Psoriatic Arthritis in a Military Aviator

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Psoriatic arthritis is a chronic spondyloarthropathy whose pathogenesis is unknown. We present a case of a naval flight officer who presented with chronic psoriatic arthritis, which ultimately became well controlled with etanercept treatment. The naval flight officer was granted military aeromedical waivers for psoriatic arthritis, cutaneous psoriasis, and chronic medication use. We also review the medical literature on psoriatic arthritis disease and etanercept and discuss their aeromedical implications in military aviation.

Keywords: psoriasis, seronegative spondyloarthropathy, sausage digits, etanercept, methotrexate, dactylitis.

IT HAS LONG BEEN recognized by the aeromedical community that rheumatologic diseases affecting the musculoskeletal system can negatively impact an aviator's duties. Joint deformity, discomfort, and limited range of motion can interfere with functional and performance capability in the cockpit (11). However, it is also important that aeromedical specialists be aware that some rheumatological diseases and their associated therapies can adversely affect other organ systems, such as the ophthalmologic and dermatological systems (4). One such rheumatological disease is psoriatic arthritis (PsA), a rare chronic seronegative autoimmune inflammatory arthritis of the joints associated with psoriasis (2,6). Clinical manifestations of PsA range from mild arthritis to severely destructive disease (4). The military flight surgeon must determine the severity of the disease and decide how it will affect function, mission success, and safety of flight. Severe disease often results in permanent disqualification, while mild disease may merit consideration of a waiver. Treatment options of the disease also merit aeromedical evaluation due to possible side effects. The following is a case report of an experienced naval flight officer (NFO) who initially presented with PsA 12 yr ago. Since his diagnosis, he has undergone multiple treatment regimens with varying success as the disease has progressed.

CASE REPORT

A 35-yr-old Caucasian F/A-18D United States Marine Corps NFO with over 2000 total flight hours reported 12 yr of joint problems in his upper and lower extremities. The patient's medical complaints began in 1993 and initially consisted of recurrent, non-traumatic, painless right knee swelling. He underwent a diagnostic arthroscopy which showed mild inflammation, but revealed no cause. He was managed with nonsteriodal anti-inflammatory drug (NSAID) therapy and the knee swelling resolved. In 1995, the patient started to have pain and swelling of the second toe on his left foot and a new scaly rash on his scalp. After initial evaluation by his flight surgeon, he was referred to internal medicine and dermatology for further assessment. The internal medicine specialist diagnosed monoarticular arthritis and suggested a possible diagnosis of PsA. However, the dermatologist diagnosed his new skin lesions as either seborrheic dermatitis or a mild form of early psoriasis. The patient was put on a NSAID for his monoarticular arthritis and a topical corticosteroid for his scalp lesions. Both problems resolved with their respective therapies.

In 1996, new red, mildly pruritic skin lesions slowly started appearing all over the patient's body. He also complained of new joint pain in the left foot, left wrist, and right hand. He denied any history of sexually transmitted diseases, bowel problems, and trauma to involved joints. He denied symptoms of fever, chills, eye trouble, oral ulcers, dysuria, chest pain, and back or neck pain. There was no family history of skin disease, arthritis, or gout. Physical examination revealed a well-nourished, medium build man. There were classic psoriatic skin lesions on his scalp, back, gluteal cleft, glans penis, elbows, and knees varying from 0.5–4.0 cm in size (**Fig. 1 and 2**). There was pitting and discoloration in his fingernails (**Fig. 3**). The first, second, third, and fourth toes of the left foot, the left wrist, and the third metacarpophalangeal joint of the right hand showed swelling, tenderness, and slightly reduced range of motion. The involved toes of the left foot were sausage shaped. The remainder of his exam was normal. The patient was then referred to dermatology and rheumatology. Numerous laboratories were drawn. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were both elevated. Both rheumatoid factor (RF) and antinuclear antibody tests were negative. HLA-B27 was positive. Complete blood count (CBC), chemistry panel, liver function tests, and urinalysis were normal. Rapid plasma reagin, HIV, purified protein derivative,

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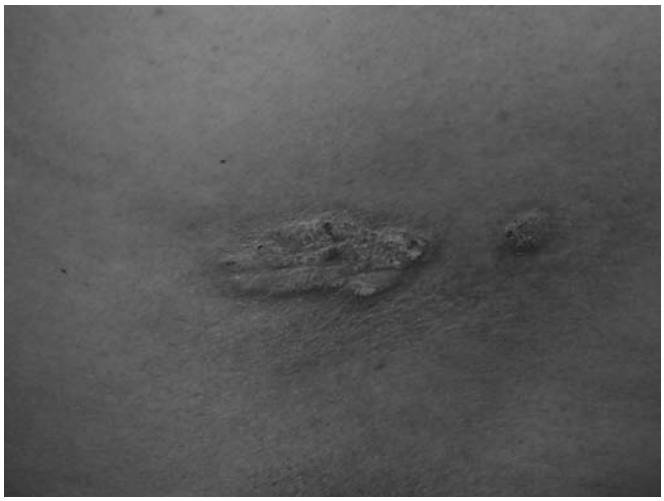

Fig. 1. Two psoriatic skin lesions on the lumbosacral area. They are well-demarcated erythematous plaques with silvery, adherent, and dry scale.

lupus anti-coagulant, and Lyme titer were all negative. Radiological films of both hands and feet were normal. The patient was diagnosed with PsA. Nearly complete resolution of joint symptoms and control of skin lesions was accomplished with use of diclofenac sodium and topical corticosteroids. Military aeromedical waivers for psoriatic arthropathy, cutaneous psoriasis, and chronic NSAID use were recommended and granted. While on this therapy, ESR and CRP levels returned to normal. The patient remained stable for 7 yr.

In 2003, he experienced acute pain, swelling, and stiffness of the left hand. The patient also complained of discomfort in both wrists. His psoriatic skin and nail lesions were stable. Exam showed the second, third, and fourth digits were sausage shaped and tender. There was reduced range of motion in the involved digits. The remainder of his exam was normal. ESR and CRP were elevated. Radiographs of his left hand demonstrated mild erosive changes and slight narrowing of the proximal interphalangeal joints. His rheumatologist advanced his therapy regimen to methotrexate, prednisone, celecoxib, and folic acid. Only marginal results were seen. Etanercept 25 mg subcutaneously twice weekly was added to the regimen with dramatic improvement of the patient's arthritic symptoms within a few months. Involved joint pain, swelling, and tenderness resolved. Additionally, his psoriatic skin lesions decreased in redness and itchiness, but the skin plaques only slightly decreased in size. Fingernail findings disappeared. ESR and CRP levels returned to normal. Overall, he reported a "90% improvement" in joint symptoms and an improved level of energy. Later, methotrexate, prednisone, and celecoxib were removed from therapy, but the patient continued to improve with etanercept alone. A waiver was requested and granted for etanercept therapy.

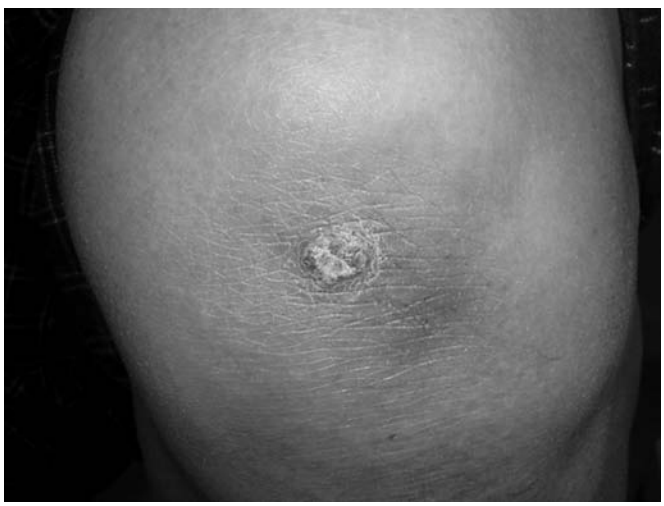

Fig. 2. A nickel-sized psoriatic plaque on the left knee. In psoriasis, skin lesions typically involve the extensor surfaces (e.g., elbows, knees), scalp, lumbosacral area, and umbilicus.

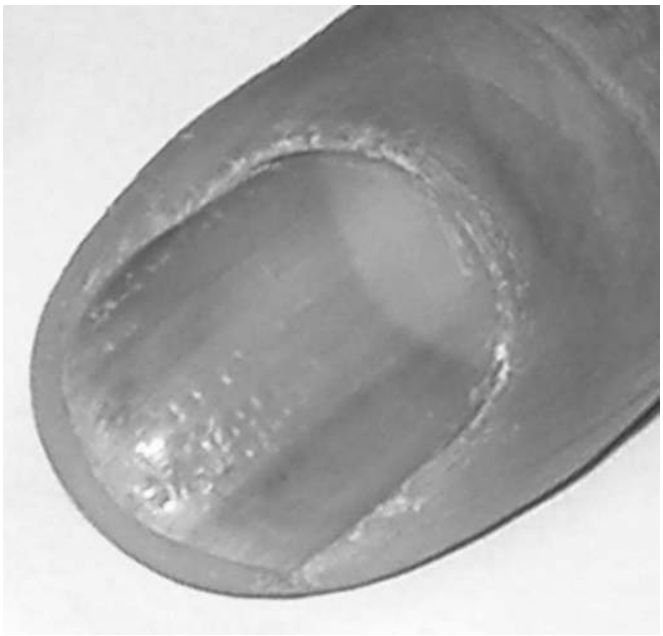

Fig. 3. Nail pitting, onycholysis, and orange-yellow discoloration. Many cases of psoriatic arthritis are associated with nail changes. This can be a helpful clue in the diagnosis of psoriatic arthritis.

The NFO has been in remission for the past 17 mo. He currently reports minimal discomfort and stiffness of the right shoulder, left third proximal interphalangeal joint, and left second, third, and fourth metacarpophalangeal joints. There has been no joint swelling, effusions, tenderness, and new or progressive pain. He has had no arthritic flare-ups while on etanercept therapy. His skin psoriasis lesions are stable with topical therapy, but are still better compared with pre-etanercept therapy. He currently flies without difficulty from PsA, psoriasis, or medication side effects.

DISCUSSION

Psoriasis is a common chronic, recurrent autoimmune disease of the skin affecting approximately 2% of the population in the United States. The etiology is unknown, but it is likely an interplay between genetic, environmental, and immunologic factors (5). PsA is a complication of psoriasis, with an estimated prevalence of 6% to 42% among psoriasis patients (2,7). It is more

common in Caucasians and affects men and women equally (3,5). It is classified as a spondyloarthropathy and defined as a seronegative autoimmune inflammatory arthritis of the joints associated with psoriatic skin lesions (2,4,6). It affects the ligaments, tendons, fascia, and joints, which results in symptoms such as stiffness, joint deformity, reduced range of motion, pain, swelling, and tenderness of the joints and surrounding soft tissue (3,7,10). Onset and progression of symptoms may be insidious, or it may develop acutely as a severely destructive arthritic disease (4,10). Psoriasis may occur before, simultaneously, or after the onset of arthritis. Typically though, psoriasis lesions predate arthritis by approximately 10 yr. PsA onset is usually around 35–55 yr, but can occur at any age (2,3,5,6). Our patient was atypical because he initially presented with right knee involvement before the development of psoriatic skin lesions at the age of 23 yr.

There are five clinical subgroups of PsA: distal interphalangeal joint arthropathy, asymmetrical oligoarthritis (inflammation of four or less joints), symmetrical polyarthritis (inflammation of five or more joints), spondylitis, and arthritis mutilans (extremely severe form). Oligoarticular and polyarticular are the most common types (2,3). Classically, the distal interphalangeal joints are affected, but any joint can be affected (6). Dactylitis (sausage shaped digits) affects up to 30% of patients (2,3,6). Pathology can also occur in the enthesis, which leads to inflammation at tendon or ligament insertions into bone (6). The long-term course of PsA is unpredictable, with periods of relapse and remission (3,7). Our patient initially presented with the oligoarthritis type, but with disease progression it later became the polyarthritis type.

No specific diagnostic tests are available for PsA (3,7). Diagnosis is based on a complete history and examination, presence of psoriasis, an inflammatory arthritis, absence of serological tests for RF, and characteristic radiological features of involved joints (3,7,9). The skin exam should look for classic psoriasis skin lesions which appear as well-demarcated erythematous papules and plaques with silvery, adherent, and dry scale. Commonly involved areas of the body include the extensor surfaces, scalp, umbilicus, lumbosacral area, gluteal cleft, and genitalia (5). Nail involvement, such as pitting, onycholysis, thickening, dystrophy, and orange-yellow discoloration can also be a helpful clinical clue because 80% of PsA patients have these findings (2,3,5,9,10). Anemia of chronic disease and elevated levels of ESR or CRP are nonspecific laboratory findings which support the diagnosis (4). In fact, ESR and CRP are frequently used to measure inflammation activity and track PsA's response to therapy (7). HLA-B27 testing is of limited value (4). During our patient's workup for PsA, he had psoriatic skin lesions and nail findings. Laboratory findings were HLA-B27 positive, RF negative, CBC normal, CRP elevated, and ESR elevated. Radiological films were initially normal. But as the disease progressed, radiological films later became positive for arthritic changes.

The differential diagnosis for PsA includes all the spondyloarthropathies (anklylosing spondylitis, reactive arthritis, inflammatory bowel disease associated spondyloarthropathy, undifferentiated spondyloarthropathy), osteoarthritis, rheumatoid arthritis, gout, septic arthritis, and Lyme disease (3). Differentiating PsA from the other diseases can be done through a complete history, physical examination, and some additional laboratories or radiological tests as needed. Difficult cases may be referred to a rheumatologist.

There is limited information on PsA waivers in the U.S. aeromedical community. PsA is not specifically addressed in the aeromedical waiver guides of the Navy, Army, and Federal Aviation Administration (13,14). All military services state psoriasis is considered disqualifying mainly because skin lesions can interfere with protective aviation equipment (helmet, mask, safety garments) and treatment options have potential side effects (12,13,14). Only the Air Force comments that PsA cases should be evaluated by a rheumatologist because of the unlikelihood of waiver (12). According to each of these agencies, chronic medication use requires individualized evaluation of its side effects prior to approval for flight duty. Our patient's job performance is more at risk from PsA than psoriasis. His psoriasis has not interfered with protective gear use and there have been no adverse effects from topical therapy.

The first concern for PsA is the patient's ability to perform flight duties. If our patient was a pilot, a waiver would not have been recommended. Pilot (class I) duties involve skillful control of an aircraft. PsA involvement of the hands and feet may cause joint deformities, pain, limited range of motion, decreased manual dexterity, and fatigue, which would interfere with precision flight, mission accomplishment, and safety. However, as a designated NFO (class II) our patient will always fly with a pilot to form a flight crew and will not have control of the aircraft. A NFO's primary duties are managing complex communications and operating advanced tactical systems, which poses less of a threat to flight safety than actual control of the aircraft. Naval pilots are also trained to perform the NFO's duties if required. In the case of a student NFO or applicant, a waiver would not be recommended because of the unpredictable course of PsA and training cost. In general, more consideration is given to designated personnel because of their valuable experience. Our patient was a designated NFO with approximately 400 h of flight time when he was first diagnosed with PsA. Therefore, he merited consideration of a waiver because of his experience in military operations and his favorable response to therapy. Other class II and III applicants, students, and designated aviation personnel (e.g., aircrew, flight surgeon, air traffic controller) would merit consideration because their duties do not involve control of aircraft and arthritic disease would have less impact on flight safety compared with pilots and NFOs. But a waiver would be dependent on disease severity and its effects on their flying duties.

Another aeromedical concern is PsA therapy. Treatment of PsA typically starts with a NSAID, which improves swelling and tenderness (4). This is especially true in patients with mild disease that only involves a few joints and occurs episodically (3,7). On initial pre-

sentation, our patient only required use of diclofenac sodium, a NSAID. If used chronically, there lies the risk of gastrointestinal ulcers and bleeding. But generally speaking, NSAIDs are safe drugs to use in the aviation environment. However, as our patient's disorder progressed, he required use of methotrexate. For progressive or moderate to severe PsA, disease-modifying therapy may be required. This therapy consists of two classes, traditional disease-modifying antirheumatic drugs (DMARDs) and new biological response modifiers. Traditional DMARDs include methotrexate, retinoids, cyclosporine, glucocorticosteroids, and other medications (2,10). These medications are effective against PsA, but most of them have significant side effects, which makes them incompatible with flying duties (10,12,14). A waiver would not have been recommended for our patient if he continued methotrexate therapy. Methotrexate has multiple side effects which can adversely affect mission accomplishment and safety. Some of the more frequently reported side effects include ataxia, hallucinations, malaise, fatigue, dizziness, nausea, abdominal upset, liver damage, anemia, and leukopenia (8,14). Methotrexate also requires regular laboratory tests (CBC, liver function tests, and periodic liver biopsy) to ensure that the patient's health is not being endangered (8). The new biological agents also demonstrate clinical effectiveness, but do not require regular laboratory surveillance and have significantly less side effects compared with the traditional DMARDs. Biologic drugs are made from living tissue and proteins and are specifically designed to act on the body to correct abnormal mechanisms that lead to disease. The biologics include etanercept, alefacept, efalizumab, and infliximab, but only etanercept is approved by the U.S. Federal Drug Administration for PsA treatment (10).

Etanercept is also the only biologic approved by the U.S. Federal Drug Administration for plaque psoriasis therapy. Etanercept is a tumor necrosis factor (TNF) α receptor fusion protein, which is stored under refrigerated conditions and administered subcutaneously. It binds to TNF and blocks its interaction with cell receptors. TNF is a biological natural cytokine involved in normal and abnormal inflammatory and immune responses. Etanercept has shown significant clinical improvement in PsA joint symptoms, psoriatic skin lesions, quality of life, and function. It has also slowed disease progression. Etanercept treatment has generally been safe, with few side effects, and has been well tolerated by patients. The most common side effect is a mild, local skin reaction at the injection site occurring in approximately one-third of patients, but this usually resolves with continued therapy. Since anti-TNF therapy affects the immune system, which is overactive and causing disease in the case of PsA, it may also affect the host's ability to fight infections and cancers. However, controlled studies have shown infection rates are not increased with etanercept compared with placebo. Nonetheless, there have been rare cases of lymphoma and tuberculosis associated with TNF antagonists. Other rare unforeseen toxicities include demyelinating disease, lupus-like syndrome, and worsening or new-onset congestive heart failure. The causal relationship of anti-TNF agents and some of these illnesses is unclear. If any of these complications develop, treatment should be discontinued and the patient should be carefully evaluated. The risk for these rare complications can be decreased by screening potential etanercept therapy patients for these disorders. For example, caution should be used in patients with tuberculosis exposure, demyelinating disease, and cardiovascular disease (1). Our patient learned how to store etanercept, reconstitute it, and administer self-injections without difficulty. He has been on etanercept therapy for 17 mo and has had significant improvement in his PsA symptoms, nail findings, and modest improvement in his psoriatic skin lesions. Laboratory results are normal with therapy. He has not developed any injection skin reactions, side effects, or complications. As a military aviator, he is restricted to global areas with medical facilities that can provide refrigerated storage of etanercept and provide tools for sterile reconstitution and injection twice weekly. He is prohibited from deploying to areas without these services.

Finally, there are aeromedical concerns regarding the complications associated with PsA. Common extra-articular complications of spondyloarthropathic disease include iritis, urethritis, mucous membrane lesions, aortic root dilation, and diarrhea (2). Approximately 30% of PsA patients have inflammatory ocular involvement, including conjunctivitis in 20% and acute anterior uveitis in 7% (3). Uveitis causes visual problems which can impair performance and affect flight safety (12,14). Aortic root dilation can lead to aortic insufficiency, which is considered disqualifying (14). This can adversely affect aviation duties, especially in tactical aircraft requiring anti-G straining maneuvers (12). Skin and mucosa lesions of the head, face, and oral mucosa can interfere with the use of the helmet and oxygen mask. The combination of chronic psoriasis and PsA can lead to physical discomfort, cosmetic disfigurement, and reduced functional capacity (7,10). These multiple factors increase the risk for psychological disease because of stress, reduced quality of life, and stigmatization issues (12). Therefore, in addition to regular follow-up to monitor for disease progression and side effects from therapy, we recommend vigilantly examining a patient's full physical and mental makeup periodically to look for any direct or indirect complications. We also recommend continual follow up with a rheumatologist and dermatologist.

In conclusion, this case illustrates that psoriasis is not a simple disease in the military aviation community. There is risk of developing PsA. Medications used to treat psoriasis and PsA may have adverse side effects. Thus, both disease and therapy may negatively affect aviation duties, mission accomplishment, and safety. These factors must be appraised before a waiver is recommended. Even after a waiver is approved, in addition to periodically following the patient for psoriasis and PsA progression, the flight surgeon must monitor for physical or mental complications from both diseases. Any complications from psoriasis, PsA progression, extra-articular spondyloarthropathic manifesta-

tions, and treatment must be thoroughly evaluated to determine the patient's fitness for aviation duties. Flight surgeons must also be aware of the differing requirements of the various classes of military physicals (class I, II, III) as they pertain to their aviation duties. It must be kept in mind that a physical defect, which may be disqualifying for a particular aviation duty, may not be disqualifying for another.

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