Lymph Node Tuberculosis Reactivation During Ruxolitinib Therapy for JAK2 Exon 12-Positive Primary Myelofibrosis: Case Report

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Introduction

Primary myelofibrosis (PMF) is a Philadelphia-negative myeloproliferative neoplasm characterized by bone marrow fibrosis, ineffective erythropoiesis, splenomegaly, and constitutive activation of the JAK-STAT pathway. Most cases are associated with JAK2 V617F, CALR, or MPL mutations, while JAK2 exon 12 mutations are exceptionally rare in PMF (<1%) and are more commonly observed in polycythemia vera.

Ruxolitinib, a selective JAK1/JAK2 inhibitor, significantly improves splenomegaly, constitutional symptoms, and survival in PMF patients. However, its immunosuppressive effect impairs cellular immunity and increases the risk of opportunistic infections, particularly tuberculosis (TB), through disruption of IFN-γ-mediated macrophage activation and granuloma maintenance.

Several cases of TB reactivation during Ruxolitinib therapy have been reported, mainly in patients with JAK2 V617F-mutated or uncharacterized PMF from TB-endemic regions. Nevertheless, no previous case has been described in a patient with JAK2 exon 12-positive PMF.

Morocco remains a moderate TB-burden country, making TB screening before initiation of JAK inhibitor therapy particularly important. Current international recommendations advise systematic screening using tuberculin skin testing or interferon-gamma release assays combined with chest imaging prior to biologic therapy.

This report presents the first described case of lymph node tuberculosis occurring in a patient with JAK2 exon 12-positive PMF treated with Ruxolitinib, highlighting the importance of systematic TB screening and vigilance regardless of the underlying JAK2 mutation subtype.

Objectif

To report the first documented case of tuberculosis reactivation in a patient with primary myelofibrosis harboring a JAK2 exon 12 mutation treated with Ruxolitinib, and to highlight the need for increased infectious vigilance throughout this treatment, regardless of the JAK2 molecular subtype.

Case presentation

A 41-year-old Moroccan male with no significant past medical history — no prior thromboembolic events, autoimmune disorders, chronic infections, known immunodeficiency, or tuberculosis exposure. Family history was non-contributory. He was a non-smoker with no alcohol or illicit drug use. He was admitted in September 2022 for acute abdominal pain of sudden onset, without gastrointestinal bleeding or bowel transit disorders.

Physical examination revealed a well-appearing individual (ECOG PS 0) with normal vital signs. Abdominal examination demonstrated massive splenomegaly, with the splenic tip palpable approximately 10 cm below the left costal margin, extending to the umbilicus — non-tender, smooth surface, no palpable nodularity. No hepatomegaly, ascites, or collateral venous circulation. Constitutional symptoms included night sweats, without fever, weight loss, or easy bruising.

Parameter	Value
Hemoglobin	14.2 g/dL
MCV	88 fL
WBC count	7,000/mm³
Platelet count	271,000/mm³
Peripheral smear	Normal (no dacrocytes, no blasts)
LDH	400 U/L
Renal & hepatic function	Within normal limits
HBsAg / anti-HCV / HIV	All negative
BCR-ABL1 transcript	Undetectable
JAK2 V617F	Negative
JAK2 exon 12 mutation	Positive (heterozygous)
CALR exon 9 / MPL W515	Both negative
Karyotype	46,XY — normal diploid, 20 metaphases

Initial management consisted of anticoagulation with heparin, subsequently switched to a vitamin K antagonist, for the management of thrombosis. Hydroxyurea 500 mg twice daily was initiated as cytoreductive therapy. However, after two months, the patient experienced persistent constitutional symptoms and progressive splenomegaly reaching 12 cm below the costal margin, leading to hydroxyurea discontinuation.

Ruxolitinib 15 mg twice daily was then introduced, with a rapid and sustained response: splenic size decreased from 12 cm to 7 cm below the costal margin — representing a reduction exceeding 35% — and the MPN Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) improved by approximately 40% from baseline. The treatment was very well tolerated, with no immediate adverse effects and stable blood counts throughout.

At the six-month treatment evaluation, the patient developed new painful peripheral lymphadenopathies involving the right supraclavicular region (1.5 cm), the left axillary region (3 cm, painful), and the left lateral cervical region (1 cm, painful). Supraclavicular lymph node biopsy revealed caseo-follicular tuberculous adenitis. GeneXpert testing on the biopsy specimen was negative. Chest CT demonstrated blunting of the left costophrenic angle and a left basal atelectatic band, consistent with pleural involvement.

Given this diagnosis of lymph node tuberculosis occurring in the context of ruxolitinib-induced immunosuppression, ruxolitinib was immediately discontinued and standard antituberculous therapy (ATT) was initiated. The regimen comprised an intensive two-month phase combining rifampicin 600 mg/day, isoniazid 300 mg/day, pyrazinamide 1,500–2,500 mg/day, and ethambutol 1,200 mg/day, followed by a four-month continuation phase with rifampicin 600 mg/day and isoniazid 300 mg/day. Pyridoxine supplementation was provided throughout to prevent isoniazid-induced peripheral neuropathy. Complete resolution of tuberculosis was achieved after six months, with excellent adherence and good tolerability of the regimen.

Ruxolitinib was reintroduced six months after completion of ATT, at the same dose of 15 mg twice daily. At the time of writing, the patient has been maintained on ruxolitinib for 18 months with an excellent myeloproliferative response and no recurrence of tuberculosis.

Disscusion

To contextualize our case within the broader experience of Ruxolitinib-associated TB, we conducted a systematic review of published case reports and case series. A PubMed/MEDLINE search using terms ("Ruxolitinib" OR "JAK inhibitor") AND ("tuberculosis" OR "mycobacterium") identified 12 individual cases reported between 2013 and 2023. Our case represents the 13th reported case. Analysis of the 13 cases (12 literature + our case) reveals:

Age/Sex	JAK2 Mutation	TB Manifestation	Ruxolitinib Mgmt	Anti-TB Treatment	Outcome	Ref.
35 / F	JAK2 V617F	Tuberculous lymphadenopathy	Discontinued	Standard HRZE	Recovered	[1]
78 / F	JAK2 V617F	Disseminated tuberculosis	Discontinued	Rifampicin-based	Recovered	[2]
72 / M	JAK2 V617F	Disseminated tuberculosis	Continued	Standard anti-TB	deces	[3]
68 / M	JAK2 V617F	Pulmonary tuberculosis	Continued	Standard anti-TB	deces	[3]
62 / M	JAK2 V617F	Disseminated tuberculosis	Discontinued	Standard anti-TB	Recovered	[4]
65 / F	JAK2 V617F	Extrapulmonary tuberculosis	Discontinued	Standard anti-TB	Recovered	[5]
82 / M	JAK2 V617F	Pulmonary TB reactivation	Discontinued	Standard anti-TB	Recovered	[6]
78 / M	JAK2 V617F	Cervical tuberculous lymphadenitis	Discontinued	Standard anti-TB	Recovered	[7]
N/A / F	JAK2 V617F	Tuberculous lymphadenitis	Continued	Standard anti-TB	deces	[8]
N/A / M	JAK2 V617F	Tuberculous lymphadenitis	Discontinued	Standard anti-TB	Recovered	[8]
N/A / M	JAK2 V617F	Disseminated tuberculosis	Discontinued	Standard anti-TB	Recovered	[9]
69 / M	JAK2 V617F	Pulmonary TB reactivation	Discontinued	Standard anti-TB	Recovered	[10]
41 / M	**JAK2 Exon 12**	**Lymph node TB (cervical, axillary, supraclavicular)**	**Discontinued**	**Standard HRZE + continuation**	**Recovered**	**Our case**

Conclusion

This clinical case illustrates the first reported observation of lymph node tuberculosis occurring during Ruxolitinib therapy in a patient with primary myelofibrosis harboring a JAK2 exon 12 mutation. It reinforces the growing evidence linking JAK kinase inhibition to the risk of tuberculosis reactivation, regardless of the molecular subtype or clinical phenotype of the myeloproliferative neoplasm. The favorable outcome observed, achieved through early discontinuation of Ruxolitinib and prompt initiation of appropriate anti-tuberculous therapy, highlights the importance of systematic screening for latent tuberculosis prior to the initiation of these therapies, as well as rigorous clinical monitoring throughout treatment.

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