than disseminated. After the introduction of highly active ART (HAART), we again observed cases of MAC disease presenting in a similar way, and we also observed infectious and/or inflammatory disease caused by other pathogens [4–6]. As argued elsewhere [4, 7], we believe that these disease events also reflected the restoration of pathogen-specific immune responses, and we have proposed the term “immune restoration disease” (IRD) to designate them [4, 7–9].

We agree with Cheng et al. that IRD must be studied further, if diagnostic methods and clinical management are to be improved. In particular, the immunopathogenesis of IRD should be clarified, because it may be different for different pathogens. Immune reconstitution may be a factor, but it is notable that disease episodes usually occur during the first 12 weeks of therapy [4, 7], before substantial immune reconstitution has taken place. Redistribution of antigen-specific T cells (reviewed in [10]) and/or reversal of T cell immunosuppressive factors, such as the effect of Th2 cytokines [11], might have a more immediate effect. Disease episodes are associated with the restoration of pathogen-specific immune responses, as exemplified by MAC or Mycobacterium tuberculosis IRD (often referred to as paradoxical reactions), and possibly by cytomegalovirus or hepatitis B and C virus IRD (reviewed in [7]). Therefore, pathogen-specific immune responses, may be the critical factor and could occur without substantial changes in CD4 T-cell counts.

It is likely that other factors are also involved, since many patients experience restoration of pathogen-specific immune responses, as indicated by their ability to cease prophylactic therapy for opportunistic infections [10], without the occurrence of IRD. Preliminary evidence from our studies suggests that proinflammatory cytokines may be implicated (S.F. Stone, P. Price, N.M. Keane, R.J. Murray, M. A. French, unpublished data). Furthermore, we have demonstrated that particular HLA haplotypes correlate with herpesvirus IRD [12] which suggests that immune mechanisms are different for different pathogens.

A case of IRD that develops after a patient had begun receiving antiretroviral therapy may be misinterpreted either as an opportunistic infection resulting from persistent immunodeficiency or as the effect of drug toxicity. In either case, therapy might be stopped prematurely. It is therefore important to establish diagnostic criteria and methods of managing this complication of antiretroviral therapy. It is also important to recognize that mycobacterial IRDs may be a complication of ART consisting of only 1 or 2 nucleoside analogues [7] and that they may become a disease-management problem in developing countries that have a high prevalence of mycobacterial coinfections.

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months before the onset of the disease, he was doing well and had undergone no procedure.

At the time of admission to the hospital, clinical examination of the patient revealed a temperature of 40°C and crepitant rales in the basis of the right lung. Laboratory tests disclosed the following values: a low WBC count of 1.8 cells/mm³ (92% neutrophils and 3.9% lymphocytes), a platelet count of 44 cells/mm³, a mild elevation of transaminase levels, and a C-reactive protein level of 101 mg/L. Abdominal ultrasonography revealed a 30-mm × 50-mm hypoechoegenous mass of the liver without dilatation of biliary tracts; the mass was confirmed as a probable liver abscess by means of CT. The CT scan also showed segmentary portal vein thrombosis close to the abscess, hepatosplenomegaly, and pulmonary tuberculosis sequelae. Neither diverticulitis nor an abscess of the large or small intestine was seen.

On day 3, the patient began receiving empirical antibiotic therapy with iv cepotaxime, 1 g t.i.d., and iv metronidazole, 0.5 g t.i.d., in association with preventive anticoagulant treatment with enoxaparine, 20 mg q.d. On day 7 after admission to the hospital, 3 of 3 cultures of blood samples yielded F. nucleatum that was susceptible to penicillin, cepotaxime (MIC, 0.25 mg/L), and metronidazole. Because the patient had persistent fever, transesophageal echocardiography was performed on day 10; no vegetation was shown. Scintigraphy of leukocytes labeled with technetium 99m–hexamethylpropyleneamine oxime showed no other site of infection (in particular, at the site of placement of the vena cava filter). Apyrexia was slowly obtained after 2 weeks of treatment. On day 24, antibiotic therapy was switched to oral metronidazole, 0.5 g t.i.d., for the next 2 weeks; preventive anticoagulation was stopped; and the patient was discharged from the hospital.

At the end of the 5 weeks of treatment, the patient was asymptomatic, and abdominal ultrasonography showed that the liver abscess had completely disappeared. Attempts to determine the portal of entry of infection revealed only uncomplicated colonic diverticles, whereas the findings of dental, airways, and small intestine explorations were normal.

Hematologic explorations performed 3 months after admission to the hospital revealed thrombocytopenia of central origin, T and B lymphocytopenia (497 cells/mm³ and 17 cells/mm³, respectively) with normal repartition among the CD4⁺, CD8⁺, CD45 RA⁺ and CD45 RO⁺ cell subsets, normal proliferation in response to mitogens, and a low percentage of IL-2–producing T cells. Results of protein electrophoresis, immunofixation, analyses of serum levels of Ig and IgG subclasses, and karyotype and hemostasis explorations were normal.

The thrombogenic ability of Fusobacterium necrophorum has been well known [2, 3] since it was first described by Lemierre in 1936 [2]. Our report confirms that F. nucleatum may display similar lesions. To our knowledge, this is the second report of F. nucleatum septicemia associated with portal vein thrombosis and the first report of F. nucleatum associated with hepatic abscess.

Like Bultink et al. [1], we considered 2 hypotheses for the pathogenesis of the pylephlebitis. First, even if hemostasis exploration did not reveal any abnormality, recent infection of a preexistent portal vein thrombosis cannot formally be excluded in our patient, who had a history of repeated pulmonary embolisms. Second, recent pylephlebitis was, however, considered very probable, because the thrombosis was in contact with the hepatic abscess, and because it disappeared with antibiotic therapy but without curative anticoagulation. In both hypotheses, an intestinal portal of entry of infection was suspected, on the basis of the natural history of hepatic abscesses and pylephlebitis [4], the lack of oropharyngeal disease, and the presence of colonic diverticles (even if such a finding is not uncommon in patients older than 60 years).

F. nucleatum can bind human plasminogen, which may be activated into plasmin by host plasminogen activators. The locally generated proteolysis is involved in tissue damage and penetration through host barriers, thereby causing serious infections [5]. F. nucleatum also displays in vitro hemagglutination activity on human erythrocytes [6], which may occur in vivo. The host immune response to F. nucleatum is mainly a T cell response [6], which may have been weak in this observation. As a matter of fact, our patient had lymphocytopenia that met the criteria for idiopathic CD4⁺ T lymphocytopenia [7, 8], a rare immunodeficiency syndrome. Of interest, F. nucleatum infections have also previously been observed in association with other immunodeficiencies [5, 9, 10].

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CORRESPONDENCE • CID 2001:32 (15 January) • 327


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