Vasculitis and Myelodysplasia

Cristina C. Belizna MD[1,2], Jean Marc Kerleau MD[1], Francois Heron MD[1], Nicole Cailleux MD[1] and Hervé Lévesque MD PhD[1]

[1]Department of Internal Medicine, Rouen University Hospital, and [2]INSERM U644, Rouen Faculty of Medicine and Pharmacy, Rouen, France

Key words: vasculitis, myelodysplasia, refractory anemia, hematology, leukemia

IMAJ 2008;10:156–157

Myelodysplastic syndromes are hematological malignancies frequently presenting as refractory anemia or acute myeloid leukemia. The etiopathogenesis of vasculitis in patients with neoplasia remains unknown. An association has been found between myelodysplastic syndromes and systemic vasculitis, especially when immunological abnormalities are present. Although autoimmune abnormalities generally follow the diagnosis of MDS, we describe the case of a patient with MDS who developed a striking spectrum of autoimmune disorders – including muscular, cutaneous and pulmonary vasculitis – which preceded the clinical appearance of MDS by several months.

Patient Description

A 71 year old man was admitted after 3 months of persistent asthenia and weight loss of 6 kg. His medical history included appendectomy, glaucoma, and excision of prostatic adenocarcinoma. He reported a progressive physical decline with dry cough, dyspnea, and fever with night sweats. The clinical examination was unremarkable.

Laboratory tests revealed the following: erythrocyte sedimentation rate 120 mm/hour, C-reactive protein 96 mg/L, elevated alpha-2 globulinemia (8.6 g/dl without monoclonal peak), red blood cells 3.9 g/L, hemoglobin 11.5 g/ml, mean globular volume 105 μ^3, leukocytes 4.4 g/L (including 55.5% neutrophils, 1.4% eosinophils, 1.5% monocytes, 41.3% lymphocytes), and platelets 193 g/L. Hepatic and renal function was normal. Cholesterol was 3.4 mmol/L and triglycerides 0.72 mmol/L. Chest X-ray highlighted several subpleural bilateral opacities confirmed by computed tomography scan. The abdominal CT scan and the lung fibroscopy with bronchoalveolar washing were non-contributory. The infectious and immunological assessment (human immunodeficiency virus, hepatitis B and C serologies, antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, cryoglobulins) was also negative. The worsening of his clinical condition, with hypoxia (PaO_2 8 kPa without hypercapnia), together with the presence of new pulmonary lesions led 4 months later to pulmonary biopsy that revealed non-specific inflammation without fibrosis. Moreover, inflammatory lesions appeared on the arms and forearms associated with feverish peaks, suggesting vasculitis with pulmonary manifestations. The macrocytosis was related to refractory anemia with an excess of blasts (10%) and karyotypic anomalies (paracentric insertion of the third chromosome). Therefore, the diagnosis was refractory anemia with an excess of blasts associated with secondary systemic vasculitis (pulmonary, muscular and cutaneous). High doses of corticosteroids (1 mg/k/day) induced a spectacular regression of the cutaneous and pulmonary lesions. The clinical outcome was characterized by cortico-dependence (20 mg/day), persistence of transitory feverish peaks, and pancytopenia.

Comment

Myelodysplastic syndromes constitute a group of stem cell disorders characterized by progressive refractory cytopenias related to poor hematopoiesis. MDS may sometimes progress to acute myeloid leukemia. Autoimmune manifestations occur frequently in patients with MDS and present mainly as cutaneous vasculitis, but other clinical features may also be observed, such as arthritis, fever, polyneuropathy, glomerulonephritis, polymyalgia, etc.

Vasculitis may also occasionally manifest as a complication during therapy for MDS (transfusion or bone marrow transplantation). However, vasculitis in MDS is currently paraneoplasic and could be isolated or systemic. Although autoantibodies are usually reported in isolated myelodysplasia and/or vasculitis, they are only occasionally observed in vasculitis related to myelodysplasia. Furthermore, asymptomatic immunological abnormalities may occur as well and include hypergammaglobulinemia.

Vasculitis accompanying myelodysplasia affects predominantly cutaneous vessels, but there is increasing evidence that large vessels may be involved as well. This is the case for giant cell arteritis and Takayasu arteritis related to MDS [1]. Moreover, medium-sized vasculitis (Wegener's granulomatosis, polyarteritis nodosa) occurs also with MDS [2].

Other rheumatological manifestations have been reported, but there are few reports of relapsing polychondritis, Sjogren's syndrome, systemic lupus erythematosus, rheumatoid arthritis, and mixed connective tissue disease concomitant with MDS. Other unusual localizations, e.g., neurological, sometimes isolated or an early clinical sign, have also been observed in MDS.

As a rule, autoimmune abnormalities follow the diagnosis of MDS. Nevertheless, the temporal relationship could not be determined in some of the reported cases

MDS = myelodysplasic syndrome

and prospective series. The originality of our case report lies in its initial pulmonary presentation, which was underlying for a long period.

The pathogenesis of the vasculitis in MDS remains controversial. Their association seems not to be accidental. Therefore, an immunological abnormality is suggested as the cause, and several mechanisms have been hypothesised. In a series of 14 patients with myelodysplasia it was recently reported that the absence of a transcription factor (interferon regulatory factor-1) seems to play a protective role against the development of autoimmune dysregulation in myelodysplasia [3]. An analysis of clinical and cytogenetic features in patients with autoimmune manifestations during MDS revealed that these complications occur mainly in young patients with secondary MDS and cytogenetic abnormalities [4]. Even though the clinical outcome of these patients appears to be aggravated by the presence of vasculitis in MDS, a 4 year prospective study indicated that this worse prognosis is related to the hematological malignancy itself and not to the autoimmune complications [5]. Treatment is mainly based on corticosteroids, but immunosuppressive therapy is an alternative in refractory cases. Recent observations have also shown the beneficial effects of new therapies such as anti-tumor necrosis factor.

In conclusion, we report a case of vasculitis with myelodysplastic syndrome. The originality of our observation is related to its initial exclusive presentation that preceded the diagnosis of refractory anemia by several months. The awareness of practitioners to this clinical presentation will enable quick diagnosis and therapy.

Acknowledgment: The authors thank Richard Medeiros, Rouen University Hospital Medical Editor, for editing the manuscript.

References

1. Liozon E, Loustaud V, Fauchais AL, et al. Concurrent temporal (giant cell) arteritis and malignancy: report of 20 patients with review of the literature. J *Rheumatol* 2006;33:1606–14.
2. Brickner LA, Scannell KA. Medium-vessel PAN-type vasculitis associated with myelodysplastic syndrome and presenting as bilateral perinephric hematomas. *Clin Exp Rheumatol* 1997;15:221–2.
3. Giannouli S, Tzoanopoulos D, Ritis K, Kartalis G, Moutsopoulos HM, Voulgarelis M. Autoimmune manifestations in human myelodysplasia: a positive correlation with (IRF-1) expression. *Ann Rheum Dis* 2004;63:578–82.
4. Billstrom R, Johansson H, Johansson B, Mitelman F. Immune-mediated complications in patients with myelodysplastic syndromes-clinical and cytogenetic features. *Eur J Haematol* 1995;55:42–8.
5. Sailler L, Joseph-Hein K, Astudillo L, et al. Pustular vasculitis in a patient with T-cell large granular lymphocyte proliferation and myelodysplasia. Successful treatment by cyclosporin. *Br J Dermatol* 2003;149:893–4.

Correspondence: Dr. C. Belizna, Dept. of Internal Medicine, Rouen University Hospital, 76031 Rouen Cedex, France.
Phone: (33-2) 3288-9003
Fax: (33-2) 3288-9026
email: cristina.belizna@wanadoo.fr