



# Chronic myelomonocytic leukaemia associated with large- and medium-sized arteries vasculitis of the small bowel

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### Chronic myelomonocytic leukaemia associated with large- and medium-sized arteries vasculitis of the small bowel

#### Rheumatology key message

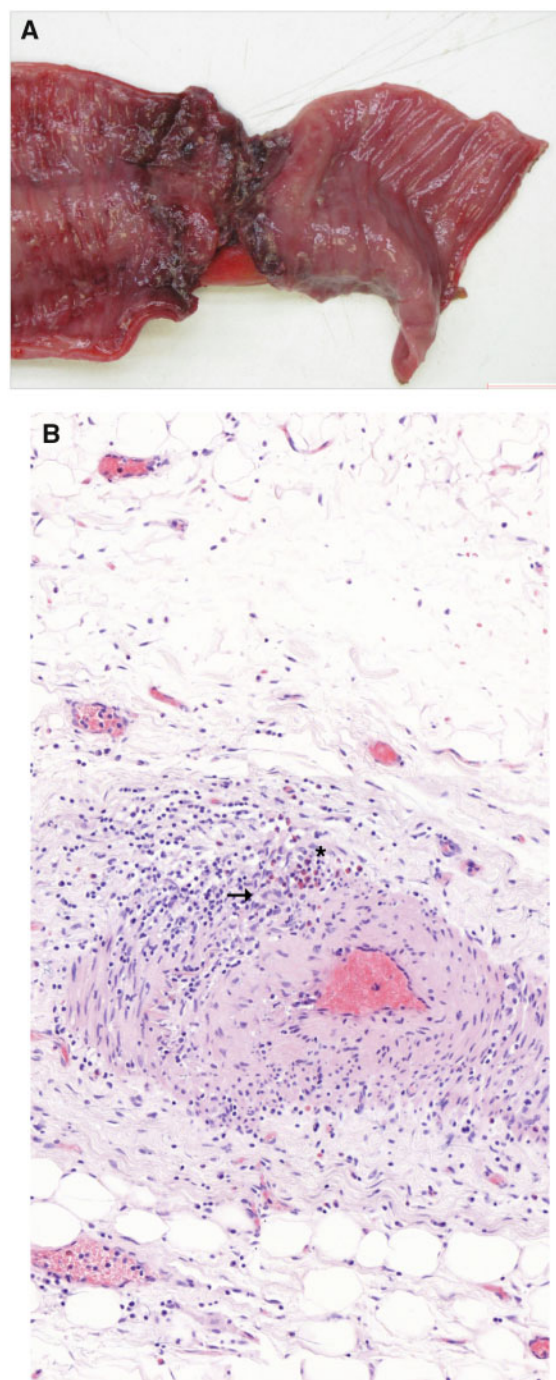
- Myelodysplastic syndromes associated vasculitis can be lethal and require early treatment of the haematological neoplasm.

SIR, Myelodysplastic syndromes (MDS) and chronic myelomonocytic leukaemia (CMML) can be associated with systemic inflammatory or autoimmune diseases (IADs) [1]. One of the most common IADs is vasculitis, mostly leukocytoclastic vasculitis or polyarteritis nodosa [2]. MDS/CMML-related IADs commonly have incomplete and atypical presentations that can make the diagnosis challenging [3]. We hereby report the case of a man consulting for fever and abdominal pain who was proven to have gastrointestinal (GI) vasculitis associated with CMML.

A 58-year-old male was admitted to surgery for abdominal pain with fever and weight loss of 4 kg. His medical history was mainly marked by arterial hypertension and gout. Laboratory tests revealed increased white blood cell count (14.600/μl) with neutrophils (5.840/μl), hypereosinophilia (2.040/μl) and hypermonocytosis (4.820/μl). C-reactive protein was increased at 50 mg/l ( $n < 3$  mg/l). Abdominal CT scan showed appendicitis. Surgeons removed a necrotic appendix surrounded by inflammatory adhesions. Anatomical pathological exam revealed tumour-free pyogenic appendix.

He was admitted one month later for asthenia, fever (38°C), abdominal pain, and livedo racemosa. Laboratory tests showed a haemoglobin level of 11.6 g/dL, platelets of 256.000/μl and the same abnormalities on white blood cell count apart from a decrease in eosinophil count (530/μl). Immunological (ANA, ANCA, type 2 anti-mitochondrial, anti-LKM1 microsome, anti-hepatic cytosol, anti-smooth muscles antibodies, Coombs' test) and infectious tests (blood cultures, parvovirus B19 PCR, HHV6 PCR) were negative apart from EBV blood PCR: 1.1 million copies/ml (6.6 log). Plasmatic protein electrophoresis was normal as were immunoglobulins subclasses (IgG 11 g/L, IgA 5.25 g/L, IgM 0.76 g/L). Screening for BCR-Abl and JAK2 mutations was negative. Abdominal CT scan showed a bridge-related occlusion, multiple mesenteric and inguinal lymphadenopathies, no sign of ischaemia, no aneurysm, no sign of small bowel lymphoma. PET-CT showed mildly hypermetabolic lymphadenopathies, spleen and colon foci. An ulcerated and stenosing lesion of the

**Fig. 1** Lesion of the small bowel secondary to large and medium-sized arteries vasculitis



**A:** stenosing lesion of the small bowel caused by large- and medium-sized arteries vasculitis; **B:** mononuclear cells and eosinophils (star) breaching the internal elastic lamina, intima thickening and giant cells (arrow).

small bowel was surgically removed. Histological analysis of the lesion showed ulcerations with large- and medium-sized arteries vasculitis, segmental, rich in eosinophils and giant cells assembled in granulomas, intima thickening and internal

elastic lamina destruction without any pathogen and negative EBV analysis (Fig. 1A and B). Staining with periodic Acid-Schiff and Grocott did not show fungal elements and Ziehl-Neelsen stain was negative as well as bacteriological cultures. Blood next generation sequencing was positive for *ASXL1* (NM\_015338) exon 12 c.17773C>A p.Tyr591\* variant allele frequency = 5.5% and *U2AF1* (NM\_001025203) exon 2 c.101C>T p.Ser34Phe variant allele frequency = 5.7%, both in favour of a myeloid neoplasm. We concluded the patient suffered from GI vasculitis associated with CMML. He died from hypoxic cardiac arrest in early postoperative time.

The most frequent vasculitis in the course of MDS/CMML are infectious and drug related, but paraneoplastic vasculitis has also been described, mainly leukocytoclastic vasculitis or polyarteritis nodosa. CMML appears to be particularly associated with polyarteritis nodosa [4], and while the GI tissues of the patient shared common features with polyarteritis nodosa, granulomas are not usually observed in this disease. Recent data also reported a new subtype of GI vasculitis similar to Behçet's syndrome associated with myelodysplastic neoplasms with trisomy 8 [5]. Extra-medullary leukaemic infiltration is moreover possible in CMML, commonly in spleen or skin, but other tropisms have been described [6].

Among single-organ vasculitis, isolated GI tract vasculitis are often non-specific in clinical and imaging features, with numerous differential diagnoses and need for histopathological analysis [7]. This type of single-organ vasculitis has a heterogeneous prognosis and when combined with the existence of MDS/CMML, the median survival for these patients is of 6 months vs 24 months for IADs-free MDS/CMML [8]. The presence of GI involvement is associated with poor prognosis, as reflected by the five factors score prognostic scale. Early diagnosis and treatment are crucial considering the high risk of secondary sepsis, perforation and occlusion as in our case. Even though data are scarce, treatment of MDS/CMML, especially with azacitidine, seems to be associated with both improvement of cytopenias and MDS/CMML associated-IADs, while immunosuppressive agents can worsen cytopenias [3].

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## Comment on: Assessments of the unmet need in the management of patients with rheumatoid arthritis: analyses from the NOR-DMARD registry

SIR. We read with interest the article by Olsen *et al.* that was published recently in the *Rheumatology* issue dealing with unmet needs in the treatment of RA, an analysis from the Norwegian DMARD (NOR-DMARD) registry [1]. In this study, the authors reported a high proportion of MTX-naïve patients who received MTX monotherapy as having an inadequate response and a large proportion of patients who discontinued MTX therapy, primarily due to a lack of efficacy. In addition, they reported that a significant number of RA patients receiving biologic DMARDs (bDMARDs) as monotherapy or in combination with MTX discontinued therapy over 24 months of treatment. All the above showed that a large proportion of patients treated with MTX as monotherapy or with bDMARDs had a huge gap in RA management and the unmet needs for treatment is very high. The authors justify their results by