Case Report

Nonspecific Numbness and Tingling

Urgent message: Though the cause of nonspecific numbness and tingling will often be benign, serious illnesses should be included in the differential diagnosis.

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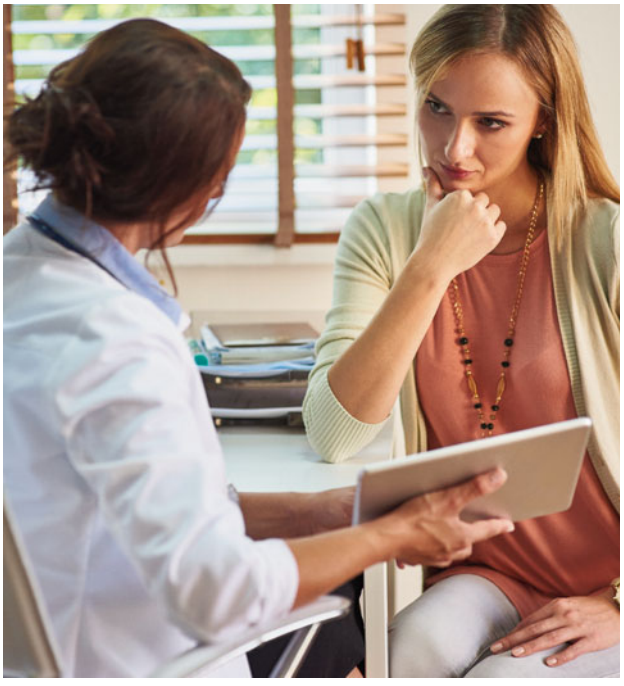
Introduction

Many patients at urgent care centers present with numbness and tingling. The symptoms can be caused by variety of underlying benign or potentially malignant pathologies.

The medical history and physical examination play a central role in the determination of the cause of numbness. Numbness that is limited to a part of a limb suggests mononeuropathy, whereas numbness that involves most of an extremity or the trunk or that occurs in a stocking-glove pattern suggests polyneuropathy.[1,2] Mononeuropathies such as carpal tunnel syndrome and cervical radiculopathy are some of the most common causes of numbness and tingling. In one study, carpal tunnel syndrome was found to have been diagnosed in 3.4% of all participants and to be undiagnosed in an additional 5.8%. Another study revealed that the average incidence of cervical neuropathy between 1976 and 1990 was 83 per 100,000, with higher rates in men between 50 and 54 years of age.[1,2]



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Case Presentation

A 43-year-old woman presented to an urgent care center with intermittent numbness and tingling in her left arm that she had experienced for 6 months. She described the symptoms as having a rapid onset each time they occurred. They lasted several days and were relieved by Chinese traditional medicine and neck and arm massage. The patient attributed her symptoms to sleeping in the wrong position and also to long work hours as a software engineer. She said that she sought consultation because she was now experiencing a "cramp in the right side of the head." She said that she had not had any related issues in the past and that she did not smoke, drink alcohol, or take drugs of abuse. The patient did

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not take any prescribed medications and did not have any allergies. Findings from her family history were unremarkable: Her parents were still living and were in their seventies. She reported that she had not had headaches, vision changes, loss of balance, speech difficultly, lack of concentration, neck pain, chest pain, shortness of breath, nausea, vomiting, pregnancy, urinary symptoms, stress, or anxiety.

Physical Examination

At initial presentation, the patient's vitals signs were as follows:

- Blood pressure: 105/70 mm Hg
- Pulse: 72 beats/min
- Respiratory rate: 16 breaths/min
- Temperature: 98.4°F (36.8°C)

The patient was not in acute distress and was sitting comfortably on the examination table, massaging her left arm with her right hand. Findings on neurologic examination were normal, including those for the cranial nerves, as were upper-extremity and lower-extremity reflexes and sensory and motor responses. Extraocular movements were normal, and the pupils were equal and reactive to light. Musculoskeletal examination revealed mild bilateral trapezius tenderness, but findings were otherwise unremarkable. Findings on cardiac and respiratory examinations were with normal limits.

Imaging

A cervical spine x-ray obtained at the urgent care center showed no abnormality. Because of the nature of the patient's symptoms, a routine outpatient computed tomography (CT) scan of the brain was ordered. The patient was discharged home with a recommendation to take nonsteroidal anti-inflammatory drugs while waiting for scan results.

The following day, the CT scan results were as follows:

- No intracranial hemorrhage
- White-matter signal abnormalities in the right periventricular region. The differential diagnosis included demyelinating plaques.

Diagnosis

The patient was contacted and informed of the scan results, which indicated that her symptoms might be due to multiple sclerosis (MS). She was referred to a neurologist, who had her undergo magnetic resonance imaging (MRI) of the brain, which confirmed the diagnosis of MS.

Discussion

Numbness and tingling are nonspecific symptoms that can be caused by a variety of underlying benign or potentially malignant pathologies related to the central or peripheral nervous system, including cardiovascular disease, musculoskeletal illnesses, an electrolyte imbalance, metabolic disorders, infectious disease, and even psychiatric illnesses. There can even be two overlapping pathologies, whether benign or malignant.

Multiple Sclerosis

It is widely accepted that the central nervous system is under constant surveillance by immune cells. The entrance and exit of immune cells from the central nervous system, however, is poorly understood. Recent research at the University of Virginia School of Medicine demonstrated the presence of functional lymphatic vessels lining the dural sinuses, but it has long been assumed that the brain has no connection with the lymphatic system. Although more research is required, scientists believe that these vessels may be the missing links between MS and the immune system.[3] An image comparing an old map of the lymphatic system with a map revised to reflect that recent research can be found at http://neurosciencenews.com/lymphatic-system-brain-neurobiology-2080/.

Differential Diagnosis

The differential diagnosis for MS includes a variety of inflammatory, infectious, vascular, and demyelinating disorders, including systemic lupus erythematosus, human immunodeficiency virus, neurosyphillis, sarcoidosis, and vitamin B_{12} deficiency. Brain MRI is a common approach to narrowing down the diagnosis. A frequent error, however, is to interpret multiple hyperintense lesions on MRI as indicating the presence of MS even when clinical manifestations of the disease are absent. A number of central nervous system inflammatory and infectious diseases can produce such lesions on MRI without clinical manifestations of MS, including systemic lupus erythematosus, Sjögren syndrome, polyarteritis nodosa, and neurosyphilis. Another common error is that many practitioners fail to pursue further diagnostic evaluation when a patient has a history of MS. Red flags that should alert physicians to consider the possibility of pathologies other than MS are as follows[4]:

- Positive family history of neurologic diseases other than MS
- Persistent back pain
- Signs and symptoms that point to a specific anatomic site

- Patients younger than 15 or older than 60 years of age
- Symptoms of systemic disease
- Rapidly progressive disease

"[Multiple sclerosis] is the most frequently occurring disabling disease of the central nervous system among young adults."

Causes

MS is a disease of the central nervous system. It is characterized by inflammation, demyelination, and degeneration of axons.[5] The exact pathophysiology of MS is unknown, but several theories exist,[6] including a widely accepted one that MS is an autoimmune disease. This theory suggests that autoreactive lymphocytes cause microglial activation and neuron degeneration.[7] A deficiency of vitamin D is another theoretical cause. Chromosome 6 consists of a region called the vitamin D response element, which enhances gene expression in the presence of vitamin D, pointing to a link between vitamin D and MS.[8] Another theory suggests that MS has infectious causes, such as chronic viral infection; however, no virus has been identified.[9] Other theories point to chronic cerebral venous insufficiency and genetic causes, as opposed to autoimmune causes.[10]

Epidemiology

MS is the most frequently occurring disabling disease of the central nervous system among young adults.[11] It is more common in women than in men, and its onset is usually between the ages of 28 and 31 years. White populations, particularly those from northern Europe, have the highest risk, though recent studies suggest that ethnic differences may be decreasing. Increased risk may be associated with latitude (greater risk farther from the equator), though some studies suggest that other factors may put this assumption into question.[12]

In recent years, there have been noticeable changes in the demographic epidemiology of MS. There has been an increase in the prevalence of MS, particularly because of increasing survival rates. There also has been an increase in MS incidence in European and North American women. These changes point to the possibility that environmental factors play a role in the disease. Lifestyle factors in Western women, including occupation, cigarette smoking, obesity, use of birth control, and childbearing at later ages, may be a focus of future study.[13]

In a recent study,[12] the overall incidence of MS was 3.6 cases per 100,000 person-years in women and 2.0 in men. Higher latitude was associated with higher incidence of MS; however, this latitude gradient was reduced after 1980 because of an increased incidence of MS in lower latitudes. The female-to-male ratio for MS incidence has increased over time, from an estimated 1.4:1 in 1955 to 2.3:1 in 2000.

Presentation

MS is categorized into four types according to pattern and course[14]:

- **Clinically isolated:** The first manifestation of MS, which may present as vision changes mimicking unilateral optic neuritis or as isolated numbness and tingling, depending on the location of demyelination
- **Relapse-remitting:** A relapse of symptoms with full recovery. This category accounts for 85% to 90% of cases at onset.
- **Secondary progressive:** A relapse attack with progressive worsening, without recovery
- **Primary progressive:** Categorized by progressive disease from the onset of symptoms

Patients with MS can present with a wide range of signs and symptoms at various stages of the disease. Clues can include progressive or intermittent numbness and tingling in limbs that lasts several days and Lhermitte sign, which is electric shocks that travel down a limb or down the spine upon cervical flexion.[15] A majority of patients with MS present with vision issues such as diplopia, which points to demyelination involving the medial longitudinal fasciculus tracts. Optic neuritis can be another presentation of MS; it is the presenting feature in 15% to 20% of patients with MS and occurs in 50% at some time during the course of the illness.[16]

Diagnosis

The diagnosis of MS is clinical, with MRI being the best supporting imaging modality. It is much more sensitive than other imaging modalities and can detect many more demyelinating lesions than CT can. It can detect plaques in the brainstem and cerebellum, which rarely appear as abnormal on CT.[17]

The prognosis of MS depends on various factors[18]:

- Older age at onset of MS has been determined to be a strong predictor of worse prognosis.
- A progressive initial course is considered the strongest clinical predictor of a poor prognosis.

- Symptoms arising from dysfunction of the spinal cord or long tracts indicate a poor prognosis.
- Male sex, incomplete recovery, a shorter time to a second episode, and a higher frequency and higher number of relapses indicate a poor prognosis.

Take-Home Points

Although numbness and tingling constitute one of the most common initial presentations of MS, they can be caused by a variety of pathologic conditions, some benign and some malignant, and can present as an overlapping symptom of more than one such condition. A thorough medical history and a detailed physical examination, and in most circumstances, a diagnostic study such as brain MRI, are needed to confirm the diagnosis of MS. ■

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