Successful treatment of a rare case of coronary vasculitis associated with diffuse large B-cell lymphoma in a patient affected by Sjögren's disease

Sirs,

Sjögren's disease (SjD) patients are burdened by higher overall cardiovascular (CV) risk, due to both disease-related and traditional factors (1-2). Clinical CV manifestations range from subclinical affections, to rare but severe entities as secondary vasculitis, including cryoglobulinaemic vasculitis, or aggressive lymphoma (3-4). Up to date, no cases of isolated coronary vasculitis in patients affected by SjD complicated with diffuse large B-cell lymphoma (DLBCL) are found in the literature.

Herein, we describe the case of a 57-year-old male patient, diagnosed with SjD in 2013, on the basis of subjective and objective sicca syndrome, Raynaud's phenomenon, purpura, arthralgia; positive minor salivary gland biopsy and major salivary gland ultrasonography; ANA and RF positivity; hypocomplementaemia. Anti-SSA/Ro, anti-SSB/La, serum cryoglobulins, anti-CCP negativity was also reported.

Anamnestic records showed only a mild isolated Bence Jones proteinuria in haematologic follow-up, and familiarity for acute myocardial infarction at early age. From 2013 to 2019 he was treated for arthro-cutaneous manifestations with hydroxy-

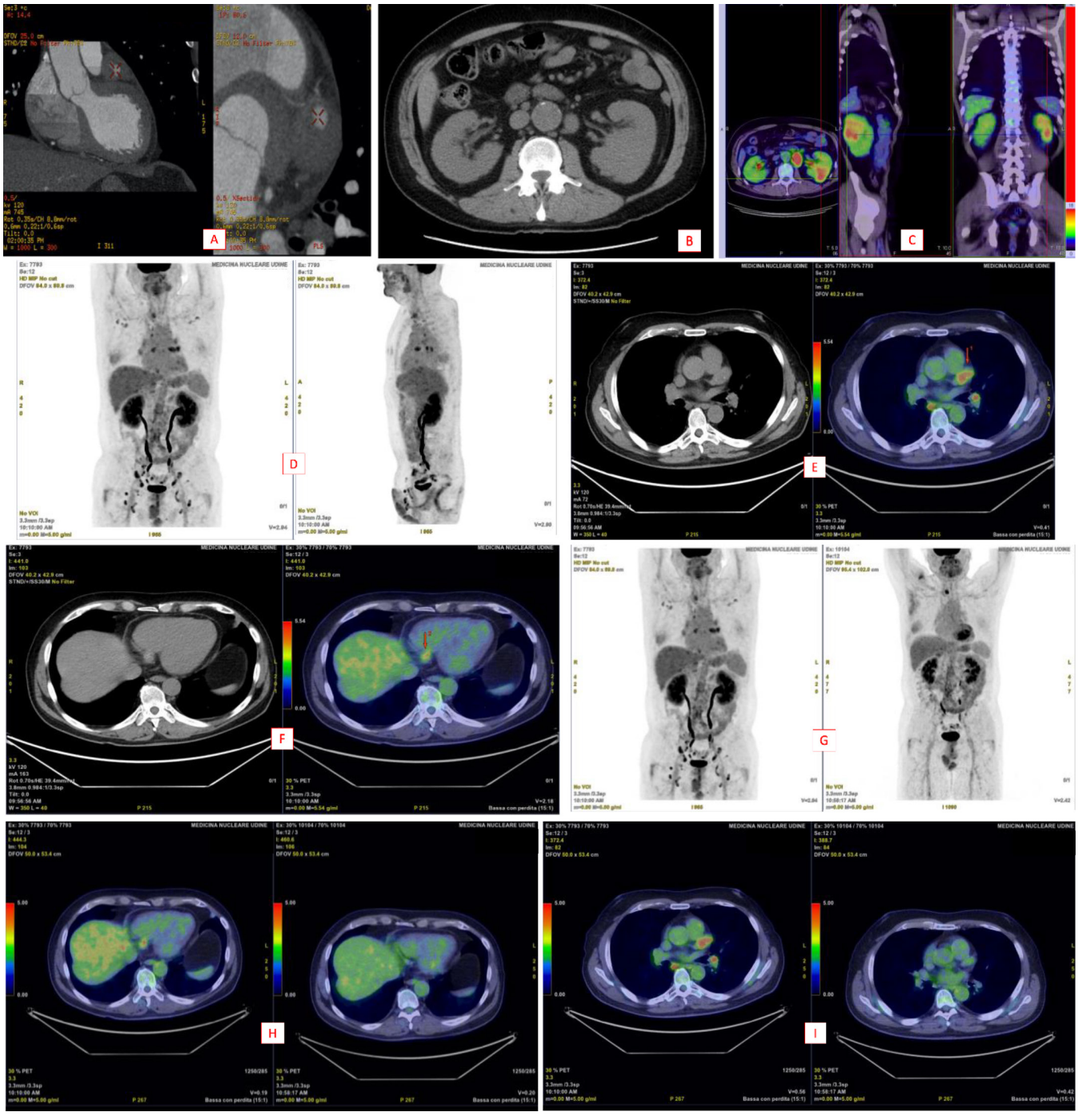

Fig. 1. Imaging details of cardiac and lymphoproliferative manifestations. **A**: Details of aneurismatic dilatation of LDA coronary artery at coronary CT. **B-C**: Left renal mass and bulky adjacent lymph adenomegalies at abdominal angio CT and PET/CT. **D-F**: PET/CT captation of diffuse lymph adenomegalies and of coronary aneurisms, suspicious for relapse of lymphoproliferative and cardiac involvement of disease. **G-I**: Details of PET/CT scan amelioration after therapy, both on lymphoproliferative and cardiac involvement.

chloroquine, colchicine, and steroid cycles, with clinical benefit. In march 2019, he was admitted to hospital due to acute chest pain, dyspnoea and ST-segment depression on ECG, and diagnosed with NSTEMI. Coronarography showed critic mono-vascular thrombotic occlusion of left anterior descending artery (LAD), associated to aneurysmal dilatation of both LAD and right coronary artery (RCA), confirmed at coronary CT as expression of inflammatory involvement (Section A of Figure 1). These data, together with elevation of inflammatory markers (CRP 50 mg/L) and in the absence of other systemic involvement and laboratory anomalies (*e.g.* negative cryoglobulins, ANCA and anti-phospholipid antibodies), posed diagnosis of isolated coronary vasculitis in SjD. The patient underwent three 500 mg i.v. boluses of methylprednisolone (MP), then gradual tapering of 1 mg/kg MP, with improvement of cardiac symptoms. Subsequent abdominal CT angiography showed a left renal mass with adjacent bulky lymphadenopathies. Consequently, a PET/CT was performed, showing captation of the renal mass (SUVmax 14.2), of adjacent lymph nodes (SUVmax 13.1) and in lesser extent of diffuse lymph-nodal stations (Fig. 1 B-C). Biopsy of the renal mass demonstrated a DLBL. The patient underwent 6 cycles of R-COMP chemotherapy with complete clinical, imaging, laboratory response of lymphoma, vasculitis and SjD manifestations, which lasted from 2019 to 2021. In March 2022, we assisted to recurrence of SjD symptoms (sicca, Raynaud's phenomenon) and laboratory abnormalities (increase of RF and gamma globulins; decrease of C4; peripheral CD19 B-cell repopulation), that led to imaging re-evaluation. Coronary CT showed increase of RCA aneurism. PET/CT showed uptake of suspicious diffuse lymphadenopathies and of RCA and LAD aneurisms, compatible with recurrence of vasculitic and lymphoproliferative disease (Fig. 1 D-F). Bioptic evaluation of peripheral up-taking lymph-nodes showed diffuse lymphocytic hyperplasia without malignant features. After a multidisciplinary discussion, a diagnosis of lymph-nodal and coronary manifestations of recurrent indolent lymphoproliferative disease in SjD was formulated. The patient was treated with rituximab 1 gr x 2 for induction, then 1 gr every 6 months as maintenance, with clinical, imaging, and laboratory persistent remission on an overall follow up of 36 months. Details of PET/CT scan improvement are shown in Figure 1 G-I, respectively.

Overall, the strict link between lymphoproliferation, even malignant, and vasculitis in SjD is reinforced. Our herein reported case might represent a paradigm of these concepts, supporting the crucial role of B-cell hyperactivity in SjD pathogenesis and clinical manifestations: in fact, both connective tissue disease symptoms, haematological and cardiac vasculitic manifestations appeared as manifestations of a common B-cell mediated lymphoproliferation, supported by an optimal response to B-cell depleting therapy. Anti-B cell therapies, such as CD20-depleting rituximab, are known for their role in haematological diseases such as DLBCL, mainly associated to other chemotherapy agents (5). In SjD, targeting B-cell with anti-CD20 and/or anti-BAFF therapies has shown promising results, but this strategy is, as of now, supported in severe, refractory systemic disease (6-7).

Overall, in this case, the prompt diagnosis of this rare manifestation of SjD, and an accurate clinical, laboratory and imaging follow up of its course, allowed a successful treatment and consequent stable remission.

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