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Atypical Trigeminal Neuralgia: A Rare Neurological Manifestation of Systemic Lupus Erythematosus

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Patient: Female, 53
Final Diagnosis: Atypical trigeminal neuralgia
Symptoms: Right sided facial pain
Medication: —
Clinical Procedure: None
Specialty: Rheumatology

Objective: Unusual clinical course





Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder of unknown etiology which can present at any age with symptoms of mucocutaneous, musculoskeletal, renal, central nervous system, and non-specific clinical pictures making the disease a “master of mimicry”.

Case Report: A 53-year-old female, who was recently diagnosed with SLE, presented with right-sided sharp and electric shock-like facial pain starting at the side of her right nostril and traveling down the naso-labial fold and then back to the angle of the jaw, mostly in the region of V2–V3 distribution with no radiation beyond trigeminal distribution. Her pain had been going for the last 2 years and was regarded as “pretrigeminal neuralgia”; however, it progressed in frequency over the last 2 weeks, with no clear identifying triggering factors. Her laboratory test results showed positive anti-nuclear antibodies (ANA) with raised titer, anti-double-stranded DNA, anti-ribonucleoprotein, anti-Sjögren’s syndrome-related antigen A, anti-Sjögren’s syndrome-related antigen B, and anti-smooth muscle antibodies. Other possibilities of migraine, postherpetic neuralgia, Bell’s palsy, and brain tumor were ruled out. A diagnosis of SLE with trigeminal neuralgia (TN) was made and carbamazepine 100 mg 2 times a day was prescribed.

Conclusions: TN is seldom mentioned as a neurological manifestation of SLE; hence, we recommend further studies to investigate the SLE-mediated injury to trigeminal fibers to make a timely diagnosis of TN and to prevent progressive autoimmune process-related vasculitic and demyelinating changes.

MeSH Keywords: Autoimmune Diseases • Lupus Vasculitis, Central Nervous System • Trigeminal Neuralgia

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/901478>

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Background

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder of unknown etiology which can present at any age with symptoms of mucocutaneous, musculoskeletal, renal, central nervous system, and nonspecific clinical pictures making the disease a “master of mimicry”. The prevalence is approximately 130/100 000 in the United States, with African Americans, Hispanics and Asians more frequently affected than non-Hispanic whites [1]. It has a female predominance with approximately 9: 1 ratio and the onset is usually during the reproductive years. The symptoms and signs may start abruptly or may take months or years before the diagnosis can be confirmed. The American College of Rheumatology case definitions collectively have detected the presence of 14–17 out of the 19 neuropsychiatric SLE syndromes among adults and reported total spectrum of headache (39–61%), seizures (8–18%), cerebrovascular disease (2–8%), psychosis (3–5%), cranial neuropathy (1.5–2.1%), and movement disorder (1%) [2].

Trigeminal neuralgia (TN) is a neuropathic disorder of one or both of the trigeminal nerves, and is more common among females and people over age 50. It can be either primary with unknown precise cause or secondary, which might be associated with some other diseases; with symptoms of extreme, sporadic, sudden burning or shock-like face pain triggered by common activities such as eating, talking, shaving, and tooth brushing. Although TN is not a fatal disorder, it can greatly impair patient quality of life [3]. Currently considered explanations are vascular pressing on the trigeminal nerve in its root entry zone, a demyelination of trigeminal sensory fibers, and jawbone cavity, but these fail to sufficiently explain the total clinical picture [4].

We report a case of an African American woman who presented to us with 2 variable presentations of SLE over a short span of time.

Case Report

A 53-year-old woman (African American, Jamaican, ex-smoker of 30 pack years) who presented with multiple joint pains and stiffness was diagnosed with SLE after thorough investigation. She was given 1 dose of intramuscular Depo-Medrol and started on oral methotrexate 20 mg weekly and oral folic acid 1 mg every day. Three months later, she complained of right-sided, sharp, electric shock-like facial pain starting at the side of her right nostril and traveling down the naso-labial fold and then back to the angle of the jaw, mostly in the region of V2–V3 distribution with no radiation beyond trigeminal distribution. She said that her pain paroxysm usually lasted for around a week, went away without warning, and

Table 1. List of positive autoimmune panel in chronological order.

Test	Patient result	Normal range
ANA	Positive	Negative
ANA titer	1: 2560	≤1: 40
ANA brightness	4+	–
ANA pattern	Speckled	–
C4 complement	16.5 mg/dl	16-47 mg/dl
C3 complement	109 mg/dl	88-201 mg/dl
Anti-dsDNA antibodies	Positive	Negative
Anti-dsDNA antibodies titer	1: 10	Negative
Anti-SS-A	Positive	Negative
Anti-SS-A titer	>8.0	≤0.9
Anti-SS-B	Positive	Negative
Anti-SS-B titer	>8.0	≤0.9
Anti-Sm antibodies	Positive	Negative
Anti-Sm antibodies titer	>8.0	≤0.9
Anti-RNP antibodies	Negative	Negative
Anti-RNP antibodies titer	0.3	≤0.9

ANA – anti-nuclear antibodies; anti-dsDNA – anti-double-stranded DNA; anti-RNP – anti-ribonucleoprotein; anti-SS-A – anti-Sjögren’s syndrome-related antigen A; anti-SS-B – anti-Sjögren’s syndrome-related antigen B; anti-Sm – anti-smooth muscle.

then returned 2–3 weeks later. She stated that the pain has been occurring for the last 2 years. It was suspected to have a dental origin, and an unnecessary dental procedure was performed. However, the pain still persisted and progressed in frequency but was limited to the region of V2–V3 distribution over the last 2 weeks, with no clear identifying triggering factors and was temporarily relieved with ibuprofen. She found no triggers of pain paroxysms by chewing, talking, brushing teeth, cold air, smiling, and/or grimacing. There was no history of fever, chills, vomiting, diarrhea, chest pain, malar rash, oral ulcers, weight loss, jaw claudication, altered taste sensations, lacrimation, conjunctival injection, rhinorrhea, difficulty in chewing, or sicca symptoms. She denied any lupus flare-up episodes and/or any other past neurological manifestations of lupus, including seizures, movement disorder, hemiparesis, peripheral neuropathy, autonomic disorder, or psychotic disorder.

On physical examination, no gross neurological abnormality, including touch, pain, and temperature sensation in all 3

Table 2. List of various neurological manifestations in lupus.

Reference	Age/Sex	CNS manifestation	SLE presentation
Kak et al. [5]	18 y/F	Encephalitis with repeated episodes of convulsions and headaches	Multiple joint pains, oral ulcer, malar rash, and lupus nephritis
Faruk et al. [6]	7 y/F	Status epilepticus	Generalized erythematous rash, oral ulcers, and fever
Hashizume et al. [7]	70 y/F	Left hemiparesis	Arthralgia and autoimmune hemolytic anemia
Altabas et al. [8]	38 y/F	Right hemiparesis with contracture of fist and epilepsy	Lupus nephritis and vasculitis
Horozoglu et al. [9]	32 y/F	Left hemiparesis	Fever, lymphadenopathy, malar rash, photosensitivity, and lupus nephritis
Krishna et al. [10]	14 y/M	Multiple infarcts in brain with left hemiparesis	Antiphospholipid syndrome, autoimmune hemolytic anemia, right central retinal vein thrombosis, hypertension and exogenous cushingoid
Malec et al. [11]	47 y/F	Schizophrenia, cognitive impairment, and mood disorder	Generalized erythematous rash
Agarwal et al. [12]	22 y/F	Acute inflammatory polyneuropathy	Photosensitivity and oral ulcerations

trigeminal divisions, was found. Her laboratory test results showed raised inflammatory markers C-reactive protein (2.07; 0–0.8) and erythrocyte sedimentation rate (76; 0–20). Her positive autoimmune panel determined by indirect immunofluorescence is listed in Table 1. Other laboratory results included normal complete cell count, basic metabolic panel, liver function test, lipid panel, folate levels, vitamin B12, syphilis IgG, lead level, quantitative rheumatoid factor (RF) levels, and anti-cyclic citrullinated protein levels, and she was negative for intrinsic factor blocking antibody, herpes zoster, human immunodeficiency virus, hepatitis panel, and quant TB gold. Her brain MRI showed no acute or chronic pathology. Other possibilities of migraine, postherpetic neuralgia, Bell's palsy, or brain tumor were ruled out. A final diagnosis of lupus associated with TN was made. She had been started on oral carbamazepine 100 mg 2 times a day and reported no complaints on her follow-up visits.

Discussion

Several neurological manifestations have been reported among SLE patients in the literature (Table 2), but very few cases showed an association between SLE and trigeminal sensory neuropathy (TSN) and TN. We hereby present a rare case of TN with SLE and propose this unique presentation of atypical trigeminal pain in SLE patient as “lupus neuropathy”.

Hagen et al. [13] reported 2 cases of TSN in SLE among 81 studied subjects; however, none of the patients had a pain syndrome similar to TN. They found 26% prevalence of TSN in mixed connective tissue disease, 19% scleroderma, 2%

rheumatoid arthritis (RA), 2% Sjögren syndrome, 1% dermatomyositis, and 47% undifferentiated connective tissue disorder (CTD). It is still unexplained why TSN occurs more frequently in certain CTDs as compared to others. However, the incidence of other neurologic manifestations in these less common CTDs is generally lower than reported among patients with SLE or RA [14].

Among the collagen vascular diseases, neurological manifestations have been most commonly recognized and well-studied in SLE. Nervous system involvement in SLE has been reported to vary from 40% to 70% [12]. It may occur at any time during the course of the disease, but is rarely the first manifestation of SLE. Interestingly, trigeminal neuropathy is seldom mentioned as a symptom in nervous system SLE but has been observed as the only neurological manifestation of the disease among 2 cases reported by Ashworth and Tait [15].

The diagnosis of TN is usually based on the characteristic clinical picture, which consists of key clinical features and physical examination showing no clinical evidence of neurological deficit or mild sensory impairment in trigeminal nerve distribution. Although there are fairly standard treatment approaches for TN, management with either anti-epileptic drugs or surgical procedures both carries risks of adverse effects, recurrence, and complications. However, there are few studies which directly compare medical and surgical treatments. Pharmacological therapy for TN has been the subject of several Cochrane systematic reviews and available evidence shows carbamazepine is the best-studied treatment and drug of choice for initial and long-term management of TN, as prescribed in our patient [16].

The pathogenesis of lupus neuropathy is multifocal processes involving vasculitis causing destructive changes in the vasa nervorum, microangiopathy, intrathecal production of proinflammatory cytokines, premature atherosclerosis, demyelination, immune complex deposition, and antibody-mediated damage [17]. However, there is little pathological information about TN cases. Vasculitis affecting the trigeminal nerve branches, particularly at the sites where they are tightly invested by dura and more susceptible to edema, as well as consequent rise in endoneurial pressure, seems to be a possible pathophysiological mechanism in the context of autoimmune disease. Fibrosis of the epineurium and perineurium might increase the endoneurial pressure and preferentially damage myelinated trigeminal fibers. Direct injury induced by vasculopathy may affect the blood-brain barrier, thereby allowing antibodies to enter the central nervous system. There is experimental evidence showing increased permeability of the trigeminal ganglion blood vessels to proteins and antibodies as compared to the blood-brain barrier [18]. It has been proven that in the rat, horseradish peroxidase passes from venous blood into the extracellular space of the trigeminal ganglion within 2 min, in comparison to penetration of the endoneurial space within 5 min [19].

Vasculitic changes, neural tissue fibrosis, and increased permeability of trigeminal blood vessels seen among SLE patients might predispose them to the development of TN. However,

why the trigeminal fibers are selectively involved still remains controversial. Further studies to investigate the SLE-mediated injury to trigeminal fibers are recommended to make a timely diagnosis of TN or any other lupus neuropathy and to prevent progressive autoimmune process-related vasculitic and demyelinating changes. Investigation of underlying autoimmune disease must be done among newly diagnosed high-risk patients with TN, as it might precede the diagnosis of SLE or any other autoimmune disease.

Conclusions

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder of unknown etiology reported to be associated with several neurological manifestations. We report a rare case of trigeminal neuralgia in a patient with SLE to raise awareness among health care providers that trigeminal neuralgia can be manifested before, after, or at the time of SLE diagnosis. Further studies to investigate the selective involvement of trigeminal fibers in SLE are recommended to make a timely diagnosis of TN and to prevent progressive autoimmune process-related vasculitic and demyelinating changes.

Conflict of interest

None.

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