BRIEF REPORTS

Clinical Efficacy of and Switch from T Helper 2 to T Helper 1 Cytokine Profile After Interferon α2a Monotherapy for Human Echinococcosis

Alveolar echinococcosis (AE) is severe liver disease caused by the cestode Echinococcus multilocularis [1]. Previous studies have demonstrated that T helper (Th)2 lymphocyte responses might be associated with a progressive form of AE in humans and that Th1 lymphocyte responses might be associated with resistance [2–4]. Peripheral blood mononuclear cells (PBMCs) from patients with AE have been shown to produce very high levels of IL-10, even without any stimulation, and relatively low levels of IFN-γ [3]. Because current therapeutic strategies are not satisfactory for AE, immunomodulation has been proposed as an alternative. Positive but limited efficacy of IFN-γ therapy on the development of AE lesions, especially metastases, in experimental mice [5] and in two patients with advanced disease [6, 7] has been described. To our knowledge, no experience with IFN-α has ever been reported. The aim of the present study was to examine the effect of IFN-α2a on AE lesions and the production of IL-10, IL-4, IL-5, and IFN-γ by PBMCs from a patient who received IFN-α2a treatment for concomitant chronic hepatitis due to hepatitis C virus (HCV).

A 34-year-old woman from eastern France underwent partial hepatectomy for AE diagnosed in 1983. Treatment with albendazole (10 mg/[kg·d]) had to be withdrawn in 1985 because of febrile urticaria with elevated levels of serum aminotransferases. HCV infection was then found by serology and reverse transcriptase PCR analysis. In 1995, treatment with recombinant IFN-α2a (Laroféron, Roche, Neuilly sur Seine, France) was initiated at a dosage of 3 million U three times weekly. Although the liver AE lesions had regularly increased in size during the 10 years without treatment, a small but significant reduction in the AE lesion size (from 5.5 × 3 cm at the initiation of treatment to 5 × 2.8 cm) was observed after 3 months of IFN-α2a treatment. After 1 year, IFN-α2a treatment was withdrawn. The size of the AE lesions stabilized, and HCV hepatitis was in remission.

During the treatment period, IL-10, IFN-γ, IL-4, and IL-5 secretions by PBMCs were similar to those measured in PBMC supernatants from non-IFN-α2a-treated patients with AE (figure 1). However, 6 months and 1 year after the 1-year treatment period, IL-10, IL-4, and IL-5 secretions were decreased after stimulation with E. multilocularis fluid antigen [3] or phytohemagglutinin and even in nonstimulated PBMC cultures (figure 1). Expression of IL-10 and IL-4 mRNA was markedly reduced in the patient’s PBMCs, especially CD8+ T cells (data not shown). Conversely, IFN-γ secretion was markedly enhanced, whatever the stimulation (figure 1).

These results suggest that IFN-α2a administration may contribute to the switch from the Th2-type cytokine profile characteristic of progressive AE to a Th1-type cytokine response able to...
enhance immunologic protection against disease progression. Reduction in lesion size is rare in AE, even after benzoimidazole therapy, and stabilization of lesions is usually considered an indicator of impairment of parasitic growth and of clinical improvement [1, 8]. This observation could indicate an early effect of IFN-α2a on the cells that infiltrate the lesion locally, before it may be apparent for the circulating cells.

Although a potential additive effect of HCV itself on the cytokine profile cannot be ruled out [9], this unique observation of a concomitant infection by E. multilocularis and HCV in the same patient treated with IFN-α2a strongly suggests that IFN-α2a could be used as an immunomodulatory agent in human AE. IFN-γ and IL-12 are the only cytokines that have been experimentally tested for their therapeutic effects and were shown to be partially [5] or totally [10] effective for controlling parasitic growth. Because of the extreme severity of AE and its resistance to chemotherapy [1], experimental studies and clinical trials should be developed to test the usefulness of IFN-α2a as treatment of AE.

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References


There was a 2 × 2-cm lesion present on the patient’s right upper arm. The surface was scabbled over and friable. There was a halo of indurated tissue beneath the lesion that was nontender. No axillary or epitrochlear lymphadenopathy was noted.

Biopsy of the lesion revealed only necrotic tissue with overlying skin. Analysis of imprints showed numerous acid-fast bacilli. Therapy with isoniazid, rifampin, and ethambutol was started based on identification of acid-fast bacilli on the touch preparation.

The three punch biopsy sites coalesced to form an ulcerated lesion 2 weeks after the procedure. One month after biopsy, the lesion became superinfected. Right axillary lymphadenopathy was noted. There was no change in the size of the lesion; however, the halo of induration was absent. Cephalexin was added to the patient’s therapeutic regimen for 2 weeks, which resulted in clearing of the superinfection.

Six weeks after biopsy, the lesion was essentially unchanged with the exception of the appearance of a sinus. Since there was no response to isoniazid, rifampin, and ethambutol, therapy with trimethoprim-sulfamethoxazole was initiated. After 3 weeks of trimethoprim-sulfamethoxazole therapy, the lesion decreased, but the patient developed a severe rash, urticaria, and pruritus. Therapy was changed to tetracycline hydrochloride (500 mg q.i.d.). Two weeks later, because of severe nausea, therapy was changed to doxycycline (100 mg b.i.d.). A CT scan of the arm was obtained at this time (figure 1). After 5 months of doxycycline therapy, the lesion had significantly decreased in size and crusted over.

Acid-fast bacilli were recovered after 2 months of incubation on chocolate agar at 30°C. The organism was identified as Mycobac-