vietnam 2 months previously, having had all relevant immunisations. There was history of neither unprotected sex nor sexual transmitted infections. The patient denied any drug use and had not been in contact with any other people with similar symptoms.

On examination, he had a low grade fever of 37.8°C. There was oral mucosal ulceration of the palate (figure 1), buccal mucosa and gingivae. Bilateral conjunctival injection with normal visual acuity (figure 2A, B) was noted. There was a widespread maculopapular rash over the trunk (figure 3)

Figure 1 Oral ulceration.

and inflammation of the glans penis, which later became ulcerated. The patient's chest was clear on auscultation.

INVESTIGATIONS

The patient underwent investigations to look for an underlying, likely infective, cause. Blood tests suggested an infective cause with raised inflammatory markers, with a C reactive protein (CRP) of 196.5 and white cell count of 9.0. All other blood tests,

Figure 2 (A and B) Conjunctival injection of right (A) and left (B) eyes.

CrossMark

To cite: Dhaliwal K, Enright K. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-214044

Figure 3 Anterior chest rash.

including full blood count, urea and electrolytes, and clotting screen, were normal. Urine dip was negative. A chest X-ray (CXR) showed consolidation in the left mid-zone (figure 4). This was repeated at 7 days and lung fields were clear (figure 5). PCR testing of a throat swab was positive for *M. pneumoniae* and serology titre was positive at 1:160.

DIFFERENTIAL DIAGNOSIS

The patient was tested for a range of infectious diseases including malaria, tuberculosis (TB) and legionella. Legionella antigen was negative. Acid-fast bacilli and TB culture were negative.

Malaria testing was negative.

TREATMENT

The patient was diagnosed with *M. pneumoniae* infection and admitted under the infectious diseases team. He was treated with oral doxycycline and a 5-day course of intravenous benzylpenicillin. His CRP dropped steadily.

He underwent regular review by both, the dermatology and ophthalmology departments.

After dermatology review, he was diagnosed with SJS and treated with a 3-day course of intravenous hydrocortisone and ongoing topical steroids and emollients.

After ophthalmology review, the patient was started on dexamethasone eye drops and chloramphenicol eye drops. However, despite treatment, his eye symptoms worsened and he developed extensive bilateral subconjunctival haemorrhage. He was

Figure 4 Chest X-ray at presentation.

Figure 5 Chest X-ray 7 days after starting treatment.

diagnosed with pseudomembranous conjunctivitis and underwent bilateral amniotic membrane grafting under local anaesthetic. There were no intra or postoperative complications.

OUTCOME AND FOLLOW-UP

The patient's symptoms improved gradually and he was discharged after 7 days, when he was able to consume adequate fluids and food. He was followed up by the infectious diseases, dermatology and ophthalmology departments.

At 1 month, the conjunctivitis, oral and genital ulcerations had fully resolved and the patient was discharged from outpatient follow-up. The patient remains in good health.

DISCUSSION

M. pneumoniae infection is the commonest cause of atypical pneumonia in children and young adults under 20 years old. It is uncommon in patients above this age, but should always be considered as a differential diagnosis in a patient presenting with chest and skin signs. The underlying pathology is not fully understood, but it is thought to involve the production of auto-antibodies.⁵ The diagnosis of the underlying cause of the atypical pneumonia is vital for the initiation of appropriate antibiotic treatment. Suspected *M. pneumoniae* infection needs laboratory testing to confirm diagnosis. It is generally accepted that PCR, used in conjunction with serological testing, is the most accurate and reliable method. Serological testing alone is unreliable; positive tests only occur 7 days after onset and patients with chronic infection may also have raised levels. PCR shows sensitivity as high as 77% and specificity as high as 97%, and is superior to serological testing during the early phase of infection.^{6 7}

The most common cause of SJS in adults is drug-induced, however, in children, it is most commonly caused by infections. There are noted differences between the course of the disease and the cause of the disease; ocular lesions are more common in *M. pneumoniae*-associated SJS and are reported in 69–81% of patients.² Traditional methods of treatment with lubricating drops can be insufficient in severe disease. If it is not treated promptly, it can have devastating long-term consequences, ultimately resulting in loss of vision. Amniotic membrane transplantation involves grafts being applied to the conjunctival surfaces of the affected eyes. It is indicated early, during the acute phase, and has been shown to improve outcome and prevent vision loss.⁸

M. pneumoniae-associated SJS is less likely to present with cutaneous manifestations, such as the typical targetoid skin lesions of SJS. Instead, cases may only present with mucositis.⁹ It is therefore important to have a high index of clinical suspicion. This is especially true in children, where cutaneous involvement is absent in 34% of cases. This is often termed 'atypical SJS', and there is a debate about whether this is actually SJS or whether it should be termed 'M. pneumoniae-associated mucositis'.^{9 10}

The management of SJS is mainly supportive with attention given to fluid balance and nutrition, as painful oral ulceration often leads to poor oral intake. Antibiotics are usually started to treat the underlying *M. pneumoniae* infection. The role of

steroid treatment in SJS has been highly debated. Some evidence suggests higher rates of complications and hospital stays.¹¹ However, there is also evidence suggesting that, when started early, steroid treatment shortens the course of the disease and patients have better outcomes.¹² Although there is no consensus, it is generally accepted for use in severe, recurrent oral disease. If complications develop, it is important to get specialist help and initiate treatment early to minimise long-term sequelae. This is particularly important with ocular complications. Patients should be followed up regularly once they have been discharged.

Contributors KD drafted the article and KE provided input on the content and was responsible for overall supervision. All the authors agreed to the final version.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Patient's perspective

The care I received was excellent throughout. I feel very fortunate to live near a facility with a full range of specialties on hand. They were very quick to respond to all potential warning signs in terms of eye conditions/rashes, etc. I can confirm that there was no drug use prior to admission.

Learning points

- ▶ As the clinical picture with *Mycoplasma pneumoniae* is varied, it should be considered in the differential diagnosis of Stevens-Johnson syndrome (SJS), given the appropriate clinical setting.
- ▶ SJS is usually a drug-induced condition; however, *M. pneumoniae* is the commonest infectious cause and should be considered as a differential diagnosis.
- ▶ Clinicians looking after patients with skin disease should be aware of the association between *M. pneumoniae* and its extra pulmonary manifestations.
- ▶ Any ocular signs or symptoms in patients diagnosed with *M. pneumoniae* need prompt review by the ophthalmology team. If neglected, they can result in permanent visual loss.
- ▶ A multidisciplinary approach is required to care for such patients given the wide variety of extra pulmonary manifestations and the subsequent complications and long-term sequelae that may develop.

REFERENCES

- 1 Hammerschlag MR. *Mycoplasma pneumoniae* infections. *Curr Opin Infect Dis* 2001;14:181–6.
- 2 Kunimi Y, Hirata Y, Aihara M. Statistical analysis of Stevens-Johnson syndrome caused by *Mycoplasma pneumoniae* infection in Japan. *Allergol Int* 2001; (60):525–32.
- 3 Yachoui R, Kolasinski SL, Feinstein DE. *Mycoplasma pneumoniae* with atypical Stevens-Johnson syndrome: a diagnostic challenge. *Case Rep Infect Dis* 2013;2013:457161.
- 4 Léauté-Labrèze C, Lamireau T, Chawki D, *et al.* Diagnosis, classification, and management of erythema multiforme and Stevens-Johnson syndrome. *Arch Dis Child* 2000;83:347–52.
- 5 Schalock PC, Dinulos JGH. *Mycoplasma pneumoniae*-induced cutaneous disease. *Int J Dermatol* 2009;48:673–80; quiz 680–1.
- 6 Chang HY, Chang LY, Shao PL, *et al.* Comparison of real-time polymerase chain reaction and serological tests for the confirmation of *Mycoplasma pneumoniae* infection in children with clinical diagnosis of atypical pneumonia. *J Microbiol Immunol Infect* 2014;47:137–44.
- 7 Beersma MF, Dirven K, van Dam AP, *et al.* Evaluation of 12 commercial tests and the complement fixation test for *Mycoplasma pneumoniae*-specific immunoglobulin G (IgG) and IgM antibodies, with PCR used as the "gold standard". *J Clin Microbiol* 2005;43:2277–85.
- 8 Chang YS, Huang FC, Tseng SH, *et al.* Erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis: acute ocular manifestations, causes, and management. *Cornea* 2007;26:123–9.
- 9 Canavan TN, Mathes EF, Frieden I, *et al.* *Mycoplasma pneumoniae*-induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: a systematic review. *J Am Acad Dermatol* 2015;72:239–45.
- 10 Wetter DA, Camilleri MJ. Clinical, etiologic, and histopathologic features of Stevens-Johnson syndrome during an 8-year period at Mayo Clinic. *Mayo Clin Proc* 2010;85:131–8.
- 11 Rasmussen JE. Erythema multiforme in children. Response to treatment with systemic steroids. *Br J Dermatol* 1976;95:181–6.
- 12 Wolverson SE. *Systemic corticosteroids. Comprehensive dermatologic drug therapy*. 2nd edn. Philadelphia, PA: Saunders Elsevier, 2007:127–61.

Copyright 2016 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