in the first hour (Westergren), Hb was 12 gr%, WBC 12,500 with 11% bands; the rest of the blood count, routine serum biochemistry, protein electrophoresis and a general analysis of the urine were normal. Rheumatoid factor, ANA, anti DNA, anti-cardiolipin, anti-β2GPI and ANCA were negative. Serum complement levels were normal. Serological tests for hepatitis B and C, Parvovirus, Shigella, Salmonella, Chlamydia and HIV were negative and repeated blood and urine cultures were sterile. Skin biopsy was denied by the patient. Cultures from vaginal swabs grew Gardnerella vaginalis. The diagnosis of Gardnerella vaginallis-induced reactive arthritis and dermatitis was posed. Treatment with small doses of corticosteroids (10 mg prednisone a day) and Flagyl (500 mg a day) was followed by a gradual reduction of the arthritis, dermatitis and vaginal discharge. Ten days later the temperature was normal, the pathological dermal and musculoskeletal signs have disappeared and the patient resumed her previous activities. Later, she was lost to follow up, therefore a planned examination of the patients was males and in one case the specimen taken from the patient’s wife. The previous activities. Later, she was lost to follow up, therefore a planned examination of the trigging agents for reactive arthritis and Reiter’s syndrome. The B. Shne Department of Rheumatology, Rambam Medical Center and School of Medicine, Technion, Israel Institute of Technology, Haifa, Israel. Please address correspondence to: Daniel Schapira, MD, DSc, Department of Rheumatology, Rambam Medical Center, POB 9602, 31096 Haifa, Israel.

References

Treatment of recurrent oral aphthous ulcers with etanercept
Sirs,
Thalidomide was banned worldwide in 1962 after its teratogenic effects had been demonstrated. However, more recently thalidomide has received increased attention due to its anti-inflammatory and immunomodulatory properties mediated primarily by tumor necrosis factor-alpha (TNF-alpha) inhibition. Thalidomide is currently being used for treatment of graft host disease, clinical manifestations of erythema nodosum leprosum, systemic lupus erythemato-
sus, Behçet’s syndrome, multiple myeloma spontaneous and secondary aphthous ulcers. Thalidomide has gained orphan drug status for several specific indications, including treatment of recurrent aphthous stomatitis in AIDS patients (1,2). Thalidomide is associated with several adverse effects besides teratogenicity. Peripheral neuropathy, often associated with paresthesias muscle weakness and drowsiness has been described frequently in patients receiving thalidomide. In the past five years several patients attending our Clinic have shown prompt response to the use of 100 to 200 mg of thalidomide for the treatment of recurrent aphthous stomatitis. Two patients, one with probable and the other with classical Behçet’s syndrome had the medication discontinued, one due to severe drowsiness and the development of neuropathy, and the other due to severe muscle weakness and mood changes.

The exact mechanism of action of thalidomide is not known. It affects TNF-alpha function by selectively affecting TNF-alpha mRNA without directly affecting other cytokines (3,4). On the two patients mentioned above the cessation of thalidomide was followed by recurrence of aphthous lesions two and three months after discontinuation of the medication. We offered the patients the possibility of receiving etanercept, an expensive form of TNF inhibition currently in use for patients with severe forms of rheumatoid arthritis (5,6). Both patients started to receive etanercept 25 mg subcutaneously twice a week. The lesions disappeared on both patients, one after three weeks and the other after five weeks, after a six-month period we discontinued the injections and in both patients the ulcers again developed five and seven weeks after, respectively. Etanercept was reintroduced with quick clinical response similar to the first period of treatment (1).

Etanercept was first introduced in clinical practice as a medication able to reduce signs and symptoms and inhibit the progression of rheumatoid arthritis. Additional indications are now being explored including psoriasis, psoriatic arthritis and vasculitides. Our findings appears to be the first report of the potential beneficial use of etanercept in patients with severe recurrent aphthous ulcers, and confirms observations reported by Robertson et al., showing that infliximab, another anti-TNF drug, is useful in the treatment of recalcitrant orogenital ulceration of Behçet’s syndrome where other forms of therapy are not available or contraindicated (7).

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Letters to the Editor

References


Lack of evidence for herpesvirus, retrovirus, or parvovirus infection in Henoch-Schonlein purpura

Sirs,

Henoch-Schonlein purpura (HSP) is an idiopathic form of vasculitis which occurs mainly in childhood. Its clinical features include palpable purpura, arthritis, abdominal pain, and nephritis (1). In contrast to most other vasculitides, HSP is usually acute and self-limited. Some studies indicate variation in incidence according to season and familial clusters have been reported (2). In addition, characteristic immunologic findings can often be demonstrated, including IgA deposits in tissues (3). These observations have led to the view that HSP represents an aberrant immune response to infection.

To examine the possible role of viral infection in HSP, we used sensitive PCR-based techniques to detect evidence of human herpesviruses (HHV) or retroviruses in patients’ peripheral blood. We chose to study these viruses because of reports of their involvement in HSP (4) and other forms of vasculitis (5), and their potential immunomodulatory effects. Because several reports have emphasized a possible association between parvovirus B19 and HSP, patient sera were also examined for parvovirus DNA.

Patients age 2-16 years were recruited at Hadassah Hospital, Mount Scopus during 1996-2001. The diagnosis of HSP was established according to American College of Rheumatology criteria. The study was approved by an Institutional Review Board, and informed consent of participants was obtained. Twenty-eight patients were examined for parvovirus and HHV, and 8 were studied for retroviruses. Sera were cryopreserved at -70°C until assay. Genomic DNA was prepared from PBMC or buffy coat by a proprietary technique (Quiagen DNA blood kit).

HHV assays were performed on DNA substrates by a nested PCR technique using degenerate primers to amplify a relatively conserved sequence of herpes viral DNA-directed DNA polymerase, as described elsewhere (6). The assay could detect as few as 10 copies of HHV-1, and HHV-3, 4, 5, and 6A DNA in very low amounts. Amplification of an unrelated DNA sequence was performed as a positive control for each specimen. Parvovirus DNA was detected by nested PCR as previously described (7). This method detects parvovirus DNA in approximately 85% of sera from immunocompetent patients containing IgM and antibodies to parvoviruses. We found it could detect 10 parvovirus copies in human serum. Sera were screened for reverse transcriptase (RT) activity, which is a generic marker of all retroviral particles using Amp-RT, an ultrasensitive PCR-based RT assay, as previously described (8). Sera were also tested for infection with human T-cell lymphotropic virus types 1 and 2 (HTLV-I and -2) by antibody screening using an HTLV-I/2 purified virus EIA spiked with recombinant HTLV-I p21E antigen (Organon-Teknika, Durham, NC).

Using these techniques, we found no evidence for HHV, retrovirus, or parvovirus infection in this group of patients. Despite epidemiologic studies pointing to a possible link between HSP and infection, a causal role for specific agents has been difficult to establish. Numerous case reports have described HSP associated with serologic evidence of recent infection by viruses including varicella, adenovirus, rubella, human immunodeficiency virus, and hepatitis viruses (1). In addition, several reports have described HSP associated with IgM antibodies to parvovirus, but these reports were not confirmed in subsequent larger studies (10). Our result is in keeping with these later reports. Amp-RT detects cell-free retrovirus. Intracellular HTLV may not be detected by Amp-RT, but antibodies to these viruses were not found in sera tested. Taken together, the results suggest that retroviruses are not a common cause of HSP.

The duration of herpesvirus infection varies according to the specific virus, lasting up to several weeks. While we found no HHV in peripheral blood, serologic studies will be necessary to exclude the possibility that a post-infectious immunologic response to one of these viruses may contribute to the pathogenesis of some cases of HSP.

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