Multifocal fibrosclerosis in a patient with HIV infection treated with rituximab

Sirs,

We describe a clinical case of multifocal fibrosclerosis (MFS) (1) in a patient with a human immunodeficiency virus (HIV) infection diagnosis, treated with steroids and rituximab (RTX).

In July 2020, a 63-year-old woman was admitted to our Rheumatology Unit for a suspicious IgG4-related disease (RD) (2).

In 2015 she was diagnosed with HIV, started treatment with dolutegavir, abacavir and lamivudine, achieving sustained suppression of HIV replication.

In November 2015, an ultrasound scan carried out because of recurrent abdominal pain, showed hyperechoic nodular tissue in the pancreas body. The abdominal magnetic resonance imaging (MRI) scan showed: heteroplastic-infiltrative tissue in the pancreas head-body extending to the retroperitoneum with the involvement of the superior mesenteric vein tract and stenosis of the Wirsung duct and chledochus. An explorative laparoscopy and a pancreas biopsy were carried out: there was fibrosis and lymphoplasmacytic peri-ductal infiltrate without evidence of neoplastic cells. Subsequently, the patient developed obstructive jaundice and hyperglycaemia, and as a result of this, she was admitted to a gastrointestinal diseases centre. The suspicion of IgG4-RD was raised, but the serum IgG4 were in the normal range. A working diagnosis of MFS was made and daily oral prednisone, 40 mg/die was started and slowly tapered to 5 mg/die.

After two weeks of prednisone therapy, there was a complete resolution of the abdominal symptoms and jaundice. MRI follow-up in May 2016 showed normal pancreas size, normal caliber of the superior mesenteric vein and choledochus. Some minimal sub-stenosis of the Wirsung's duct was observed. At the end of 2016 the patient was lost at the follow-up. Four years later, without prednisone therapy, she was admitted to the emergency room due to a hyperglycaemic crisis and, considering her past medical history, was transferred to our Rheumatology Unit.

On admission, fever, signs and symptoms of active infection diseases were absent. There was: hypereosinophilia (900/uL), an increase in erythrocyte sedimentation rate (ESR) (98 mm/h), C-reactive protein (CRP) (7.2 mg/dl), gamma-glutamine transferase (γ-GT) (64 U/l, n.r. 5-36) and alkaline phosphatase (ALP) (209 U/l, n.r. 35-107). Total bilirubin, liver enzymes, total IgE and IgG subclasses were normal. Anti-nuclear-antibodies with fine speckled pattern were positive at low dilution (1:80) in the absence of anti-ENA and ANCA. Revaluation of the pancreatic tissue, biopsied in 2015, showed discrete IgG$^+$ plasma cells infiltrate, with only 2 IgG4$^+$ plasma cells/high power field. The abdominal MRI showed a reduction in pancreas size, minimal ectasia of the Wirsung duct and a new infiltrative-heteroplastic tissue around the thoracoabdominal-aortic-tract. The MFS diagnosis was confirmed. HIV 1 RNA was not detectable and T-CD4$^+$ and CD20$^+$ cell count was in the normal range. Therefore, low dose steroid therapy and RTX (August 2020), 1000 mg iv at time 0 and after 14 days, were introduced.

After one month from the second RTX dose, we observed a normal eosinophil count and an improvement in ESR (25 mm/h), CRP (0.9 mg/dl) and ALP (141 U/l).

After six months, in February 2021, the values of ESR, CRP, ALP, γ-GT were normal and HIV 1 RNA was still undetectable with a normal T-CD4$^+$ cell count. A new MRI scan showed a significant improvement of the peri-aortic fibrosis, both in the thoracic and abdominal tract, and the normalisation of the Wirsung and biliary ducts (Fig. 1).

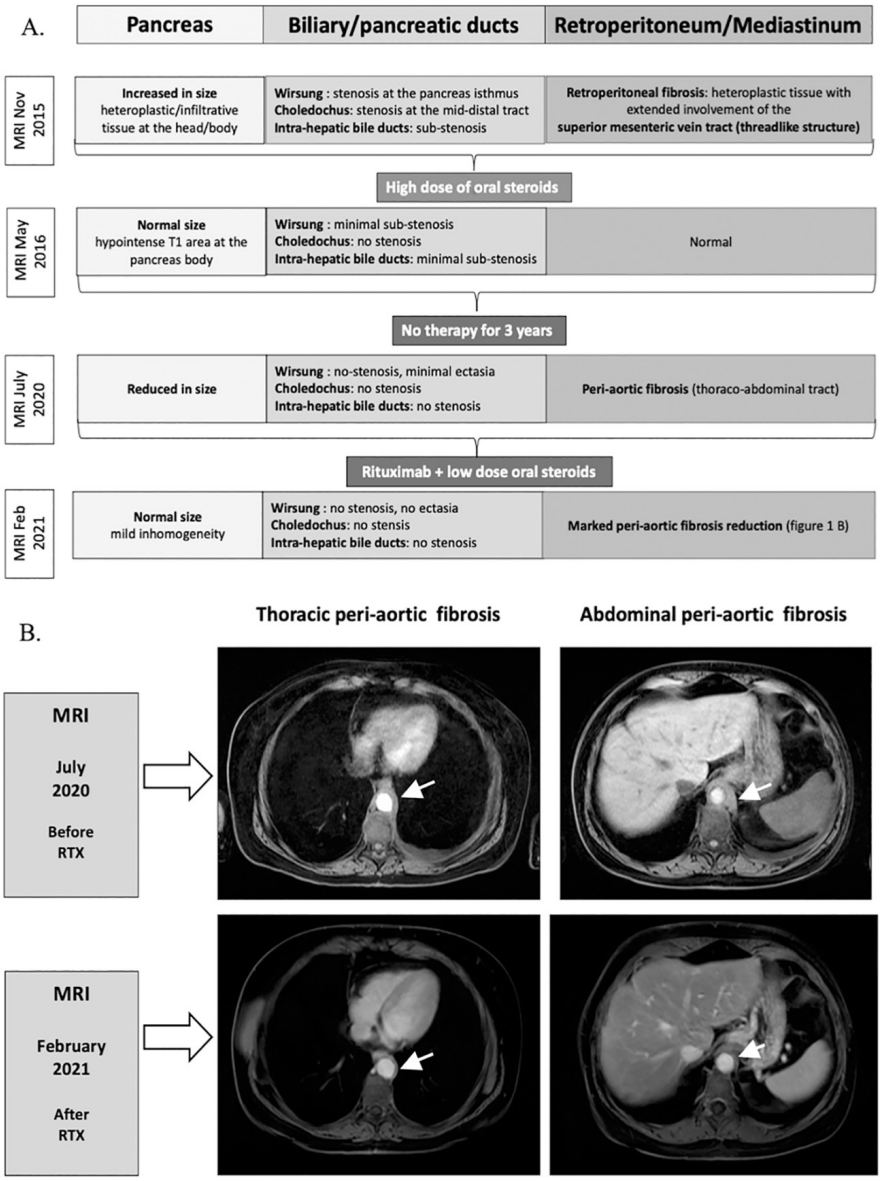

Fig. 1. A: Treatments and their effect on the involved tissues during the follow-up period.
B: The peri-aortic fibrosis before and six months after rituximab (RTX) and steroids, on MRI.

We found only two described IgG4-RD cases in patients with HIV infection (3,4), and a case of HIV infection that mimicked an IgG4-RD (5).

Interestingly, RTX showed efficacy for IgG4-RD (6) and safety during HIV infection (7).

To the best of our knowledge, this is the first clinical case of MFS in a patient with HIV infection, in which RTX therapy showed a good clinical response and a safety profile.

S. Scriffignano, *MD*
D. Mauro, *MD, PhD*
M. Raimondi, *MD*
F. Ciccia, *MD, PhD*
R. Tirri, *MD*

Dipartimento di Medicina di Precisione, Reumatologia, Università degli Studi della Campania L. Vanvitelli, Napoli, Italy.

Please address correspondence to:
Rosella Tirri,
Dipartimento di Medicina di Precisione, Section of Reumatology,
Università degli Studi della Campania L. Vanvitelli,
via Pansini 5,
80131 Napoli, Italy.
E-mail: rosella.tirri@unicampania.it

Competing interests: none declared.

References

1. COMINGS DE, SKUBI KB, VAN EYES J, MOTULSKY AG: Familial multifocal fibrosclerosis. Findings suggesting that retroperitoneal fibrosis, mediastinal fibrosis, sclerosing cholangitis, Riedel's thyroiditis, and pseudotumor of the orbit may be different manifestations of a single disease. *Ann Intern Med* 1967; 66: 884-92.
2. UMEHARA H, OKAZAKI K, MASAKI Y *et al*.: Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. *Mod Rheumatol* 2012; 22: 21-30.
3. BUTEL-SIMOES G, WOOLLEY I, MCMAHON J, YEO A: IgG4-related disease masquerading as a fungating groin lesion in a patient with HIV and incomplete immune reconstitution. *AIDS* 2021; 35: 706-7.
4. RON R, RUZ-CARACUEL I, GARCÍA E, MONTES-RAMÍREZ ML: IgG4-related disease in a patient with HIV infection. *BMJ Case Rep* 2019; 12: e226809.
5. YU HT, LEE CH, HUANG SC, YU SF: Unsuspected human immunodeficiency virus infection presenting as immunoglobulin G4-related lymphadenopathy: a case report. Int J STD *AIDS* 2018; 29: 92-5.
6. ARRUTHERS MN, TOPAZIAN MD, KHOSROSHAHI A *et al*.: Rituximab for IgG4-related disease: a prospective, open-label trial. *Ann Rheum Dis* 2015; 74: 1171-7.
7. SERRA-PEINADO C, GRAU-EXPÓSITO J, LUQUE-BALLESTEROS L *et al*.: Expression of CD20 after viral reactivation renders HIV-reservoir cells susceptible to rituximab. *Nat Commun* 2019; 10: 3705.