EXPERIENCE AND REASON—Briefly Recorded

“In Medicine one must pay attention not to plausible theorizing but to experience and reason together. . . . I agree that theorizing is to be approved, provided that it is based on facts, and systematically makes its deductions from what is observed. . . . But conclusions drawn from unaided reason can hardly be serviceable; only those drawn from observed fact.” Hippocrates: Precepts.

(Short communications of factual material are published here. Comments and criticisms appear as Letters to the Editor.)

Acute Monarticular Arthritis Caused by Herpes Simplex Virus Type I

Numerous viruses have been described as potential causes of acute arthritides.1-3 Recently, herpes simplex virus (HSV) type I has been implicated as a possible etiologic agent in acute arthritis in adults.4-6 The purpose here is to review evidence of the role of herpes viruses in acute arthritis and to report the isolation of HSV from the synovial fluid of a child with arthritis.

CASE REPORT

A 6-year-old girl of Mexican descent was admitted to the hospital because of the acute onset of pain and swelling in her right knee. The patients had been well until four days prior to admission when she developed fever and painful oral lesions. Fever persisted through the day of admission; however, oral lesions were no longer painful and appeared to be healing. On the day of admission, the patient complained of right knee pain and she refused to walk. Physical examination revealed a well-developed, well-nourished child. She appeared apprehensive and guarded against movement of her right leg. Her temperature was 39.4°C. Several 1-2-mm shallow ulcers covered by grayish-yellow exudate were noted on the anterior tongue. A single crusted ulcer was present on the mucosal surface of the lower lip. The pharynx was erythematous, and multiple 1x1-cm anterior cervical lymph nodes were palpated. The right knee was in the position of mild flexion. The knee was warm, swollen, and markedly tender, but not erythematous. The parapatellar fossae were obliterated, and the patella was ballotable. The passive range of motion at the knee was between 30 and 100 degrees of flexion.

Roentgenograms showed a right knee effusion with normal bony structures. The hemoglobin level was 12.1 g/dL. The WBC count was 7,000/μL with 60% neutrophils, 7% band forms, 28% lymphocytes, and 5% monocytes. The ESR (Westergren) was 41 mm/h. An ECG was normal for age.

Aspiration of the knee effusion yielded 7 mL of turbid, straw-colored fluid of low viscosity. The synovial fluid protein level was 4.1 g/dL; the lactic dehydrogenase (LDH) level was 987 U/L; and the glucose level was 33 mg/dL. A simultaneous blood glucose level was 80 mg/dL. Microscopic examination revealed many WBCs, of which 90% were lymphocytes and 10% were neutrophils. Methylene blue and Gram-stained smears of the fluid revealed no bacteria.

Further investigations included antistreptolysin, antihyaluronidase, and anti-DNAse antibody titers which were within normal limits. Measurement of the third component of complement was also normal. A PPD skin test was negative. Antinuclear antibodies and rheumatoid factor (latex fixation) were absent. No bacterial pathogens were isolated from a throat culture. Synovial fluid cultures were negative for bacteria. Herpes simplex virus was isolated from the synovial fluid, as evidenced by the formation of a cytopathic effect compatible with HSV infection on both human embryonic kidney and human lung cells. Attempts at resolation from the original specimen were successful. An increase in serologic response from 1:4 to 1:256 was detected by complement fixation after a period of 25 days. By immunofluorescence, the first passage isolate was characterized as type I.

The patient was treated with bed rest, elevation of the leg, and aspirin. She became afebrile in 12 hours, walked with mild discomfort at 48 hours, and showed complete resolution of pain and swelling by the fourth day. Physical examination at 1 and 2 months after hospitalization revealed no abnormalities.

DISCUSSION

This report documents the occurrence of herpes simplex type I virus arthritis in a child. The virus
was isolated from synovial fluid. A significant increase in antibody titer was also observed.

Several cases of suspected HSV arthritis in older patients have been reported. Naraqi et al described a 30-year-old woman who developed stomatitis, disseminated vesiculopustular lesions, and arthritis after nephrectomy and splenectomy. Blood and oral cultures grew HSV type I. However, a joint aspirate was not productive of fluid for viral culture. Friedman et al reported a 26-year-old woman with fever, ankle pain and swelling, uterine and adnexal tenderness, and a vesiculopustular rash. Arthrocentesis was unproductive; however, HSV type I was cultured from skin vesicles. In these cases, it was unclear whether the arthritis was caused by a viral infection of the joint or was an inflammatory response to infection at another site. The etiology of ankle swelling in the latter case is further complicated by antibiotic therapy prior to bacterial cultures and by a positive ANA noted on follow-up examination.

From a third patient, HSV was isolated from the synovial fluid. Shelley and Friedman et al both described an 18-year-old wrestler with a swollen knee and a diffuse vesicular rash (herpes gladiatorum). Arthrocentesis yielded 0.5 mL of fluid from which HSV type I was isolated. As with our patient, mononuclear cells predominated in the synovial fluid.

In the past decade, other herpes viruses have been associated with acute arthritis. Adebonojo described a 7-year-old girl with ankle pain and swelling during an episode of infectious mononucleosis, diagnosed by a positive Monospot test and suggestive clinical findings. Friedman et al isolated cytomegalovirus from the synovial fluid of a patient who developed knee pain after renal transplant. There are also numerous reports of arthritis as a complication of chickenpox. Priest et al reviewed these cases and documented the isolation of varicella-zoster virus from the synovial fluid of an 8-year-old child with chickenpox and a tender, swollen knee.

Unlike the previously described patients with diffuse vesicular eruptions, the child in this report had a mild, resolving stomatitis. The occurrence of viremia with mucocutaneous HSV infections is well-documented, and we suggest that the patient’s arthritis is secondary to a hematogenous seeding of the joint during an episode of stomatitis. The viremia does not appear to be related to the magnitude of skin and mucous membrane involvement.

This patient’s clinical presentation recalls features of arthritis caused by varicella as summarized by Shuper et al and Priest et al. Varicella arthritis occurs most often in young girls. Typically, large joints are preferentially affected, lymphocytes predominate in the synovial fluid, and inflammation resolves rapidly and without sequelae. This clinical profile may be typical of arthritis caused by herpes viruses. We suggest that HSV arthritis should be considered in the differential diagnosis of acute nonbacterial arthritis, particularly when these clinical features are present.

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