Multiple arterial thrombosis and pericarditis revealing histiocytosis successfully treated with MEK-inhibitor cobimetinib

Sirs,

Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis characterised by long bone and peri-nephric involvement (“hairy-kidney”) associated with compatible histology. Vascular sheathing involving adventitia of vessels (“coated-aorta”) is described and is usually non symptomatic. Cardiac involvement includes pericarditis, atrium pseudo-tumour or coronary infiltration.

A 71-year-old man suffered from lower limb pain and arthritis of the ankles and knees for three years. He had medical history of hypertension and prostatic hypertrophy. He had no smoking or drinking habits and no coronary heritage. Imaging (x-ray/magnetic resonance imaging) showed no fracture or arthritis. Repeated laboratory investigations were normal except elevated C-reactive protein (CRP) between 20 and 40 mg/L (n<10mg/L). Patient described fatigue, pain and dyspnea. Physical examination showed a wound of the third toe of the right foot.

Laboratory examinations including lipid tests were unremarkable except CRP level at 45 mg/L and platelets at 555 G/L (n: 150-450 G/L). Body computed tomography (CT) showed multiple thrombosis – popliteal artery at his origin, right anterior tibia artery, left superficial femoral artery – stenosis of coeliac trunk and renal arteries. Other abnormalities – infiltration of peri-nephric fat, right ureter dilatation, mesenteric enlarged lymph nodes – were present on the CT. Cardiac echocardiography showed left ventricle ejection fraction at 30% with abundant pericardial effusion. Pericardial puncture appeared as exudate made of 82% of neutrophils. Malignant cells were absent and culture for infectious agents was negative. Coronary angiography showed a 70% stenosis of left anterior descending artery requiring percutaneous coronary intervention. The patient also underwent urgent femoral and popliteal angioplasty. Due to pericardial effusion, multiple thrombosis and stenosis, the main diagnosis suspected was neoplasm.

Fluorodeoxyglucose positron emission tomography (18FDG-PET) showed radiotracer uptake on vessels, heart, and peri-nephric fat. Bone scintigraphy showed radiotracer uptake of metaphyseal/diaphyseal region of long bones suggestive of ECD. Peri-nephric fat biopsy was infiltrated by Cd68+ , Cd1a and S100+ foamy histiocytes surrounded by fibrosis. BRAFV600E mutation was positive on biopsy samples. Bone marrow biopsy showed essential thrombocythaemia (TE) with mutation on JAK2 gene. Due to cardiovascular involvement and association with myeloproliferative neoplasm, patient received cobimetinib (MEK-inhibitor). The metabolic response was good on bones, vessels and heart at 6 months. Platelets counts became normal under cobimetinib.

Erdheim-Chester disease is a rare non Langerhans-cell histiocytosis affecting adults. Diagnosis is based on clinical/imaging presentation and typical histology (1). Imaging shows long bones involvement (bi-lateral symmetric metaphyseal/diaphyseal osteoclerosis of legs), infiltration of peri-nephric fat (“hairy kidney”) and vascular sheathing. Adventitia of aorta is the preferential site of infiltration (i.e. “coated aorta”) but it can affect all vessels and might lead to stenosis/thrombosis at ending stage. Pericarditis, right-atrium pseudo-tumour and coronary infiltration are described in ECD (2). It is usually asymptomatic and diagnosis is mostly performed with imaging (MRI or CT or US) (3). Orbital occlusion is exceptional. Main predicting factor of aortic/
coronary infiltration is BRAF V600E mutation present in 60% of patients (4, 5).

Tissue biopsy is mandatory to confirm infiltration of Cd 68+, Cd1a- and S100+ histiocytes, to rule out differential diagnosis (lymphoma, solid tumour, vasculitis, hyper-IgG4 syndrome or other histiocytosis), and identify somatic mutations in MAP-kinase pathway gene present in almost 80% of patients (mostly BRAF and MAP2K1) (5). From those findings, ECD is now considered as a myeloid neoplasia (6). Co-occurrence of myeloproliferative neoplasm confirm the myeloid origins of cells in ECD (7, 8). This presentation also confirms the MEK-inhibitors efficiency in Erdheim-Chester disease (associated with TE) (9, 10).

To conclude, this case highlights the diagnosis of Erdheim-Chester disease presenting as multiple stenosis, thrombosis associated with pericarditis and efficiency of Mek-inhibitor.

J. RAZANAMAHERY1, MD
A. MALAKHIA2, MD
B. GUILLON3, MD
S. HUMBERT4, MD
N. MAGY-BERTKAND5, MD PhD

1Department of Internal Medicine, 2Department of Radiology, 3Department of Cardiology, University Hospital, Besancon, France.

Please address correspondence to: Dr Jerome Razanamahery, CHRU Besancon, 3 boulevard Alexander Fleming, 25000 Besancon, France.

E-mail: jrazanamahery@chu-besancon.fr

Competing interests: none declared.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2019.

References


