Case Report

Paraneoplastic Polyarthritis in an Ovarian Teratoma

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ABSTRACT. A 34-year-old woman presented to the rheumatology clinic with severe low back pain and arthralgia; later she developed bilateral knee pain and swelling, with limitation in ambulation and minimal improvement with nonsteroidal antiinflammatory drugs. Two weeks later she developed pain on the volar aspect of the right wrist and on the hypothenar region of the right hand. Examination showed swelling and tenderness of the right hypothenar region, tenderness and decreased flexion and extension of the right wrist, and bilateral knee effusions. The combination of arthritis and tenosynovitis raised the possibility of an ovarian tumor. A pelvic ultrasound revealed a complex, hyperechoic ovarian mass consistent with a cystic teratoma. Four weeks after removal of the teratoma, the polyarthritis and related symptoms resolved without therapy. (J Rheumatol 2004;31:1854–7)

Key Indexing Terms:
PARANEOPLASTIC SYNDROME ARTHRITIS TENOSYNOVITIS
OVARIAN NEOPLASM TERATOMA

Paraneoplastic syndromes are systemic manifestations of tumors that are neither explained by the tumor itself nor by its metastases. These syndromes are almost always indicative of a malignancy[1] and rarely have benign tumors been associated with paraneoplastic manifestations[2-5]. Paraneoplastic syndromes have been associated with ovarian cancer[6-9]. We describe a woman with inflammatory polyarthritis and tenosynovitis with resolution after the resection of a benign ovarian teratoma.

CASE REPORT

A 34-year-old woman presented to the rheumatology clinic with a dull and severe low back pain awakening her from sleep, more pronounced in the morning, and exacerbated by walking. Two days later she developed pain and swelling in the knees with limitation in ambulation, and difficulty in climbing stairs and standing. Treatment with nonsteroidal antiinflammatory drugs produced minimal improvement. Three months earlier she had noted hypersomnolence, fatigability, night sweats, and periodic mouth ulcers. She also had dry eyes and frequent painful mouth ulcerations, but denied fever, changes in menstrual pattern, or sexually transmitted diseases. The history was significant for allergic rhinitis and one episode of iritis treated topically 3 years before. She gave a history of allergy to codeine and to penicillin. Medications included fexofenadine, oral contraceptives, and naproxen for treatment of arthritis. The family history was not contributory. She denied alcohol consumption, cigarette smoking, and the use of illicit drugs.

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Examination showed that she was in no acute distress. Her height was 5'0 and her weight was 118 lbs. She was afebrile and her blood pressure was 128/85. She had a few shallow ulcerations in the mouth, slight thyromegaly, and discrete, painless, mobile lymphadenopathies less than 0.5 mm in diameter. Cardiopulmonary examination was normal. The abdomen was minimally tender in the right lower quadrant. Trace pitting edema to mid shin in both lower extremities was present. Musculoskeletal examination showed warmth in both knees with small bilateral effusions. Mobilization of the knees elicited pain on extreme flexion. Neurologic examination was unremarkable. Laboratory studies revealed hemoglobin 14 g/100 ml, white blood cell count $7.6 \times 10^3/mm^3$, and erythrocyte sedimentation rate 26 mm/h. Alkaline phosphatase, ALT, AST, and urinalysis were normal. Antinuclear antibodies by indirect immunofluorescence and rheumatoid factor were negative.

Two weeks after the initial visit, she developed severe pain in the volar aspect of the right wrist, and pain and swelling on the right hypothenar region, below and above the wrist. Examination again showed mild bilateral knee effusions. The volar aspect of the right wrist was swollen and exquisitely tender to touch on the flexor carpi ulnaris tendon and the hypothenar region. Slight motion of the wrist elicited pain.

On the basis of seronegative arthritis and history of remote iritis, a reactive arthritis was suspected. Alternatively, the combination of arthritis and tenosynovitis suggested the possibility of an ovarian tumor. Gynecologic examination showed the vulva and cervix without abnormalities and right ovarian fullness and tenderness. Transvaginal and color Doppler sonography of the pelvis revealed a right hyperechoic attenuating ovarian mass, measuring 4.6 × 3.8 × 3.0 cm. The ovarian mass had a central anechoic cystic component without discernible vascularity.

Pathologic examination of the ovarian mass, removed by laparoscopy, was consistent with a mature ovarian cystic teratoma containing hair, skin, and bony tissue. Microscopy findings were notable for keratinizing squamous epithelium, sebaceous glands, hair (Figure 1), and an area with perivascular inflammation (Figure 2).

Western blots[10,11] of nuclear extracts of HeLa cells showed high titer (1:500) IgG antibodies recognizing antigens of 36, 65, and > 120 kDa (Figure 3).

Four weeks after laparoscopic removal of the teratoma, the arthritis and tenosynovitis subsided without therapy, with resolution of all systemic symptoms. Two years after removal of the teratoma she continued to be asymptomatic. Examination and laboratory studies, including a repeat immunoblot, were normal.

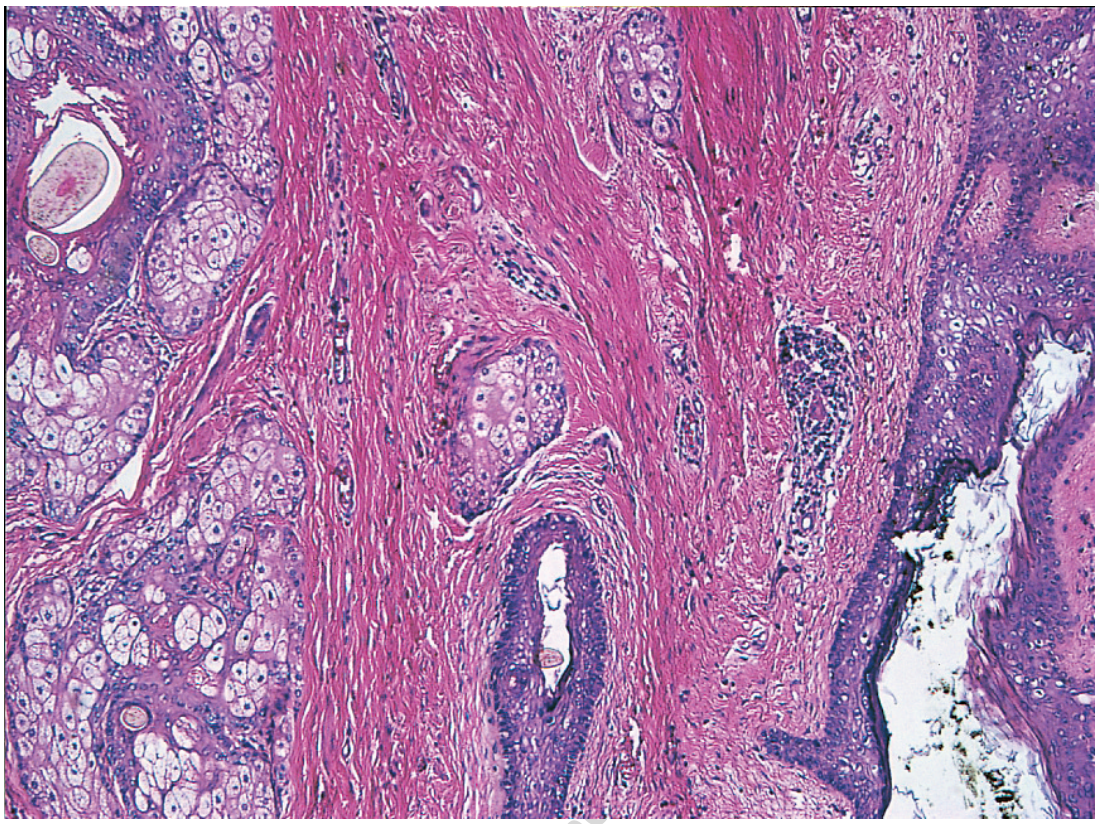

Figure 1. Photomicrograph of mature cystic teratoma. Nests of keratinizing squamous epithelium with underlying sebaceous glands are present. Note the hair follicle in the lower right hand corner. Stained with hematoxylin and eosin; magnification ×400.

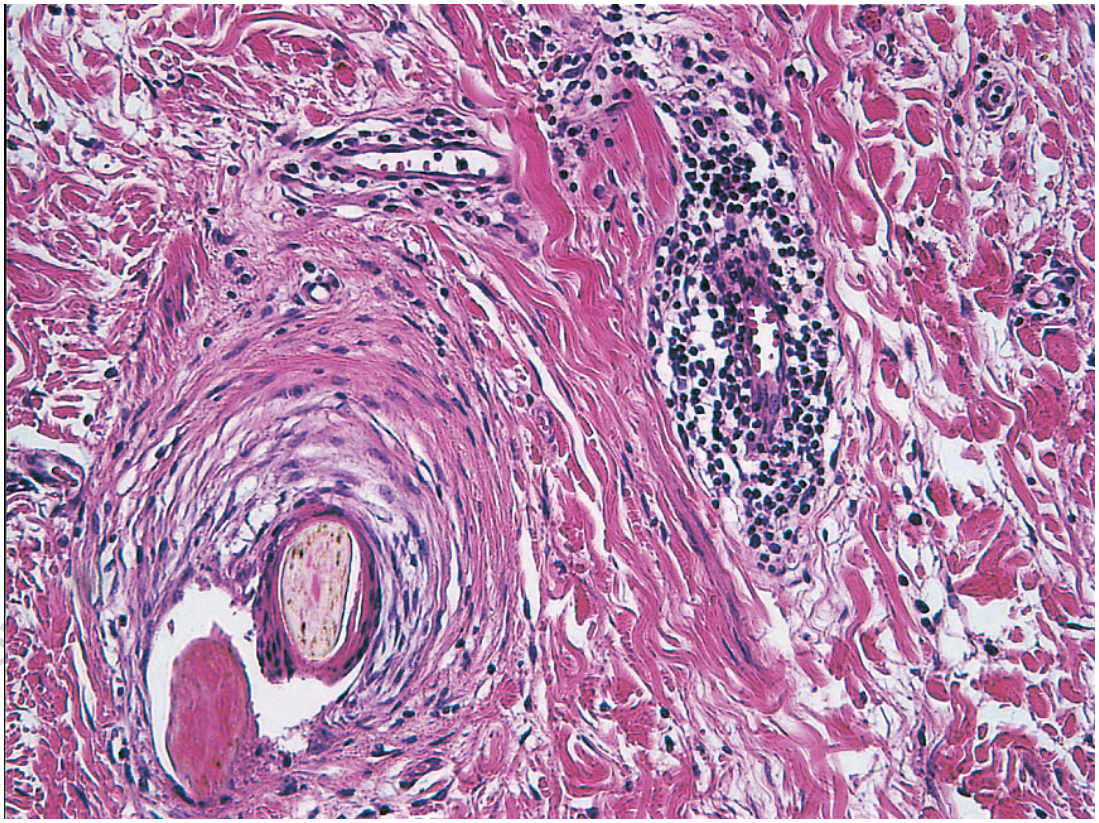

Figure 2. Photomicrograph of mature cystic teratoma showing a perivascular lymphocytic reaction.

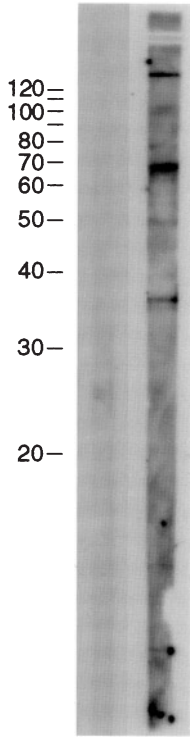

Figure 3. Immunoblot of nuclear extract of HeLa cells. Blots were probed with control serum (a) and with patient serum (b) at 1:500 dilution. Relative scale on the left (kDa).

DISCUSSION

The spontaneous resolution of an inflammatory seronegative polyarthritis with tenosynovitis, after the excision of a benign ovarian tumor, suggested that our patient had paraneoplastic manifestations triggered by a benign ovarian teratoma. Although musculoskeletal symptoms related to benign ovarian tumors have not been reported, polyarthritis, tenosynovitis, and palmar fasciitis were initially reported by Medsger in 1982 in association with ovarian carcinomas[6]. Subsequently, the syndrome of polyarthritis and palmar fasciitis was also reported with other non-ovarian carcinomas such as pancreatic and small-cell lung cancer and in association with the use of antituberculous drugs[7,12,13]. This syndrome is characterized by morning stiffness and involvement of multiple joints, most frequently the metacarpophalangeal and interphalangeal joints, preceding the diagnosis of malignant disease. Palmar changes including local warmth and erythema and diffuse swelling are prominent features in this syndrome. Although some improvement may occur with removal or debulking of the tumor[6,7] the prognosis is usually poor, since the malignant tumors are often advanced[14]. The arthritis and tenosynovitis reported here in a benign ovarian teratoma lacked the palmar fasciitis[6], but its rapid resolution after debulking of the tumor with no therapy suggests a cause-and-effect relationship between the benign ovarian teratoma and the picture of arthritis and tenosynovitis. The coexistence of a clinical picture of systemic lupus erythematosus and ovarian seminoma, with rapid disappearance of the symptoms after removal of the tumor, has also been reported[15]. Other germ cell tumors, such as malignant sacrococcygeal teratoma, have also presented with polyarthritis[16].

Benign teratomas have been associated with a variety of diverse conditions including autoimmune hemolytic anemia[3], limbic encephalitis[4,5,22], and endocrine syndromes such as sexual precocity[17], hyperthyroidism and hyperadrenalism[2,18]. The clinical features of hemolytic anemia and reversible paraneoplastic limbic encephalitis are thought to be mediated by an autoimmune reaction to the contents of the teratoma[3-5]. Although immunological mechanisms have been suggested as the basis for the polyarthritis-palmar fasciitis syndrome, its pathogenesis is poorly understood[19]. Antibodies to a number of tissue antigens have been identified in patients with ovarian tumors[20,21]. The antibodies reacting with HeLa antigens in our patient are compatible with, but not proof of, an autoimmune pathogenesis, which remains speculative.

This report suggests that disabling arthritis and tenosynovitis appearing in a young woman can be associated with a benign ovarian teratoma despite the absence of gynecological symptomatology.

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