Secondary Syphilis Presenting With Arthritis, Hepatitis, and Glucose Intolerance

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The prevalence of syphilis in the US population has not changed over the last ten years, with approximately 20,000 cases reported each year. Though less common in the antibiotic era, the disease remains quite visible and still deserves the name originally given to it—the great imitator. This case report serves as a reminder to consider testing for this disease whenever evaluating a condition in which the more obvious diagnoses are ruled out.

CASE REPORT

A 53-year-old woman presented with a four- to six-week history of bilateral joint pain and stiffness in the knees, shoulders, fingers, wrists, and elbows. Associated symptoms included malaise, anorexia, 20-lb weight loss, low-grade fever, polyuria, and polydipsia. She had taken several doses of naproxen one month before her initial visit, but had discontinued the medication when she developed a rash over her extremities and trunk. She had not worked for one month because of malaise and pain, and was essentially nonfunctional at the time of initial visit.

The patient had been seen by a local rheumatologist and referred to the Family Practice Center after an inconclusive evaluation including a normal complete blood count, erythrocyte sedimentation rate of 90 mm/h, a positive antinuclear antibody with a titer of 1:50 with a coarse speckled pattern, a negative rheumatoid arthritis latex, sheep cell agglutination test, and anti-deoxyribonucleic acid antibody test. Her serum glucose level was 13.8 mmol/L (249 mg/dL) with an alkaline phosphatase of 10.5 μkat/L (631 U/L), serum glutamic oxaloacetic transaminase of 0.82 μkat/L (49 U/L), and creatine phosphokinase of 0.83 μkat/L (50 U/L). There was no history of rheumatic fever, lupus erythematosus, or arthritis except for a two-year history of intermittent gout. Medications included methyldopa, 500 mg, and hydrochlorothiazide, 25 mg daily, both of which she had discontinued one month prior because of anorexia secondary to the infection. She had been taking indomethacin intermittently for gouty arthritis.

The patient had worked for the past 21 years as a surgical nurse. She was divorced and had not been sexually active for 11 months before her visit.

Physical examination was remarkable for marked tenderness, redness, warmth, and bilateral swelling of the shoulders, wrists, and knees. A faint maculopapular rash was present over the back and upper extremities. New laboratory studies revealed a platelet count of 660×10^9/L (660×10^3/mm^3), and fractionation of the alkaline phosphatase suggested a liver source. A chest roentgenogram and abdominal computerized tomography (CT) scan were normal.

The patient was treated with NPH insulin, 10 units daily, and sulindac, 200 mg twice daily. A rapid plasma reagin, sequential multiple automated chemistry (SMAC), repeat rheumatology screening test, and cervical culture were obtained. Subsequently a reactive rapid plasma reagin test was reported with a titer of 1:256, and microhemagglutination was positive for treponemal pallidum. All previous rapid plasma reagin tests obtained in conjunction with this patient's employment had been nonreactive. The most recent determination had been made five months earlier, but these results were not immediately available and thus initial staging was difficult. A lumbar puncture was performed, which showed increased protein of 0.96 g/L (96 mg/dL), increased glucose of 9.4 mmol/L (169 mg/dL), and a white cell count (WBC) of 4.4×10^9/L (4.4×10^6/μL), with 0.34 polymorphonuclear cells and 0.66 mononuclear cells. A VDRL test of the cerebrospinal fluid was negative.

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TABLE 1. SURVEILLANCE SEROLOGY FOLLOWING TREATMENT

VDRL*	Recommended guidelines—Quantitative VDRL at 1, 3, 6, 12 months following treatment
	Course—75% seronegative at 1 year in primary stage 75% seronegative at 2 years in secondary stage 80% will remain positive indefinitely if treated in later stage
	Treatment goal—≥ Fourfold decline in titer

** Rapid plasma reagin may be substituted*
Note: Fluorescent treponemal antibody-absorption and microhemagglutination-treponemal pallidum tests generally remain positive following treatment

The patient was treated with 2.4 million units of benzathine penicillin intramuscularly. Within two days the joint pain, inflammation, and constitutional symptoms were dramatically improved. The patient returned to work full time three weeks after initial therapy. Dramatic improvement was noted by the patient, her family, and her health care providers. Despite the extreme embarassment the patient felt due to the nature of her disease, she was overjoyed at feeling well enough to work and play again. A daughter who lives in town was quite supportive of the patient throughout the illness.

Two months after the initial presentation, the insulin was replaced with an oral agent. After six months the patient required no further hyperglycemic therapy. Six months following treatment, the rapid plasma reagin test was reactive with a titer of 1:8, alkaline phosphatase was 1.2 μkat/L (70 U/L), erythrocyte sedimentation rate was 13 mm/h, and fasting glucose was 5.0 mmol/L (90 mg/dL).

COMMENT

The manifestations of secondary syphilis are extensive. The most common include generalized lymphadenopathy, skin rash, and constitutional symptoms of fever, malaise, and anorexia. This stage generally begins six weeks after healing of the primary chancre, and a VDRL titer of greater than or equal to 1:32 is expected.[1]

The patient had no history of a primary lesion. Transmission was most likely through occupational exposure, although case review failed to reveal a source. The incidence of such transmission is rare, and the lesion is generally an atypical sore on the hand.[2]

The secondary rash of syphilis may easily be mistaken for a drug reaction, since most patients are initially treated with nonsteroidal anti-inflammatory agents for their joint pains. This co-occurrence may prevent or delay accurate diagnosis, as occurred in this case.[3]

Joint manifestations of syphilis were described soon after the identification of Treponema pallidum permitted accurate diagnosis in 1905.[1] Much earlier lay literature had noted rheumatism as a consequence of the "pockes."[2] The etiology of the joint pain includes osteitis, periostitis, synovitis, and neuropathy. Gummata of the joints are rare. Synovitis, the primary cause of rheumatic complaints in secondary syphilis, usually presents as a migratory polyarthralgia or arthritis involving bilateral knees, shoulders, hips, and proximal phalangeal joints. Pain is typically most severe at night, exacerbated by heat, and eased by movement.[4–7]

The diagnosis rests on serologic testing and is confirmed by the response to appropriate therapy, ie, long-acting penicillin. As in this patient, relief of joint pain is rapid and dramatic. Dark-field examination of synovial fluid may occasionally reveal spirochetes, but this test is invasive and frequently does not reveal the organism.[8] Recommended serologic surveillance following treatment is shown in Table 1.

The presence of predominately elevated alkaline phosphatase without apparent cause in this patient led to a costly evaluation, but has been well described in syphilitic hepatitis.[9,10]

The patient described here had significant elevations of white cell count and protein, but negative findings on cerebrospinal fluid serologic testing. Neurosyphilis is characterized by increased cell count, increased protein, and reactive VDRL on cerebrospinal fluid, but a negative VDRL does not exclude the diagnosis.[11] In view of the nonreactive rapid plasma reagin test five months earlier and the time course implicated by the rash, the patient had secondary syphilis rather than neurosyphilis, which occurs in the tertiary stage. Indeed, approximately 30 percent of cerebrospinal fluid examinations in secondary syphilis reveal these nonspecific findings.[1]

This patient developed significant glucose intolerance during her illness. Normal glucose levels obtained five and 11 months earlier essentially excluded occult disease. With resolution of the infection, the intolerance resolved. Glucose intolerance has not been specifically reported in secondary syphilis.

Sir William Olser stated, "Know syphilis in all its manifestations and relations and all other things clinical will be added unto you." This case clearly illustrates the diversity of its presentation and reminds one of its role as a great impostor in medicine. Serologic tests for syphilis are essential in evaluating arthritis and hepatitis of uncertain cause.

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