Transverse myelitis and chronic urticaria in systemic lupus erythematosus. Case report

Vitorino Modesto dos Santos¹, Érica Correia Garcia², Fabiana Leão Rabelo², Gina Eliane Menezes Haase Lobo³, Maria Aparecida Santos Damasceno⁴.

We report a 40 years old woman with chronic urticaria and acute transverse myelitis associated with systemic lupus erythematosus. The urticaria appeared in her adolescence and after 26 years was followed by photosensitivity, peripheral polyarthritis and acute transverse myelitis, with positive antiphospholipid and antinuclear antibodies. Both chronic urticaria and acute transverse myelitis have been described associated with or appearing as the first manifestation of systemic lupus erythematosus. Transverse myelitis is a rare and still poorly understood condition reported in about 2% of patients with systemic lupus (Rev Méd Chile 2005; 133: 209-213).

(Key Words: Lupus erythematosus, systemic; Myelitis, transverse; Urticaria)

Mielitis transversal y urticaria crónica en el lupus eritematoso sistémico

Se relata un caso de urticaria crónica y mielitis transversal aguda en asociación con lupus eritematoso sistémico en una mujer de 40 años. La urticaria se inició en su adolescencia y, después de 26 años, presentó fotosensibilidad, poliartritis, meningitis aséptica y mielitis transversal aguda, con anticuerpos antifosfolípidos y antinucleares positivos. Se ha descrito urticaria crónica y mielitis transversal en asociación, o como la primera manifestación del lupus eritematoso sistémico. La mielitis transversal es una condición rara y poco comprendida, diagnosticada en cerca de 2% de los pacientes con lupus eritematoso sistémico y, muy frecuentemente asociada con anticuerpos antifosfolípidos. Los autores describen un caso de esta rara asociación y resaltan la necesidad de evaluaciones sistemáticas del diagnóstico en pacientes con urticaria crónica, porque esta condición suele ser una manifestación cutánea de enfermedades sistémicas, la puede anteceder por mucho tiempo y dificultar la correcta caracterización del lupus eritematoso sistémico, correlacionado a la usual corticoterapia prolongada.

Address correspondence to: Prof. Dr. Vitorino Modesto dos Santos. SMPW Quadra 14 Conjunto 2 Lote 7, Casa A. Setor de Mansões Park Way, 71745-140, Brasilia-DF, Brazil. Fax: (0xx55) 61 2330812. E mail: vitormodesto@ig.com.br
Transverse myelitis (TM) is a rare and still poorly understood condition reported in 1-2% of patients with systemic lupus erythematosus (SLE), and is associated with the presence of antiphospholipid antibodies (aPA)1. The diagnosis of SLE must be discarded in patients with chronic urticaria, because urticanform lesions may occur associated with collagen diseases2,3.

Although without clear distinction among the acute and chronic forms and the urticarial vasculitis, Yell JA et al (1966), described occurrence of urticaria in 44% of 73 patients with SLE4. In the study of López de Maturana et al, 72% of 32 patients with pathological diagnosis of cutaneous vasculitis were women, with a mean age of 43.5 years, and palpable purpura, erythematos macules and urticaria were the most frequently observed skin lesions, while connective tissue diseases and systemic vasculitis were the most commonly associated diseases5. Noteworthy, those authors did not find fibrinoid necrosis in 59.4% of their cases associated with systemic diseases and autoimmune disorders, including systemic vasculitis, rheumatoid arthritis, progressive systemic sclerosis and SLE5. As autoimmunity also plays an important role in the development of chronic urticaria associated with SLE2,4,6 and both conditions may be influenced by the use of corticosteroids, the correct characterization of SLE can result delayed or mistaken, favouring eventual diagnostic pitfalls.

We describe a case of TM and aPA positive in a middle-aged woman with SLE, in whom the urticaria was treated with corticosteroids during 26 years before the characterization of this collagen disease. Both, urticaria and TM may constitute an early manifestation of SLE1,7.

CASE REPORT

A 40 years old Brazilian housewife attended to hospital complaining of non-scarring alopecia and ascending paresthesia and paraparesis in the lower limbs which rapidly evolved to paraplegia. She also referred urinary and bowel dysfunction. Beginning at the age thirteen (1976), she related episodes of itching and fugacious reddish papules and plaques in the skin soon after hot baths. Since 28 years of age, these lesions have been recurring at yearly intervals, persisting for 3 to 12 months in spite of the use of corticosteroids and hydroxyzine. Two years later, she noticed photosensitivity and, at 36 years, a spontaneous abortion occurred. In 2002, she developed recurrent headaches and migratory arthralgia involving the temporomandibular, elbow, wrist, metacarpophalangeal, interphalangeal, coxofemoral, knee, ankle and metatarsophalangeal joints, in addition to episodes of asymmetric peripheral polyarthritis, coinciding with a positive HEp-2 rim ANA indirect immunofluorescence test.

On admission, she was conscious and well-oriented, with Cushitoid facies and urticaria lesions (Figure 1) predominantly on the trunk. Body mass index: 25.3 kg/m². Skin temperature was 36.5°C. The heart was rhythmic, 88 bpm, and there were no murmurs. Blood pressure: 140/90 mmHg. The lungs were clear and the respiratory rate 20 ipm. There was a discrete abdominal distension and tympanism, with bilateral sensory abolition below the epigastrium level. The liver and spleen were normal, and there was leg weakness and muscle flaccidity, with ankle jerk and plantar hyporeflexia, mainly on the right side.

Erythrocyte count 4.65 x 10⁶/mm³, hemoglobin 13.4 g/dl, hematocrit 41.5%, mean cell volume 89.2 fl, leukocyte count 17,500/mm³ (neutrophils: bands 11%, segmented 83%, eosinophils and basophils 0%, lymphocytes 14%, monocytes 2%).

FIGURE 1. Aspect of the skin lesions in the dorsum.
platelets 224,000/mm³; Erythrocyte sedimentation rate (ESR) 7 mm. INR 1.03, prothrombin time 12.3 sec, albumin 3.4 g/dL, globulins 2.53 g/dL (α1 0.26, α2 0.51, β 0.68, γ 1.08 g/dL); glucose 104 mg/dL, urea 19 mg/dL, creatinine 0.9 mg/dL, sodium 137 mEq/L, potassium 4.2 mEq/L, magnesium 2.1 mEq/L, chloride 104 mEq/L, calcium 1.21 mmol/L; TSH 1.32 µU/mL; antibodies antithyroglobulin negative, and antiperoxidase 10 U/mL; complement levels C3 134 mg/dL and C4 50 mg/dL; acid α1-glycoprotein 83 mg/dL. Rheumatoid factor and C-reactive protein titers were normal. Anti-Ro (SS-A) and anti-RNP were positive; anti-La (SS-B) and anti-Sm were negative; antibodies anticardiolipin IgM and IgG were positive and the lupus anticoagulant was negative. Hepatitis B and C and syphilis tests were negative. The urinalysis was normal. The cerebrospinal fluid (CSF) was clear, with 8 cells (neutrophils 51%, lymphocytes 47%, monocytes 2%); protein 90 mg/dL, glucose 57 mg/dL, chloride 123 mEq/L; serologic tests were negative for herpesvirus, cytomegalovirus, toxoplasmosis, syphilis, cysticercosis and schistosomiasis; Gram-stained smear and routine cultures resulted negative. The radiographic studies of the thorax, hands and knees revealed normal. The complete neuro-ophthalmologic evaluation resulted normal.

An electroneuromyography study showed absence of motor units recruitment in the lower right limb, without signs of peripheral neuropathy. The uncontrasted computed tomography of thoracic spinal cord resulted normal, while in magnetic resonance imaging (MRI) the T2-weighed images after gadolinium disclosed multiple focal areas of hyper signal, aspect suggestive of spinal cord demyelinating neuropathy (Figure 2). Moreover, the nerve conduction evoked responses showed normal responses to visual and auditory stimuli, and dysfunction of the sensory fast conducting fibers mainly in right side of spinal topography. In addition, the T2-weighed and FLAIR images of the cranium with gadolinium revealed multiple bilateral focal areas of abnormal enhancement in the white matter, more conspicuously in the posterior parietal lobes and in the left temporal lobe, a finding compatible with demyelization and vasculitis (Figure 3).
The skin biopsy disclosed edema, lymphangiectasia, perivenular infiltrate predominantly of mononuclear cells, some degranulated mast cells and rare eosinophils (Figure 4). The direct immunofluorescence tests with IgA, IgG, IgM and C3 were negative and leukocytoclasia, fibrinoid necrosis and deposits of immunocomplexes were not found in the sample. The diagnoses of chronic urticaria and transverse myelitis associated with SLE were well established. The treatment for TM was initiated immediately after the establishment of this diagnosis, in order to halt eventual progression of cord compression, and consisted of pulse therapy with methylprednisolone (20 mg/kg/day) during five days, which resulted in rapid clinical improvement. The patient remains symptomless and she is under outpatient surveillance.

**DISCUSSION**

Although urticaria can not be considered among the diagnostic criteria for SLE, this condition may represent the first complain in persons that further have developed the classical features of SLE\(^7\). Our patient received prednisone for long-standing treatment of chronic urticaria, and presented SLE 26 years after the onset of the cutaneous lesions. More recently, she developed signs and symptoms indicative of myelopathy\(^1,8,9\) associated to SLE, characterized by acute bilateral signs and symptoms of motor disturbance and sphincter dysfunction; well defined upper level of sensory disturbance; elevated proteins and pleocytosis in CSF; exclusion of spinal cord compression by MRI; and progression to nadir into the period of 3 weeks after the onset of symptoms.

Neuropsychiatric changes occur in about 80\% of patients with SLE; seizures and psychosis are diagnostic criteria and the most frequent features\(^8,10\), in addition to anxiety and depression, dementia, deficit of cranial nerves, headache, peripheral neuropathy, cerebellar dysfunction, chorea, Guillain-Barre syndrome, strokes, aseptic meningitis, and myelopathy\(^1,8,10\).

In this patient, the lupus anticoagulant was negative, and the anticardiolipin antibodies were positive. In general, the aPA may be detected in 30-50\% of patients with SLE\(^1,8\), while the incidence of aPA in SLE patients with TM has been somewhat higher (55-64\%)\(^1\).

We emphasize the unusual long evolution (26 years) of skin changes before at least four diagnostic criteria for SLE could be fulfilled. Our patient showed 1) photosensitivity; 2) arthritis involving more than two peripheral joints; 3) immunologic disorder (IgG and IgM anticardiolipin, anti-RNP and anti-Ro antibodies); 4) antinuclear antibody in the absence of drug use; in addition to neurological disorders (aseptic meningitis and transverse myelitis)\(^1,8,11\), and the chronic urticaria\(^7\). Brey et al (2002) found neuropsychiatric syndromes associated with SLE (NPSLE) in 80\% of 128 patients\(^10\). Although aseptic meningitis and TM were not characterized in the subjects of that study, the role of NPSLE syndromes includes aseptic meningitis and myelopathy\(^1,8,11\).

With respect to urticaria, a possible concern could be the hypothesis of Schnitzler’s syndrome (SS)\(^12\), characterized by fever; arthritis and bone pains, associated with urticarial vasculitis (UV) due to autoimmune diseases as SLE. In fact, she presented skin lesions aggravated by sunlight and lasting more than 36 hours, in addition to aseptic meningitis and anti-Ro (SS-A) antibodies positive, suggesting the presence of UV\(^4,7\). However, differing from this case, in SS occurs enlargement of...
liver, spleen and lymph nodes, high ESR and globulin changes; moreover, UV is usually seen in patients with a more severe disease\(^4\), in which skin lesions characteristically show leukocytoclasia\(^3,5\). Our report emphasizes the need of systematic diagnostic evaluations in patients with chronic urticaria, because this condition constitutes a feature of some cutaneous vasculitis\(^5\), may antecede and can hinder the correct characterization of systemic diseases favouring diagnostic pitfalls, in special after long-standing treatment with corticosteroids.

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Transverse Myelitis: Symptoms, Causes and Diagnosis

1 author:

Joanne Lynn
The Ohio State University

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Transverse Myelitis: Symptoms, Causes and Diagnosis

Joanne Lynn, M.D.

Transverse myelitis (TM) is a neurologic syndrome caused by inflammation of the spinal cord. TM is uncommon but not rare. Conservative estimates of incidence per year vary from 1 to 5 per million population (Jeffery, et.al., 1993). The term myelitis is a nonspecific term for inflammation of the spinal cord, transverse refers to involvement across one level of the spinal cord. It occurs in both adults and children. You may also hear the term myelopathy, which is a more general term for any disorder of the spinal cord.

Clinical Symptoms

TM symptoms develop rapidly over several hours to several weeks. Approximately 45% of patients worsen maximally within 24 hours (Ibid.). The spinal cord carries motor nerve fibers to the limbs and trunk and sensory fibers from the body back to the brain. Inflammation within the spinal cord interrupts these pathways and causes the common presenting symptoms of TM which include limb weakness, sensory disturbance, bowel and bladder dysfunction, back pain and radicular pain (pain in the distribution of a single spinal nerve).

Almost all patients will develop leg weakness of varying degrees of severity. The arms are involved in a minority of cases and this is dependent upon the level of spinal cord involvement. Sensation is diminished below the level of spinal cord involvement in the majority of patients. Some experience tingling or numbness in the legs. Pain (ascertained as appreciation of pinprick by the neurologist) and temperature sensation are diminished in the majority of patients. Appreciation of vibration (as caused by a tuning fork) and joint position sense may also be decreased or spared. Bladder and bowel sphincter control are disturbed in the majority of patients. Many patients with TM report a tight banding or girdle-like sensation around the trunk and that area may be very sensitive to touch.

Recovery may be absent, partial or complete and generally begins within 1 to 3 months. Significant recovery is unlikely, if no improvement occurs by 3 months (Feldman, et. al., 1981). Most patients with TM show good to fair recovery. TM is generally a monophasic illness (one-time occurrence); however, a small percentage of patients may suffer a recurrence, especially if there is a predisposing underlying illness.

Causes of Transverse Myelopathy and Myelitis

Transverse myelitis may occur in isolation or in the setting of another illness. When it occurs without apparent underlying cause, it is referred to as idiopathic. Idiopathic transverse myelitis is assumed to be a result of abnormal activation of the immune system against the spinal cord. A list of illnesses associated with TM includes:

Table: Diseases Associated with Transverse Myelitis
**Parainfectious** (occurring at the time of and in association with an acute infection or an episode of infection).

**Viral:** herpes simplex, herpes zoster, cytomegalovirus, Epstein-Barr virus, enteroviruses (poliomyelitis, Coxsackie virus, echovirus), human T-cell, leukemia virus, human immunodeficiency virus, influenza, rabies

**Bacterial:** Mycoplasma pneumoniae, Lyme borreliosis, syphilis, tuberculosis

**Postvaccinal** (rabies, cowpox)

**Systemic autoimmune disease**

- **Systemic lupus erythematosis**
- **Sjogren's syndrome**
- **Sarcoidosis**

**Multiple Sclerosis**

**Paraneoplastic syndrome**

**Vascular**

- **Thrombosis of spinal arteries**
- **Vasculitis secondary to heroin abuse**
- **Spinal arterio-venous malformation**

The cause of idiopathic transverse myelitis is unknown, but most evidence supports an autoimmune process. This means that the patient's own immune system is abnormally stimulated to attack the spinal cord and cause inflammation and tissue damage. Examples of autoimmune diseases which are more common include rheumatoid arthritis, in which the immune system attacks the joints, and multiple sclerosis, in which myelin, the insulating material for nerve cells in the brain, is the target of autoimmune attack.

TM often develops in the setting of viral and bacterial infections, especially those which may be associated with a rash (e.g., rubeola, varicella, variola, rubella, influenza, and mumps). Approximately one third of patients with TM report a febrile illness (flu-like illness with fever) in close temporal relationship to the onset of neurologic symptoms. In some cases, there is evidence that there is a direct invasion and injury to the cord by the infectious agent itself (especially poliomyelitis, herpes zoster, and AIDS). A bacterial abscess can also develop around the spinal cord and injure the cord through compression, bacterial invasion and inflammation.
However, experts believe that in many cases infection causes a derangement of the immune system which leads to an indirect autoimmune attack on the spinal cord, rather than a direct attack by the organism. One theory to explain this abnormal activation of the immune system toward human tissue is termed "molecular mimicry." This theory postulates that an infectious agent may share a molecule which resembles or "mimics" a molecule in the spinal cord. When the body mounts an immune response to the invading virus or bacterium, it also responds to the spinal cord molecule with which it shares structural characteristics. This leads to inflammation and injury within the spinal cord.

Vaccination is well known to carry a risk of the development of acute disseminated encephalomyelitis (ADEM) which is an acute inflammation of the brain and spinal cord. This was particularly common with the older antirabies vaccine which was grown in animal spinal cord cultures; the use of the newer antirabies vaccine grown in human tissue culture has almost eradicated this complication. This is also thought to occur as an immune system response.

Transverse myelitis may be a relatively uncommon manifestation of several autoimmune diseases including systemic lupus erythematosus (SLE), Sjogren's syndrome, and sarcoidosis. SLE is an autoimmune disease of unknown cause which affects multiple organs and tissues in the body. Features of this illness include arthralgias (joint pain) and arthritis (joint inflammation), rashes, kidney inflammation, low blood counts (including white and red blood cells, platelets), oral ulcers and the presence of abnormal autoantibodies (antibodies which are directed against the person's own tissues) in the blood. The fully developed syndrome of SLE is easy to recognize; however, this illness may begin with just one or two signs and is then more difficult to diagnose.

Sjogren's disease is another autoimmune disease characterized by invasion and infiltration of the tear and salivary glands by (lymphocytes) white blood cells with resultant decreased production of these fluids. Patients complain of dry mouth and dry eyes. Several tests can support this diagnosis: the presence of a SS-A antibody in the blood, ophthalmologic tests that confirm decreased tear production and the demonstration of lymphocytic infiltration in biopsy specimens of the small salivary glands (a minimally invasive procedure). Neurologic manifestations are unusual in Sjogren's syndrome, but TM can occur.

Sarcoidosis is a multisystem inflammatory disorder of unknown cause manifested by enlarged lymph nodes, lung inflammation, various skin lesions, liver and other organ involvement. In the nervous system, various nerves, as well as the spinal cord, may be involved. Diagnosis is generally confirmed by biopsy demonstrating features of inflammation typical of sarcoidosis.

Multiple sclerosis is an inflammatory autoimmune disease of the central nervous system (brain and spinal cord) which results in demyelination or loss of myelin (the insulating material on nerve fibers) with resultant neurologic dysfunction. A definite diagnosis of MS is not given until a patient has had at least two attacks of demyelination (hence, multiple) at two different sites in the central nervous system. The spinal cord is frequently affected in multiple sclerosis and may be the site of involvement of the first attack of MS. This presents the possibility that patients with acute transverse myelitis could later go on to have a second episode of demyelination and receive a diagnosis of MS.
Just what percentage of patients with a first attack of acute transverse myelitis will go on to develop MS is unclear in the medical literature, ranging from 15 to 80%; however, the majority of studies show a low risk. We do know that patients who have abnormal MRI scans of the brain with lesions like those seen in MS are much more likely to go on to develop MS than those who have normal brain MRIs at the time of their myelitis (between 60 and 90% for those with abnormal brain scans, less than 20% for those with normal scans in one study). It is also suggested in the medical literature that patients with "complete" transverse myelitis (which means severe leg paralysis and sensory loss) are less likely to develop MS than those who had a partial or less severe case. The literature also suggests that patients who have abnormal antibodies in their spinal fluid, called oligoclonal bands, are at higher risk to develop MS subsequently.

Myelitis related to cancer (called a paraneoplastic syndrome) is uncommon. There are several reports in the medical literature of a severe myelitis occurring in association with a malignancy. In addition, there are a growing number of reports of cases of myelopathy associated with cancer in which the immune system produces an antibody to fight off the cancer and this cross-reacts with the molecules in the spinal cord neurons. It should be emphasized that this is an unusual cause of myelitis.

Vascular causes are listed because they present with the same problems as transverse myelitis; however this is really a distinct problem primarily due to inadequate blood flow to the spinal cord instead of actual inflammation. The blood vessels to the spinal cord can close up with blood clots or atherosclerosis or burst and bleed; this is essentially a "stroke" of the spinal cord.

**Diagnosis**

The general history and physical examination are first performed, but often do not give clues about the cause of spinal cord injury. The first concern of the physician who evaluates a patient with complaints and examination suggestive of a spinal cord disorder is to rule out a mass-occupying lesion which might be compressing the spinal cord. Potential lesions which might compress the cord include tumor, herniated disc, stenosis (a narrowed canal for the cord), and abscess. This is important because early surgery to remove the compression may sometimes reverse neurologic injury to the spinal cord. The easiest test to rule out such a compressive lesion is magnetic resonance imaging of the appropriate levels of the cord. However, if MRI is not available or the images are equivocal, myelography must be performed. A myelogram is a set of X-rays taken after a lumbar puncture has been performed either in the neck or in the low back and a contrast agent (dye) is injected into the sac that surrounds the spinal cord. The patient is then tilted up and down to let the dye flow and outline the spinal cord while the X-rays are taken.

If the MRI or myelogram shows no mass lesion outside or within the spinal cord, then the patient with spinal cord dysfunction is thought to have transverse myelitis or vascular problems. The MRI can sometimes show an inflammatory lesion within the cord. It is difficult to get to the cause of the inflammation, because biopsy is rarely done on the spinal cord because of the
damage this would cause. The physician would next send blood for general bloodwork and studies for SLE and Sjogren's syndrome, HIV infection, vitamin B12 level to rule out deficiency, and a test for syphilis. The next test which is commonly performed is a lumbar puncture to obtain fluid for studies, including white cell count and protein to look for inflammation, cultures to look for infections of various types, and tests to examine for abnormal activation of the immune system (immunoglobulin level and protein electrophoresis). A MRI of the brain is often performed to screen for lesions suggestive of MS. If none of these tests are suggestive of a specific cause, the patient is presumed to have idiopathic transverse myelitis or parainfectious transverse myelitis, if there are other symptoms to suggest an infection.

References


Dr. Lynn is an Assistant Professor of Neurology at The Ohio State University. She received her medical degree from The Ohio State College of Medicine and then served residencies in internal medicine and neurology at Strong Memorial Hospital, University of Rochester. She then returned to The Ohio State University for fellowship training in neuromuscular disease. She is currently on the staff of The Ohio State University Multiple Sclerosis Center and has special interests in clinical research on the treatment of MS. Document Date: October 1997
SLE

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SYSTEMIC LUPUS ERYTHEMATOSUS

Posted by DR BURHAN ULLAH BARKI

Introduction

Background

Systemic lupus erythematosus (SLE) is a chronic, multifaceted inflammatory disease that can affect every organ system of the body. SLE is protean in its manifestations and follows a relapsing and remitting course. This article addresses what is known regarding the etiology, pathophysiology, clinical features, and treatment of SLE.

Pathophysiology

SLE is an autoimmune disorder characterized by multisystem microvascular inflammation with the generation of autoantibodies. Although the specific cause of SLE is unknown, multiple factors are associated with the development of the disease, including genetic, racial, hormonal, and environmental factors. Many immune disturbances, both innate and acquired, occur in SLE, as illustrated in below.

In systemic lupus erythematosus (SLE), many genetic-susceptibility factors, environmental triggers, antigen-antibody responses, B-cell and T-cell interactions, and immune clearance processes interact to generate and perpetuate autoimmunity.

One proposed mechanism for the development of autoantibodies involves a defect in apoptosis that causes increased cell death and a disturbance in immune tolerance. The redistribution of cellular antigens during apoptosis leads to a cell-surface display of plasma and nuclear antigens in the form of nucleosomes. Thus, dysregulated (intolerant) lymphocytes begin targeting normally protected intracellular antigens.

Immune complexes form in the microvasculature, leading to complement activation and inflammation. Moreover, antibody-antigen complexes deposit on the basement membranes of skin and kidneys. In active SLE, this process has been confirmed based on the presence of complexes of nuclear antigens such as DNA, immunoglobulins, and complement proteins at these sites. Serum antinuclear antibodies (ANAs) are found in virtually all individuals with active SLE, and antibodies to native double-stranded DNA (dsDNA) are relatively specific for the diagnosis of SLE.

Frequency

United States

According to a recent report from the National Arthritis Data Working Group, approximately 250,000 Americans have systemic lupus. The frequency of SLE varies by race and ethnicity, with higher rates reported among black and Hispanic people. The prevalence of SLE is approximately 40 per 100,000 whites in Rochester, Minnesota, versus 100 per 100,000 Hispanic persons in Nogales, Arizona.

International

Worldwide, the prevalence of SLE varies. Although the prevalence of SLE is high in black persons in the United Kingdom, the disease is rarely reported among blacks who live in Africa.
Mortality/Morbidity

The natural history of SLE varies from relatively benign disease to rapidly progressive and even fatal disease. SLE often waxes and wanes in affected individuals throughout life, and features of the disease vary greatly between individuals. The disease course is milder and survival rate higher among persons with isolated skin and musculoskeletal involvement than in those with renal and CNS disease.

SLE carries an average 10-year survival rate that now exceeds 90%. Prior to 1955, the 5-year survival rate was less than 50%. Decreased mortality rates associated with SLE can be attributed to earlier diagnosis (including milder cases), improvement in disease-specific treatments, and advances in general medical care. According to the CDC, one third of SLE-related deaths in the United States occur in patients younger than 45 years, making this a serious issue despite declining overall mortality rates. In 1976, Urowitz first reported bimodal mortality in early versus late SLE, noting that SLE-related deaths usually occur within the first 5-10 years of symptom onset.

Infectious complications related to active SLE and immunosuppressive treatment are now the most common cause of death in early active SLE, and accelerated arteriosclerosis is a key cause of late mortality. The Framingham Offspring Study demonstrated that women aged 35-44 years with SLE were 50 times more likely to develop myocardial ischemia than healthy women. Causes of accelerated coronary artery disease (CAD) in persons with SLE are likely multifactorial, including endothelial dysfunction, inflammatory mediators, corticosteroid-induced atherogenesis, and dyslipidemia associated with renal disease.

Race

Worldwide, the prevalence of SLE appears to vary by race. However, because of different prevalence rates among people of the same race in different geographical locations, a clear conclusion cannot yet be drawn. Low reported rates of SLE in Africa in contrast to a high prevalence in black women in the United Kingdom suggests the importance of environmental influences. In addition, the influence of race on prognosis has been widely debated. The LUMINA study group examined SLE among black, white, and Hispanic patients in the United States (including Puerto Rico) and reported that both disease activity and poverty predicted higher mortality among racial and ethnic minorities.

Sex

SLE frequently starts in women of childbearing age, and the use of exogenous hormones has been associated with lupus onset and flares, suggesting a role for hormonal factors in the pathogenesis of the disease. The risk of SLE development in men is similar to that in prepubertal or postmenopausal women. Interestingly, SLE is more common in men with Klinefelter disease than in men without the disease, also supporting a hormonal hypothesis.

Age

A correlation between age and incidence of SLE mirrors peak years of female sex hormone production. The prevalence of SLE is highest among women aged 14-64 years. SLE does not have an age predilection in males.

Clinical History

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect almost any organ system. Its presentation and course are highly variable, ranging from indolent to fulminant. The following is an overview of the multitudinous protean manifestations.

* Constitutional symptoms: Nonspecific fatigue, fever, arthralgia, and weight changes are the most common symptoms in new cases or recurrent active SLE flares. Fatigue, the most common constitutional symptom associated with SLE, can be due to active SLE, medications, lifestyle habits, or concomitant fibromyalgia or affective disorders. Fatigue due to active SLE generally occurs in concert with other clinical and laboratory markers. Fever, another common yet nonspecific symptom of SLE, may also result from many causes, the most common of which include active SLE, infection, and drug fever. Careful history
taking may help to differentiate these. Weight loss may occur in patients with active SLE. Weight gain may also be due to corticosteroid treatment or active disease such as nephrotic syndrome anasarca.

* Musculoskeletal symptoms: Joint pain is one of the most common reasons for the initial clinical presentation in patients with SLE. Arthralgia, myalgia, and frank arthritis may involve the small joints of the hands, wrists, and knees. In contrast to rheumatoid arthritis, SLE arthritis or arthralgia may be asymmetrical, with pain that is disproportionate to swelling.

* Dermatological symptoms
  + Cutaneous manifestations of SLE comprise 4 diagnostic criteria and multiple other clues to a potential diagnosis of lupus.
    + The first is malar rash, which is characterized by an erythematous rash over the cheeks and nasal bridge. It lasts from days to weeks and is occasionally painful or pruritic.
    + The second feature is photosensitivity, which may be elicited from patients who are asked if they have any unusual rash or symptom exacerbation after sun exposure.
    + The third feature may be discoid rash. Discoid lesions often also develop in sun-exposed areas but are plaquelike in character, with follicular plugging and scarring. They may be part of systemic lupus or may represent discoid lupus without organ involvement, which is a separate diagnostic entity.
    + Alopecia is the fourth and often less-specific cutaneous feature of SLE. It often affects the temporal regions or creates a patchlike pattern of hair loss.
  + Other cutaneous manifestations related to but not specific to SLE include Raynaud phenomenon, livedo reticularis, panniculitis (lupus profundus), bullous lesions, vasculitic purpura, telangiectasias, and urticaria.

* Renal features: The kidney is the most commonly involved visceral organ in SLE. Although only approximately 50% of patients with SLE develop clinically evident renal disease, biopsy studies demonstrate some degree of renal involvement in almost all patients. Glomerular disease usually develops within the first few years of SLE onset and is usually asymptomatic. Acute or chronic renal failure may cause symptoms related to uremia and fluid overload. Acute nephritic disease may manifest as hypertension and hematuria. Nephrotic syndrome may cause edema, weight gain, or hyperlipidemia.

* Neuropsychiatric features
  + Because of the difficulty in distinguishing causal SLE associations from certain neurological features of the disease, only seizure and psychosis are included among the diagnostic criteria. Psychosis may manifest as paranoia or hallucinations. Delirium represents a spectrum of fluctuating altered consciousness characteristic of SLE. Delirium may be caused by CNS vasculitis, encephalopathy, or the manifestations previously called organic brain syndrome. Seizures related to SLE may be generalized or partial and may precipitate status epilepticus. Aseptic meningitis, optic neuropathy, or other demyelinating disorders may also require urgent evaluation. Transverse myelitis with spastic paraparesis is a rare but serious complication of SLE. The CNS Lupus nomenclature has been revised to catalog many manifestations.
  + Cognitive disorders may be variably apparent in patients with SLE. Formal neuropsychiatric testing reveals deficits in 21-67% of patients with SLE. Whether this represents true encephalopathy, neurological damage, medication effects, depression, or some other process is unclear. Stroke and transient ischemic attack (TIA) may be related to antiphospholipid antibody syndrome or vasculitis. Migraine headaches may also be linked to antiphospholipid syndrome, although this is less clear. Headache and mood disorders may be the most commonly reported neurologic manifestation of SLE, but cause and effect may be difficult to distinguish.
  + For additional information on neurologic manifestations of SLE, see the article Systemic Lupus Erythematosus in eMedicine's Neurology volume.

* Pulmonary features: Pulmonary manifestations of SLE may manifest acutely or indolently, representing many complications. Pleurisy with pleuritic chest pain with or without pleural effusions is the most common feature of acute pulmonary involvement in SLE. Shortness of breath or dyspnea may be due to many causes. Serositis due to pericardial or pulmonary effusions, pulmonary embolism, lupus pneumonitis, chronic lupus interstitial lung disease, complement-mediated pulmonary leukoaggregation, or infection may be related to lupus disease. Pulmonary hypertension without underlying parenchymal lung disease rarely occurs with symptomatic dyspnea or right-sided heart failure. Most seriously, hemoptysis may herald diffuse alveolar hemorrhage, a rare, acute, life-threatening pulmonary complication of SLE.

* Gastrointestinal features: Gastrointestinal symptoms secondary to primary SLE and adverse effects of medication are common among persons with SLE. Abdominal pain in SLE is significant because it may be directly related to active lupus, including peritonitis, pancreatitis, mesenteric vasculitis, and bowel
infarction. Nausea and dyspepsia are common symptoms in patients with active SLE and are sometimes difficult to correlate with objective evidence of gastrointestinal involvement. Jaundice due to autoimmune hepatitis may also occur.

* Cardiac features: Heart failure or chest pain must be carefully examined in patients with SLE. Pericarditis that manifests as chest pain is the most common cardiac manifestation of SLE, manifesting as positional chest pain that is often relieved when the patient leans forward. Myocarditis may occur in SLE with heart failure symptomatology. Coronary vasculitis manifesting as angina or infarction is rarely reported. Libman-Sacks endocarditis is noninfectious but may manifest as symptoms similar to those of infectious endocarditis. More commonly, accelerated ischemic CAD is associated with SLE and may present indolently as atypical anginal equivalents.

* Hematologic features: A history of multiple cytopenias such as leukopenia, lymphopenia, anemia, or thrombocytopenia may suggest SLE, among other etiologies. Leukopenia and, more specifically, lymphopenia are common in SLE; this and hypocomplementemia may predispose persons with SLE to frequent infections. Anemia is occasionally overlooked in young menstruating women. Thrombocytopenia may be mild or part of a thrombotic thrombocytopenic purpura (TTP)–like syndrome or antiphospholipid antibody syndrome. History of recurrent early miscarriages or a single late pregnancy loss may be clues to lupus or isolated antiphospholipid antibody syndrome. A family history of autoimmune disease should also raise further suspicion of SLE.

Physical
As discussed above, almost any organ system can be involved in active SLE. The constellation of several physical findings may suggest a diagnosis of SLE. The American College of Rheumatology (ACR) diagnostic criteria are discussed in Lab Studies. Examination findings are discussed by system.16,17

* Constitutional/lymph findings: Fever may signal infection or an acute SLE flare. Lymphadenopathy or splenomegaly may be found.

* Cutaneous findings
  o Malar rash describes an erythematous rash over the cheeks and nasal bridge, with classic nasolabial fold sparing, as seen in the image below.

  The classic malar rash, also known as a butterfly rash, with distribution over the cheeks and nasal bridge. Note that the fixed erythema, sometimes with mild induration as seen here, characteristically spares the nasolabial folds.
  o Photosensitive rash is often macular or diffusely erythematous in sun-exposed areas of the face, arms, or hands, as in the image below.

  Photosensitive systemic lupus erythematosus (SLE) rashes typically occur on the face or extremities, which are sun-exposed regions. Photo courtesy of Dr. Erik Stratman, Marshfield Clinic.
  o Discoid lesions are plaquelike in character, with follicular plugging, which may create scarring. Again, these may represent limited discoid lupus or SLE.
  o Alopecia in SLE often affects the temporal regions or creates a patchy pattern.
  o Oral ulcers may be noted, with palatal ulcers being most specific for SLE.
  o Many other cutaneous findings are not explicitly diagnostic features of SLE. Livedo reticularis is characterized by a lacy, mottled, erythematous skin pattern that develops in some patients with SLE or antiphospholipid antibody syndrome. Raynaud phenomenon may be observed with blue, white, and red color change at the distal digital tips. Capillaroscopy can be performed with an ophthalmoscope to search for dilated capillary nailfold loops. Panniculitis, bullous lesions, vasculitic purpura, and urticaria are other skin lesions that are sometimes seen in SLE.

* Musculoskeletal findings: Small-joint arthritis of the hands and wrists is the most common musculoskeletal finding in SLE, followed by arthritis of the knees. Pain reports may be out of proportion to synovitis or swelling upon examination. Jaccoud arthropathy is the term used to describe the nonerosive hand deformities due to chronic arthritis and tendonitis that develop in 10% of patients with SLE. Myositis that may manifest as weakness rarely occurs and is more commonly related to overlap syndromes or corticosteroid-induced myopathy. Fibromyalgia, which should be distinguished by myofascial tenderness without weakness, is commonly concomitant with SLE, causing generalized widespread pain, arthralgia, and myalgia.
Relapsing transverse myelitis.

Tippett DS¹, Fishman PS, Panitch HS.

¹Department of Neurology, University of Maryland School of Medicine, Baltimore 21201.

Abstract

Acute transverse myelitis is a monophasic disorder, the recurrence of which raises the question of multiple sclerosis (MS) or other multifocal CNS disease. We now report three patients with a previously undescribed syndrome of relapsing isolated acute transverse myelitis. Each had two to five attacks over periods of 3 to 8 years, characterized by ascending paresthesias, urinary retention, sensory loss with a thoracic or cervical level, paraparesis, hyperreflexia, and bilateral Babinski signs. MRI demonstrated areas of increased signal intensity on T2- and proton density-weighted scans and decreased signal intensity on T1-weighted scans of the cervical or thoracic spinal cord consistent with an inflammatory or demyelinating process. All patients had normal complete myelograms, oligoclonal IgG bands were consistently absent from the cerebrospinal fluid, cranial MRIs were normal, and there was no other clinical or laboratory evidence of MS, collagen-vascular disease, or active viral infection. They were treated with high doses of intravenous corticosteroids, stabilized between episodes, and had partial or complete recovery. The recognition of these three patients at a single medical center in a 1-year period suggests that relapses of acute transverse myelitis may not be rare.