Defective erythropoiesis in myelodysplastic syndromes

We read with interest the report of William-son et al describing uncommon cases of red cell aplasia (RCA) in patients with myelo-dysplastic syndromes (MDS). The rarity of RCA in their first three cases was attributed to an intrinsic defect of maturation and proliferation of erythroid precursors occurring as part of the myelodysplastic disorder. We believe that RCA is a different, and possibly autoimmune aetiology, was suggested. We believe that cytogenetic and molecular study of such unusual cases is important. In the second three cases, a different, and possibly malignant haematological disorders are associated with structural chromosomal abnormalities. Cytogenetic study of unusual cases with common features, such as these cases of RCA, might indicate a common chromosomal abnormality which would point to the existence of genes which encode key regulators of erythroid lineage development at or near the junction of the chromosomal aberrations. The key regulators of lineage commitment and differentiation in haemopoi-esis remain unknown, and an investigative approach through the study of nature's genetic errors might lead to their discovery.

Using such an approach we have previously described a possible association between defective erythropoiesis and an abnormality of chromosome 11. A case of primary myelofibrosis was identified which showed morphological features of red cell aplasia and failure of circulating erythroid progenitors. The patient had greatly increased numbers of circulating granulocyte-monocyte progenitor cells (CFU-GM). Co-culture of peripheral blood mononuclear cells with irradiated allogeneic normal bone marrow stroma generated increased numbers of CFU-GM compared with controls but failed to generate erythroid progenitors, providing further evidence for an intrinsic defect in eryth-ropoiesis. Our patient exhibited a previously unreported complex karyotype. Only once previously has the absence of erythroid progenitors in primary myelofibrosis been studied in relation to cytogenetic abnormalities, and this case also indicated a complex karyotype which shared with our case a defect on chromosome 11. The relevance of this to our case was 11q—with the break point at 11q13. A literature review showed that the proto-oncogene SEA (S13 avian erythroblastosis oncogene homolog) maps to the 11q13 region and we intend to study the possible role of this gene at the molecular level.

Visceral leishmaniasis in human immunodeficiency virus disease

I read the very interesting article by Curry, Turner, and Lucas.1 It is important to include visceral leishmaniasis (VL) as an opportunistic protozoan infection in patients infected with HIV, as it is common in endemic areas.2 Although the authors comment on some of the salient diagnostic and therapeutic features of VL in patients with HIV, the description is perhaps incomplete as it is based on only a few cases. Over the past few years, most cases of VL in HIV infection have been reported from Spain, probably due to a high incidence of both VL and HIV infection and a greater awareness about this association once the first few cases had been described. In 1990 two independent studies described the features of VL in many cases of HIV.3,4 More recently, our own retrospective study of 47 patients, including most cases that had appeared in Spain up to the beginning of 1990, has updated that experience.5

Although in some patients VL can be the cause of weight loss and disease, suggesting that 92.5% of the patients were inavres- sional drug misusers suggested that the disease could be transmitted intravenously (which is an occasional route of transmission in immunocompetent). VL can occur at all stages of HIV infection, but 77% of patients were classified as stage IV with CD4 counts below 4 ×10⁹/L, suggesting that it is com-mon in the later stages of HIV infection. Most patients present with a clinical picture of "classic" Kala-azar with fever, hepatospleno-megaly, and pancytopenia, but some are asymptomatic and are diagnosed incidentally. In all patients Leishmania amastigotes were demonstrated in the spleen, liver, and in the serum of 94.5% of the patients who had a biopsy. In four cases L. amastigotes were found in normal skin, and were also present in skin lesions of 40% of sarcoma in one case. This is not a surprising finding.6 L. amastigotes are found in normal skin in immunocompetent patients with VL. The two most remarkable findings were the absence of VL in HIV seropositive patients, such as tuberculosis or Pneumocystis carinii, showing a good response to initial treatment but persisting as latent chronic disease. Conventional treatment with antimony drugs was not effective in half the cases. We report two therapeutic approaches are needed. Production of α-interferon (α-IFN) and other lymphpoines are essential to activate macrophages, but these are defective in both VL and HIV infections. Adjuvant treatment with γ-IFN has been effective in animals, in experimental models of human macrophages, and in refractory VL in immunocompetent patients.7 These results suggest that γ-IFN could also be effective in VL in HIV seropositive patients and a therapeutic trial is currently being conducted in Spain. VL is an opportunistic infection in HIV seropositive patients who is found increasing- ly often. It must be suspected and precluded in patients presenting with fever, hepatosplenomegaly, and pancytopenia, and even in less ill patients living in or travelling to endemic areas.8

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