Aplastic Crisis as Primary Manifestation of Systemic Lupus Erythematosus

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Keywords
Systemic lupus erythematosus · Aplasia · Bone marrow

Summary
Aplastic crisis is an unusual feature of systemic lupus erythematosus (SLE). We report the case of a 54-year-old woman presenting with both (extravascular) Coombs-positive hemolytic anemia and laboratory findings of bone marrow hyporegeneration with concomitant severe neutropenia. A bone marrow biopsy confirmed aplastic crisis. Diagnostic work-up revealed soaring titers of autoantibodies (anti-nuclear, anti-double-stranded DNA, anti-cardiolipin-IgM, and anti-β2-glycoprotein-IgM antibodies), indicating a connective tissue disease as the most plausible reason for bone marrow insufficiency. As the criteria for SLE were fulfilled, we initiated an immunosuppressive therapy by steroids, which led to a rapid complete hematologic and clinical remission in our patient. In this case, we could report on one of the rare cases of SLE-induced aplastic crisis showing that this condition can be entirely reversed by immunosuppressive treatment and that SLE-induced aplastic crisis yields a good prognosis. In conclusion, in a case of aplastic crisis, physicians should be aware that SLE can be a rare cause that is accessible to specific treatment.

Introduction
Anemia, leukopenia and thrombocytopenia due to peripheral destruction are common features in systemic lupus erythematoses (SLE). Aplastic crisis, however, is rare. In this case report we describe a patient with severe hemolytic anemia and neutropenia as the first manifestation of SLE. Treatment with corticosteroids resulted in a complete clinical and hematological remission.

Case Report
Medical History
A 54-year-old woman was admitted to our hospital due to fever that had persisted for 3 weeks. Furthermore, she complained of loss of appetite, lassitude, night sweats, and very subtle and fluctuating joint pain. The patient remembered polytope arthralgias without swelling at the elbows, knees, wrists and fingers, which had occurred several months before admission. The patient reported no further complaints; no skin lesions or other clinical signs of lupus were detectable in the physical examination. Extensive anamnesis revealed no photosensitivity, oral ulcers, rash, oral and/or genital ulcers, Raynaud’s or signs of arthritis. Beyond, there was no history of thromboembolic events. Of concern, the medical history revealed an episode of steroid refractory autoimmune hemolytic anemia.
in 1994, resolved after splenectomy. Thereafter, the patient remained free of symptoms. The immediate previous history showed no signs of infection like cough, dysuria or diarrhea. Amoxicillin had been prescribed by the primary practitioner 3 weeks before admission since she had then suffered from cough and fever.

**Physical Examination**

At admission, the patient had fever (39°C), an increased respiratory rate of 25/min and palpable cervical, axillary and inguinal lymphadenopathy. Blood pressure was normal at 110/75 mmHg, oxygen saturation at 95% without insufflation of oxygen.

**Laboratory Findings**

A hemogram revealed a white blood cell (WBC) count of 800 cells/µl with only 14% neutrophils, a hemoglobin concentration of 2.3 g/dl (normal range 12–16 g/dl), a hematocrit of 7% (37–46%) and reticulocytes of 8% (4–15%). Reticulocyte production index 0.1 (normal value 1); absolute reticulocyte count 8 x 10⁹/µl. The platelets at 295 G/L (150–400 G/L), mean corpuscular hemoglobin (MCH) and mean corpuscular volume (MCV) were within normal range. Ferritin was elevated (7155 µg/l, normal range 30–200 µg/l), transferrin at 1.8 g/L (2–4 g/l), transferrin saturation at 25% (20–45%), albumin at 3.2 g/dl (3.5–5.5 g/dl), C-reactive protein at 1.5 mg/l (0–5 mg/l), ferritin at 295 g/L (150–400 G/L), mean corpuscular hemoglobin concentration (MCHC) at 28% (32–36%), mean corpuscular volume (MCV) at 84 fL (80–100 fL), red cell distribution width (RDW) at 16.2% (11.5–14.5%), lymphocyte count 8 x 10⁹/µl, and neutrophil count 14% (50–70%).

**Discussion**

Hematological manifestations are not rare in SLE and occur in up to 85% of patients during the course of the disease [2, 3]. Peripheral destruction of cells is responsible for most changes. Aplastic anemia is very rare finding in SLE, and only a few case reports are found in the literature [4–6]. Here, we show a case with SLE presenting as aplastic crisis with neutropenia and anemia. Therapy with steroids led to a complete recovery of the peripheral blood count and laboratory changes of hemolysis.

**Hematological abnomalities in SLE are common.** Anemia frequently occurs in SLE due to chronic inflammation, renal disease, or immunosuppressive therapy. Autoimmune hemolysis, particularly, occurs in about 10% of all cases with SLE [7]. Pure red cell aplasia, in which autoantibodies are directed against erythropoietin, is rather rare. Thrombocytopenia, also

![Fig. 1. Morphologic changes in bone marrow cytology.](image)
a common complication of SLE, may be caused by autoimmune thrombocytopenia (ITP) or immunosuppressive therapy. ITP may be the initial presentation of disease in about 15% of all patients with SLE [8]. In our patient, thrombocytopenia was absent. Leukopenia is also very common in patients with SLE. It is mostly due to immunosuppressive drugs or mediated by autoantibodies directed against neutrophils and/or lymphocytes.

Aplastic anemia is a severe disorder of the bone marrow with an incidence of 4/1,000,000 per year. The disease is idiopathic in 80% of all cases. Drugs might be responsible; other causes could be viral infections (EBV, CMV, hepatitis and parvo B19 virus), chemicals and a few others. The responsiveness of aplastic anemia to immunosuppressive agents is the best evidence for the underlying immune mechanism of this disease: Autoreactive T cells lead to the destruction of hematopoietic stem cells and can be inhibited by immunosuppressive agents, especially antithymocyte globulins (ATG) [9, 10]. Besides the pivotal role of autoreactive T cells, autoantibodies against various proteins like kinectin, moesin and diazepam-binding inhibitor-related protein have been described and their at least subsidiary role in the pathophysiology of aplastic anemia has been suggested [11–15].

In SLE, aplastic anemia is a rare finding and only a few cases have been reported in the literature [16]. Like idiopathic aplastic anemia, SLE-induced aplastic anemia seems to be immune mediated. Both cellular-mediated and antibody-mediated inhibition of hematopoietic cell growth have been reported so far. Several authors described a cryptic serum inhibitor, for example in the acute phase of aplastic anemia, that inhibits colony-forming units in vitro through complement-dependent IgG [17]. Furthermore, Wolach et al. [18] described a case of anti-Ro-positive SLE, and Bailey et al. [6] described a case of lupus with evidence of anti-neutrophil antibodies. Others report cell-dependent mechanisms for aplastic anemia in SLE [5, 18]. However, the exact mechanisms of SLE-induced aplastic anemia to date are not yet fully understood and might be multifaceted. Yet, in contrast to idiopathic aplastic anemia [19], prognosis of SLE-induced aplastic anemia is good, with no documented recurrence or transfusion dependence.

Cornerstones of supportive care in patients with SLE-induced aplastic anemia are red cell and platelet transfusions and antibiotics. Considering therapy of SLE-induced aplastic anemia, some patients respond to oral steroids alone [5, 18], while others need parenteral steroid or plasmapheresis or even further immunosuppression using cyclophosphamide [16]. Other treatment options include cyclosporine A [20]. Steroid non-responders might benefit from azathioprine or methotrexate.

Disclosure Statement
The authors declare that they have nothing to disclose.

References