

CASE REPORT

Pneumocystis jiroveci pneumonitis complicating ruxolitinib therapySamantha C Lee,¹ John Feenstra,^{1,2} Paul R Georghiou³¹School of Medicine, University of Queensland, St Lucia, Queensland, Australia²Department of Thoracic Medicine, The Wesley Hospital, Auchenflower, Queensland, Australia³Department of Infectious Diseases, The Wesley Hospital, Auchenflower, Queensland, Australia**Correspondence to**

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SUMMARY

Ruxolitinib is a novel inhibitor of the Janus kinase (JAK) pathway that has become available for the treatment of myelofibrosis. There are increasing reports of opportunistic infections associated with ruxolitinib therapy. We present a case of *Pneumocystis jiroveci* pneumonitis complicating ruxolitinib therapy. Clinicians should consider the use of pneumocystis prophylaxis when using ruxolitinib.

BACKGROUND

Pneumocystis jiroveci is recognised to cause pneumonitis in patients with AIDS, those being treated for lymphoid haematological malignancy, and those receiving therapies which suppress cell-mediated immunity. We report a case of pneumocystosis in a patient with myelofibrosis receiving treatment with ruxolitinib, a novel inhibitor of the Janus kinase (JAK) pathway.

CASE PRESENTATION

In January 2009 a 69-year-old man was diagnosed with myelofibrosis after routine blood test revealed thrombocytosis and neutrophilia. An allele burden test later confirmed a positive JAK2 V617 activating mutation. He was placed on intermittent hydroxyurea to control thrombocytosis. By July 2012, the patient was experiencing constitutional symptoms and had palpable splenomegaly. In November 2012 he started ruxolitinib. His constitutional symptoms abated promptly and splenomegaly improved.

Now aged 73 years, the patient was recently hospitalised with 3 weeks of constitutional symptoms, cough and intermittent fevers. He continued ruxolitinib and had received no other immunosuppressive therapy. On admission, the lungs were clear to auscultation. A CT of the chest demonstrated widespread patchy ground glass and nodular changes. PCR testing of bronchoalveolar lavage fluid returned positive for *P jiroveci*, and histology of a transbronchial lung biopsy was consistent with an infective pneumonitis. The patient demonstrated steady clinical and radiological improvement after treatment with high-dose cotrimoxazole over 2 weeks. He remains on low-dose cotrimoxazole as pneumocystis prophylaxis.

DISCUSSION

Ruxolitinib has now been available for several years for the treatment of myelofibrosis. Phase III trials in myelofibrosis patients treated with this drug demonstrated amelioration of constitutional

symptoms and a reduction in splenomegaly.¹ However, those patients treated with ruxolitinib experienced a near threefold increase in the incidence of herpes zoster,¹ suggesting that the drug may promote clinically significant suppression of cell-mediated immunity in at least some patients. Indeed, a profound and prolonged reduction in T-regulatory cells may be observed in patients treated with ruxolitinib.² This might result from ruxolitinib's inhibition of both the JAK1 and JAK2 tyrosine kinases involved in the JAK/STAT signal transduction pathway, thereby arresting the release of proinflammatory cytokines and clonal myeloproliferation,¹ or the recently described effect of ruxolitinib on dendritic cells, whereby dendritic cell differentiation and function are reduced with resulting impairment of T-cell activation.³

There have been recent isolated reports of toxoplasma retinitis,⁴ cryptococcal pneumonia,⁵ disseminated tuberculosis,⁶ progressive multifocal leukoencephalopathy⁷ and sino-orbital mucormycosis⁸ in patients receiving ruxolitinib. Treatment with ruxolitinib has also been associated with the reactivation of latent infections with hepatitis B virus⁹ and herpes simplex virus.¹⁰ Our case of pneumocystosis expands the spectrum of opportunistic infections which might complicate ruxolitinib therapy. As the use of this agent increases, we might expect further reports of opportunistic infection. Physicians should consider the use of pneumocystis prophylaxis in patients receiving ruxolitinib, particularly if other immunosuppressive agents are also employed.

Learning points

- ▶ Ruxolitinib is a novel therapy used to treat myelofibrosis.
- ▶ Treatment with ruxolitinib is associated with opportunistic infections including *Pneumocystis jiroveci* pneumonitis.
- ▶ Clinicians should consider using pneumocystis prophylaxis when treating patients with ruxolitinib.

Contributors SCL, JF and PRG contributed equally to the research, creation and writing associated with this case report.

Competing interests None.

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