IMPROVEMENT OF ERDHEIM–CHESTER DISEASE–RELATED RENAL FAILURE FOLLOWING TREATMENT WITH ANAKINRA

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INTRODUCTION

Erdheim Chester disease (ECD) is a rare non-Langherans cell histiocytosis characterized by massive xanthogranulomatous infiltrates of lipid-laden CD68+/CD1a- histiocytes usually surrounded by fibrosis. The etiology and pathogenesis of ECD remain poorly understood and also its classification as a tumoral or inflammatory disease is controversial [***1***]. Commonly involved sites are bones, heart, retro-orbital soft tissue, pituitary gland, lungs and central nervous system. About 30% of patients with ECD have renal failure, often caused by vascular, ureteral or kidney infiltrates. Due to the large pleomorphism of ECD, the diagnosis is challenging, and the treatment is generally based on administration of Interferon-alpha (IFNα). This therapy improved prognosis in about 67% of patients, but myocardial, renal, pulmonary or central nervous system complications remain a frequent cause of death [***2***]. Recently, encouraging results have been reported with Anakinra, the recombinant form of interleukin-1 receptor antagonist [***3***].

CASE REPORT

A 76-year old man was admitted to our unit for hypertension and renal function deterioration. His medical history was remarkable for chronic kidney disease with a baseline creatinine of 1.6 mg/dL. Physical examination was unremarkable. Laboratory investigations showed: creatinine 2.6 mg/dL, phosphate 5.2 mg/dL, Hb2Ac 7.2%. All the other tests were normal. Urinary tract ultrasonography (US) showed bilateral hydronephrosis. A contrast-enhanced computed tomography (CT) revealed also the presence of an extra-pelvic fibrous tissue extended up to the ureteral origin, determining a significant bilateral constriction of the renal pelvis, with retro-dilatation of the calyces. At subsequent magnetic resonance imaging (MRI) the extra-pelvic tissue signal resulted compatible with a slowly evolutionary fibrous tissue [***Figure 1***]. A biopsy showed a fibro-muscular tissue diffusely infiltrated by foamy histiocytes, along with areas of steatonecrosis. On direct immunofluorescence the histiocytes were CD68+ and CD1a-. A cardiac MRI showed pericardial effusion and a mass infiltrating the interatrial septum, extended up to the junction of the cava veins. The mass signal was not homogeneous, with punctiform nodulations, strongly suggesting a diagnosis of histiocytosis [***Figure 2***]. A bone X-ray showed medullary osteosclerosis [***Figure 3***]. Tests for lung and cerebral involvement resulted negative. A diagnosis of ECD was made and treatment with subcutaneous pegylated IFNα was started at a dose of 180 µg per week, which was afterwards reduced to 135 µg per week. A heart MRI imaging at 12 months showed reduction of the pericardial effusion and decrease of the right atrium wall thickening from 18 to 9 cm. However, treatment was poorly tolerated because of weakness, edema and hypotension. Of more concern, serum creatinine progressively increased up to 3.9 mg/dL. IFNα was withdrawn, and subcutaneous Anakinra (100 mg/day) was started. After one year of therapy, the patient symptoms improved, along with renal function, and a follow-up ultrasound showed the absence of hydronephrosis. After one further year of follow-up serum creatinine was still stable around 2 mg/dL.

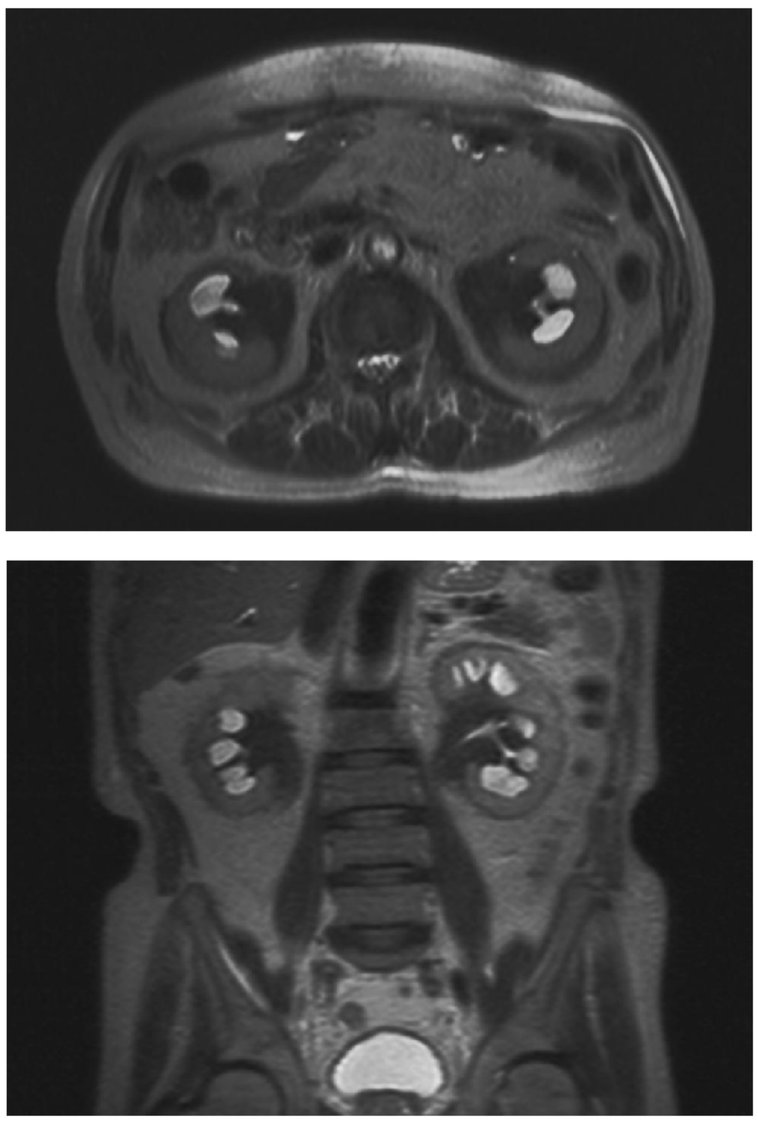

FIGURE 1 – Abdominal T2-Weighted MRI (Trasversal and Coronal Planes)

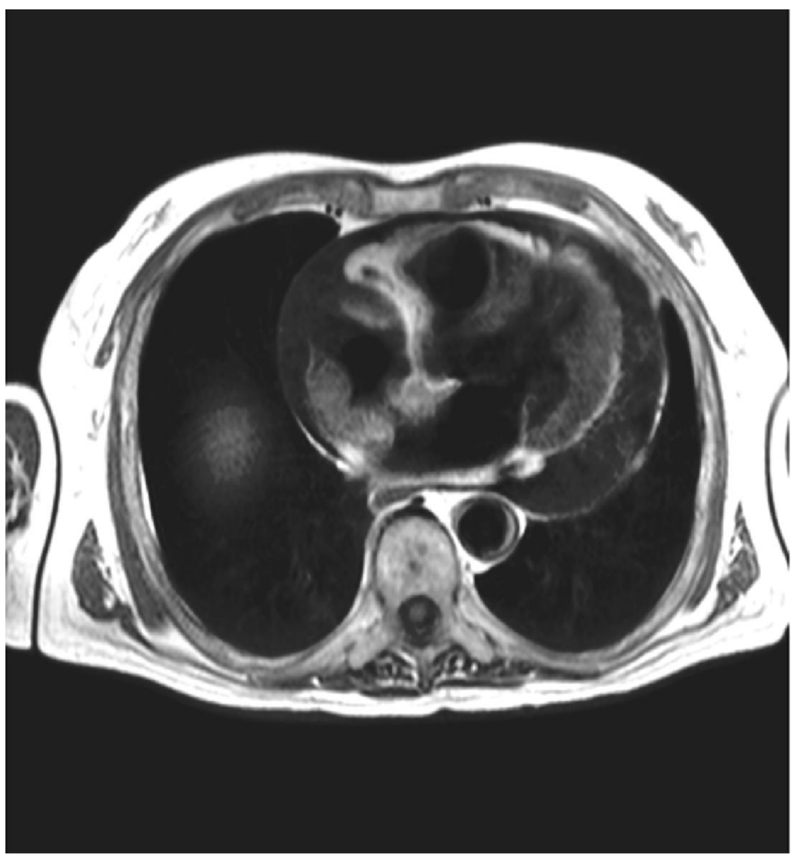

FIGURE 2 – Cardiac MRI showing pericardial effusion and a mass infiltrating the interatrial septum

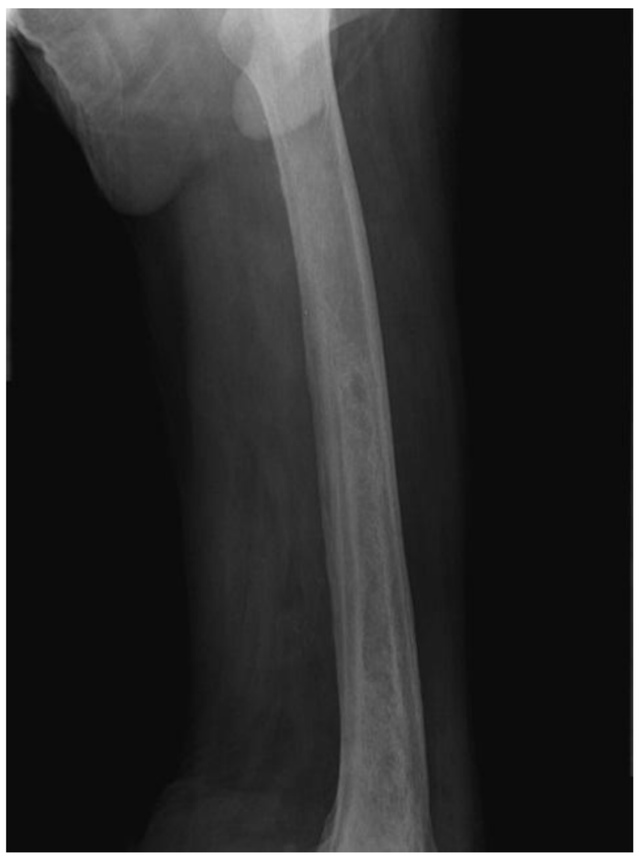

FIGURE 3 – Femur RX showing Medullary Osteosclerosis

CONCLUSIONS

Anakinra is a recombinant, form of IL-1 Receptor antagonist, which binds to IL-1 membrane receptor and down-regulates the biologic activities of IL-1, including inflammation. Aouba et al first reported a significant reduction of IL-1α (expressed at the monocytes membrane surface after cell stimulation) following treatment with Anakinra, a finding that, along with clinical improvement, supported the hypothesis of IL-1 as a primary actor in ECD systemic Th1-oriented immune perturbation. Anakinra also showed important results in some ECD patients with skeletal and cardiac involvement. In all cases a reduction of inflammatory markers, fever and ECD symptoms was observed. We used Anankira as a rescue therapy: general conditions of the patient improved and plasma creatinine reduced from 4 to 2 mg/dl. Neither renal artery nor ureteral stenting were necessary to obtain this result. Moreover, in contrast to IFNα therapy, which caused severe side-effects, Anakinra was well tolerated, even in the long-term.

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H) Clinical Nephrology, CKD. H1) Lab methods, progression & risk factors for CKD 1-5, nutrition in CKD, renal diseases (except GNs and cystic diseases).
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