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Letter to the Editor

Successful Treatment of De Novo Acute Myeloid Leukemia-Associated Aortitis by Induction Chemotherapy Alone

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To the editor.

A 42-year-old woman presented to the emergency department for a seven-day history of lumbar pain and night fever. On admission, she was febrile at 38.2°C. Associated symptoms included cough, dyspnoea on exertion, and left scapular pain. Physical examination showed sinus tachycardia and a single lingual aphtha. All peripheral pulses were well palpable with no headache, visual loss, focal neurological deficit, signs of polymyalgia rheumatica, history of chondritis, peripheral lymphadenopathy, and splenomegaly. Laboratory studies showed a white blood cell count of 46.67 x 10^9/L, including 66% of myeloid blasts; haemoglobin was 80 g/L, platelet count was 124 x 10^9/L, and C-reactive protein was 386 mg/L. Creatinine level, electrolytes, and bilirubin were within normal range. The thoracic-abdominopelvic CT scan showed a wall thickening (arrows) of the aortic arch (**Figure 1 A**), the proximal left subclavian artery (**Figure 1 B**), and the abdominal aorta (**Figure 1 C**) and a periaortic fat stranding (**Figure 1 C**, arrowhead) evocative of a panaortitis. A mild left pleural effusion was also detected. The bone marrow aspiration showed 87% of M1 myeloid blasts, confirming the diagnosis of acute myeloblastic leukaemia (AML) without maturation. Further examinations revealed normal cytogenetics (karyotype and chromosome 8 *in situ* hybridization) and mutations of the *NPM1*, *DNMT3A*, *IDH2* R140Q, *KIT* D816V, and *CEBPA-bZip* genes with variant allele frequencies of 32%, 42%, 38%, 17%, and 2% respectively. All complementary laboratory tests (blood cultures, *Coxiella burnetii* and *Treponema pallidum*, interferon-γ release assay, antinuclear, anti-neutrophil cytoplasmic and anti-CCP antibodies, rheumatoid factor, IgG4 antibodies) were negative, rendering alternative aetiologies of aortitis highly unlikely. All this led to the final diagnosis of *de novo NPM1*-mutated AML associated with paraneoplastic aortitis. The patient received induction chemotherapy with idarubicin 9mg/m²/day from day 1 to day 5 and cytarabine 200mg/m²/day from day 1 to day 7 according to the experimental arm of the BIG-1 trial (registration number: NCT02416388). The initial symptoms receded on day 10 of the induction therapy. A CT scan performed on day 13 showed a complete disappearance of the aortitis (**Figure 1 D-F**). A post-induction evaluation performed on day 38 demonstrated complete remission (CR) with *NPM1*-based minimal residual disease at 0.087%.

Discussion. The association between aortitis and myelodysplastic neoplasms (MDS) or chronic myelomonocytic leukaemia (CMML) is well documented,[1] whereas the co-occurrence of aortitis and de novo AML is extremely rare: to our knowledge, only three certain cases have been reported so far. All three were characterized by exclusive abdominal aorta involvement,[2,3,4] whereas in our case, the patient presented with panaortitis. The pathophysiology of this association is unknown. One can speculate that abnormal expression of antigens by AML blasts could stimulate immune dysregulation (particularly of dendritic cells and T lymphocytes), leading to the development of vessel wall inflammation, similar to what is described in MDS.[5]

MDS or CMML-associated large vessel vasculitis often benefits from treatment with corticosteroids (CS); however, CS dependency or refractoriness is a frequent eventuality.[1,6,7] In two of the three published cases of AML-associated aortitis, precise information about the patient's management is available. In both cases, a treatment with CS for the inflammatory disorder was associated with AML induction therapy. In the acute promyelocytic leukaemia (APL) associated case, the authors indicate that treatment led to "amelioration of the patient" and CR of APL;[3] in the second case,

evolution was characterized by progression of

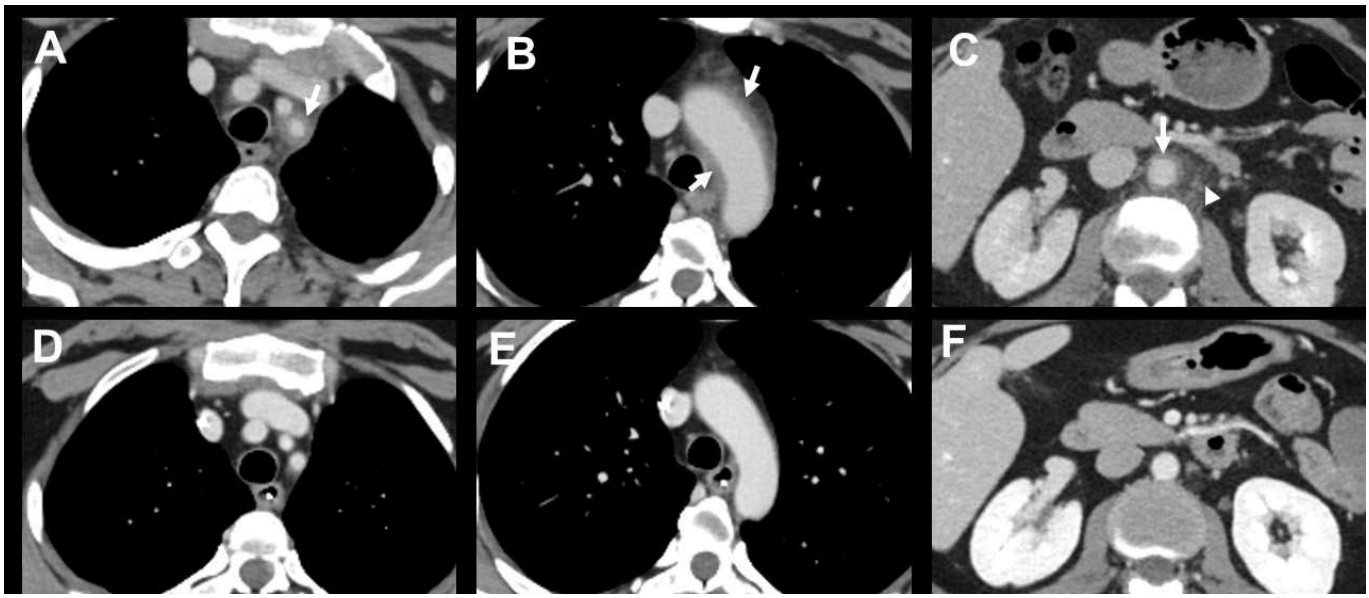

Figure 1. CT scan: panaortitis before chemotherapy (A-C). Complete resolution of abnormalities after chemotherapy (D-F).

inflammatory manifestations and early death due to acute coronary syndrome.[2] In the case of our patient, we chose the sole induction chemotherapy regimen, which led to both early and total disappearance of the aortitis and CR of AML, thus confirming the hypothesis of AML-associated paraneoplastic aortitis.

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