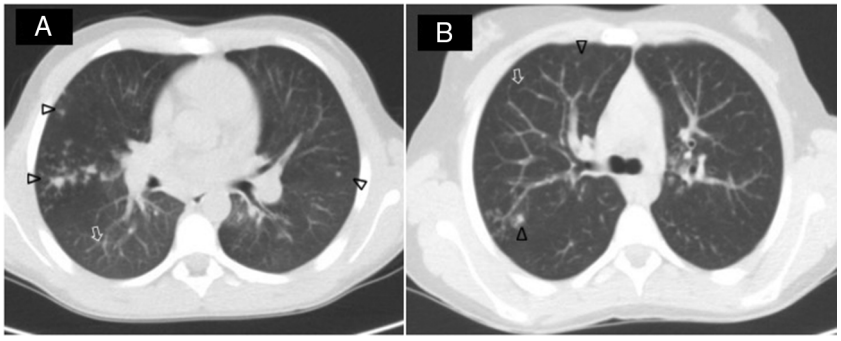

Fig. 1. Lung CTs of 2 patients with a diagnosis of *M. lentiflavum* infection. Both patients revealed a clear tree-in-bud image (arrows) with acinar nodules (Δ), mainly in the right upper lobes.

References

1. Lopes-Pacheco M. CFTR modulators: shedding light on precision medicine for cystic fibrosis. Front Pharmacol. 2016;7:275–95.
2. Skolnik K, Kirkpatrick G, Quon BS. Nontuberculous mycobacteria in cystic fibrosis. Curr Treat Options Infect Dis. 2016;8:259–74.
3. Martiniano SL, Davidson RM, Nick JA. Nontuberculous mycobacteria in cystic fibrosis: Updates and the path forward. Pediatr Pulmonol. 2017;52(S48):S29–36.
4. Quintana-Gallego E, Delgado Pecellín I, Calero Acuña C. Infección bronquial crónica en pacientes con fibrosis quística. Monogr Arch Bronconeumol. 2014;1:86–91.
5. Floto RA, Olivier KN, Saiman L, Daley CL, Herrmann JL, Nick JA, et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis. Thorax. 2016;Suppl. 1:i1–22.
6. Tortoli E, Mattei R, Russo C, Scarparo C. *Mycobacterium lentiflavum*, an emerging pathogen? J Infect. 2006;52:185–7.
7. Jeong BH, Song JU, Kim W, Han SG, Ko Y, Song J, et al. Nontuberculous mycobacterial lung disease caused by *Mycobacterium lentiflavum* in a patient with bronchiectasis. Tuberc Respir Dis. 2013;74:187–90.
8. Shin S, Yoon JH, Song SH, Kim EC. Isolation of *Mycobacterium lentiflavum* from a patient with a lung destroyed by tuberculosis. Korean J Lab Med. 2007;27:124–7.
9. Piersimoni C, Goteri G, Nista D, Mariottini A, Mazzarelli G, Bornigia S. *Mycobacterium lentiflavum* as an emerging causative agent of cervical lymphadenitis. J Clin Microbiol. 2004;42:3894–7.
10. Galarraga MC, Torreblanca A, Jiménez MS. Isolation of *Mycobacterium lentiflavum* in a case of suspected lung cancer. Enferm Infecc Microbiol Clin. 2002;20:92–7.
11. Molteni C, Gazzola L, Cesari M, Lombardi A, Salerno F, Tortoli E, et al. *Mycobacterium lentiflavum* infection in immunocompetent patient. Emerg Infect Dis. 2005;11:119–22.
12. Satana D, Erkose-Genc G, Tamay Z, Uzun M, Guler N, Erturan Z. Prevalence and drug resistance of mycobacteria in Turkish cystic fibrosis patients. Ann Clin Microbiol Antimicrob. 2014;13:28–34.
13. Phelippeau M, Dubus JC, Reynaud-Gaubert M, Gomez C, Stremler le Bel N, Bedotto M, et al. Prevalence of *Mycobacterium lentiflavum* in cystic fibrosis patients, France. BMC Pulm Med. 2015;15:131–6.

María Moreno Ortega,[a,b,*] Esther Quintana Gallego,[b,c] Laura Carrasco Hernández,[b,c] Esther Pérez Borrego,[a] Isabel Delgado Pecellín[b,c]

[a] *Unidad de Pediatría y áreas específicas, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[b] *Unidad de Fibrosis Quística, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[c] *Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Spain*

* Corresponding author.
E-mail address: bebarrabaja@gmail.com (M. Moreno Ortega).

1579-2129/

Radiological Improvement of Bronchiolitis Obliterans Following Hematopoietic Stem Cell Transplantation in a Patient Treated With Ruxolitinib☆

Mejoría de la bronquiolitis constrictiva tras trasplante de progenitores hematopoyéticos: demostración radiológica en paciente tratado con ruxolitinib

To the Editor,

Bronchiolitis obliterans (BO) after hematopoietic stem cell transplantation (HSCT) is a serious, potentially fatal complication, which appears in association with chronic graft-vs-host disease (GVHD).[1] Lung function testing, and to a lesser but growing extent, computed tomography (CT) are the most important diagnostic tests in the detection of post-HSCT BO.[2] Systemic corticosteroids remain the cornerstone of treatment, but one of the most important new therapies is ruxolitinib, a drug that is showing encouraging results in patients with GVHD.[3]

We report the case of a 39-year-old man with a history of Stage IV diffuse large B-cell lymphoma treated with several lines of chemotherapy who, after achieving complete remission, underwent HSCT from a matched donor in April 2015. Ten months after the procedure, the patient developed GVHD with cutaneous, gastrointestinal and pulmonary manifestations that did not respond favorably to treatment with corticosteroids and extracorporeal photopheresis. Lung function tests prior to developing GVHD were normal, but subsequently showed an obstructive pattern of moderate intensity, with forced expiratory volume in 1 second (FEV1) 59% predicted value, forced vital capacity (FVC) 78%, and FEV1/FVC 68%, along with a 71% decrease in CO diffusion capacity from pre-GVHD values. Dynamic computed tomography (dCT) of the chest in inspiration and expiration showed extensive areas of air trapping in both lungs (Fig. 1A and B), while infectious complications were ruled out. Bronchoalveolar lavage revealed no opportunistic infections. Given these findings, a diagnosis of BO refractory to corticosteroids and extracorporeal photopheresis associated with post-HSCT GVHD was given. The patient received ruxolitinib and

☆ Please cite this article as: Gorospe Sarasúa L, Chinea-Rodríguez A, Almonacid-Sánchez C, Almeida-Aróstegui NA. Mejoría de la bronquiolitis constrictiva tras trasplante de progenitores hematopoyéticos: demostración radiológica en paciente tratado con ruxolitinib. Arch Bronconeumol. 2018;54:640–642.

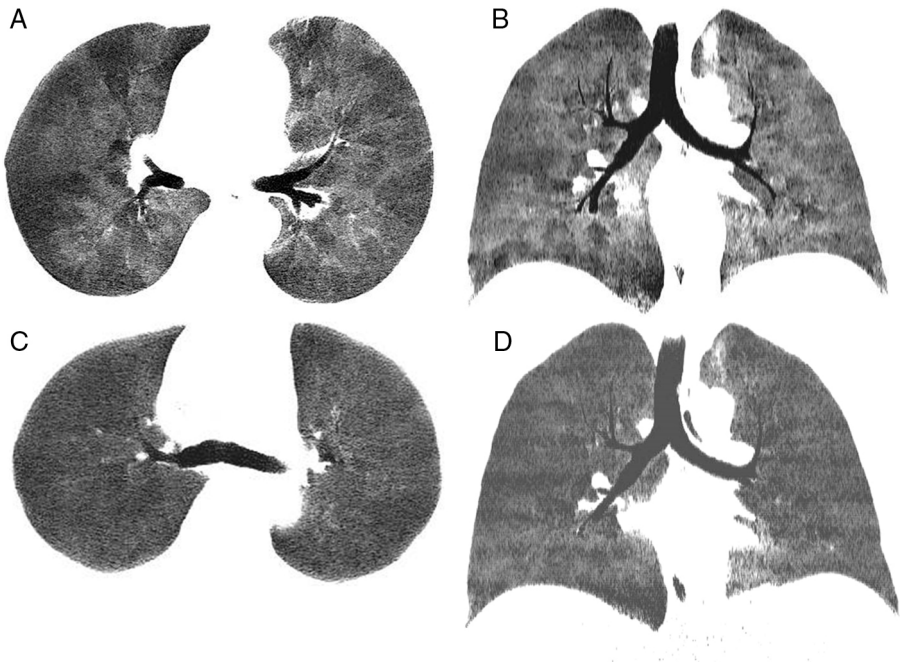

Fig. 1. Chest minIP (Minimum Intensity Projection) CT axial (A) and coronal (B) images in expiration showing a marked mosaic attenuation pattern in the pulmonary parenchyma, with geographical regions of low density alternating with areas of greater attenuation. The areas of lower density correspond to air trapping. Chest minIP (Minimum Intensity Projection) CT axial (C) and coronal (D) images in expiration showing less heterogeneity and greater uniformity of the attenuation of the pulmonary parenchyma with compared to images (A) and (B).

achieved progressive improvement of the GVHD manifestations, including BO. Four months after starting ruxolitinib, lung function tests showed significant improvement, with an increase in FEV1 (72%), FVC (80%), and FEV1/FVC (71%), although mild air trapping persisted on plethysmography, with a residual volume of 128% and residual volume/total lung capacity ratio of 127%. Reduced signs of air trapping in the expiratory phase were also observed on dCT 3 months after starting ruxolitinib (Fig. 1C and D).

BO is the most common non-infectious pulmonary complication of HSCT (and among the most serious), and one of the most important risk factors is the presence of chronic GVHD. Clinical presentation of BO is often insidious, and symptoms are non-specific (cough, dyspnea), although 20% of patients can be asymptomatic.[4] The National Institutes of Health of the United States specify the following criteria for the diagnosis of post-HSCT BO: (1) demonstrated airflow obstruction (FEV1/FVC <0.7 and FEV1 <80% of predicted value); (2) air trapping on CT, residual volume >120% predicted or histological confirmation of BO; and (3) absence of respiratory tract infection.[5] The most common CT findings are: air trapping, thickening of the bronchial walls, mosaic attenuation pattern, and bronchial dilation.[6] The long-term prognosis of BO is generally poor (5-year survival ranges between 13% and 56%),[4] and the aim of treatment is to prevent progression of airflow obstruction. Treatment with systemic corticosteroids continues to be the mainstay of BO treatment, although other therapeutic options have been used in combination with extracorporeal photopheresis, corticosteroids and/or inhaled bronchodilators, montelukast, ofatumumab, and bortezomib.[7] Ruxolitinib is a new targeted therapy that selectively inhibits Janus kinases which interfere in the synthesis of various cytokines and growth factors required for hematopoiesis and immune function; its efficacy in the treatment of corticosteroid-resistant GVHD has recently been demonstrated.[8,9] In our case, the clinical benefit of ruxolitinib was noted in the first weeks after administration, with corresponding clinical, spirometric, and radiological improvements. Very few descriptions are available in the literature of cases of post-HSCT BO responding to treatment with ruxolitinib, and we believe that the case presented illustrates the benefit of this promising drug in patients with post-HSCT BO, while at the same time reminding us of the importance of dCT studies to correlate radiological findings with spirometry in these patients.[10]

References

1. Soubani AO, Uberti JP. Bronchiolitis obliterans following haematopoietic stem cell transplantation. Eur Respir J. 2007;29:1007–19.
2. Aguilar PR, Michelson AP, Isakow W. Obliterative bronchiolitis. Transplantation. 2016;100:272–83.
3. Jagasia M, Zeiser R, Arbushites M, Delaite P, Gadbaw B, Bubnoff NV. Ruxolitinib for the treatment of patients with steroid-refractory GVHD: an introduction to the REACH trials. Immunotherapy. 2018, http://dx.doi.org/10.2217/imt-2017-0156.
4. Grønningsæter IS, Tsykunova G, Lilleeng K, Ahmed AB, Bruserud Ø, Reikvam H. Bronchiolitis obliterans syndrome in adults after allogeneic stem cell transplantation – pathophysiology, diagnostics and treatment. Expert Rev Clin Immunol. 2017;13:553–69.
5. Gazourian L, Rogers AJ, Ibanga R, Weinhouse GL, Pinto-Plata V, Ritz J, et al. Factors associated with bronchiolitis obliterans syndrome and chronic graft-versus-host disease after allogeneic hematopoietic cell transplantation. Am J Hematol. 2014;89:404–9.
6. Song I, Yi CA, Han J, Kim DH, Lee KS, Kim TS, et al. CT findings of late-onset noninfectious pulmonary complications in patients with pathologically proven graft-versus-host disease after allogeneic stem cell transplant. AJR Am J Roentgenol. 2012;199:581–7.
7. Williams KM. How I treat bronchiolitis obliterans syndrome after hematopoietic stem cell transplantation. Blood. 2017;129:448–55.
8. Khoury HJ, Langston AA, Kota VK, Wilkinson JA, Pusic I, Jillella A, et al. Ruxolitinib: a steroid sparing agent in chronic graft-versus-host disease. Bone Marrow Transplant. 2018, http://dx.doi.org/10.1038/s41409-017-0081-5.
9. Maldonado MS, Ramírez Villanueva P, Bertín Cortes-Monroy P, Jara Arias V, Soto Donoso K, Uribe Gonzalez P, et al. Compassionate use of ruxolitinib in acute and chronic graft versus host disease refractory both to corticosteroids and extracorporeal photopheresis. Exp Hematol Oncol. 2017;6:32.
10. Miller WT Jr, Chatzkel J, Hewitt MG. Expiratory air trapping on thoracic computed tomography. A diagnostic subclassification. Ann Am Thorac Soc. 2014;11:874–81.

Luis Gorospe Sarasúa,[a,*] Anabelle Chinea-Rodríguez,[b]
Carlos Almonacid-Sánchez,[c] Nicolás Alejandro Almeida-Aróstegui[a]

[a] *Servicio de Radiodiagnóstico, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[b] *Servicio de Hematología, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[c] *Servicio de Neumología, Hospital Universitario Ramón y Cajal, Madrid, Spain*

* Corresponding author.
E-mail address: luisgorospe@yahoo.com (L. Gorospe Sarasúa).

1579-2129/