Carpal tunnel syndrome caused by Mycobacterium fortuitum and Histoplasma capsulatum

Report of two cases

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Two unusual cases are presented in which carpal tunnel syndrome was found to be the presenting manifestation of Histoplasma capsulatum and atypical mycobacterial infection. General diagnostic and therapeutic points are reviewed.

KEY WORDS  * carpal tunnel  * median nerve  * Histoplasma  * Mycobacterium

The carpal tunnel syndrome (CTS) can be caused by any space-occupying lesion in the carpal tunnel. Systemic diseases, trauma, tumors, endocrine disorders, and infectious diseases have all been reported to manifest as CTS. Infectious causes include mycobacteria, Histoplasma capsulatum, Coccidioides immitis, pyogenic infections, Sporothrix schenckii, and rubella. The purpose of this report is to record two unusual cases of CTS caused by Histoplasma capsulatum and Mycobacterium fortuitum, respectively.

Case Reports

Case 1

This 43-year-old woman developed carcinoma of the right breast in February, 1979. A right mastectomy was performed, followed by weekly chemotherapy with 5-fluorouracil, Cytoxan (cyclophosphamide), and methotrexate for 2 years. In October, 1979, she noted a tingling sensation in her thumb and index and middle fingers. The symptoms progressed to numbness over the same distribution and became associated with pain in the palm and wrist. She received an injection of cortisone in the volar aspect of the left wrist which relieved her symptoms for 3 months. In July, 1980, a repeat cortisone injection afforded her no relief. Surgical debridement and decompression of the carpal tunnel space was performed in September, 1980. An inflammatory mass displacing the structures of the space was seen at surgery. Histopathologically, granulomatous inflammation was present.

The patient did well until November, 1980, when she noticed a small white plaque on the right inferior aspect of her tongue. This lesion increased in size and became ulcerated, but she denied systemic symptoms. In January, 1981, a tongue biopsy was performed which showed yeast-like organisms compatible with Histoplasma capsulatum on silver staining. The patient was subsequently admitted to the hospital. On physical examination, several white plaques of various sizes (2 mm to 2 cm in diameter) were found on the inferior and lateral margins of the right side of the tongue and mouth floor. These lesions were tender and associated with mild posterior cervical lymphadenopathy. The remainder of the physical examination was unremarkable.

Routine laboratory data were normal. The white blood count was 4100/cc. Serum antibodies to Histoplasma yeast and mycelial antigens were found to be absent on complement fixation. Chest x-ray films, bone scan, and liver scan were unremarkable. Excisional biopsy was performed on the tongue lesion, and tissue was submitted for cultures and special stains. Silver staining revealed oval structures suggestive of Histoplasma capsulatum. Ulceration and granulomatous inflammation were also present. Tissue sections...
from the previous carpal tunnel decompression were reexamined on silver stained slides. Sparse, faintly staining yeast-like organisms consistent with \textit{Histoplasma capsulatum} were identified in areas of granulomatous inflammation. Slides of bone marrow aspirate demonstrated granulomatous lesions at scattered sites in the clot sections. Cultures of the tongue biopsy and bone marrow aspirate grew no fungi. The patient received a total dose of 1 gm amphotericin B (50 mg intravenously three times per week). The oral lesions had completely resolved by the time she had received 500 mg, and no recurrence was evident at 4-month evaluation.

\textbf{Case 2}

This 56-year-old man developed symptoms of right carpal tunnel syndrome which became progressively worse over the course of a year. In July, 1979, he presented with positive Phalen's and Tinel's signs. His symptoms progressed to include paresthesias and pain, but he denied systemic symptoms. Although he was a farmer, there was no history of trauma or puncture wound. Physical examination was unremarkable except for the signs noted above and the absence of the left arm below the elbow as a result of a farming accident.

All laboratory values and a chest x-ray film were normal. Surgical decompression and debridement of the right carpal tunnel was performed in May, 1980. On release of the flexor aponeurosis, a granulomatous mass was found compressing the median nerve. Histopathological examination showed a chronic inflammatory infiltrate composed of lymphocytes, plasma cells, and mononuclear cells with multiple epithelioid granulomas scattered throughout the stroma. Many giant cells were also visualized. Acid-fast, fungal, and bacterial stains were negative.

In 9 days, cultures on Lowenstein-Jensen medium showed growth of nonpigmented acid-fast bacilli. The organisms were confirmed by the Nebraska State Laboratory as \textit{Mycobacterium fortuitum}. The organism was susceptible to isoniazid \textit{in vitro}, but resistant to para-aminosalicyclic acid, streptomycin, rifampin, and ethambutol by indirect testing on Middlebrook agar. Other cultures for bacteria and fungi were negative. Because of the localized nature of this patient's disease, it was decided to withhold medical therapy and observe his progress. He was doing well at his 1-year follow-up examination.

\textbf{Discussion}

Few cases have been reported of CTS as the presenting manifestation of infection with \textit{Histoplasma capsulatum}. None of the previous cases of CTS caused by \textit{Histoplasma} has presented with systemic symptoms, although our Case 1 was later discovered to have mucocutaneous lesions and granulomas in the bone marrow. This patient also differed from the others in that she was immunosuppressed. Iverson and Vistnes' implicated immunosuppression as a major pathogenic factor in a report of CTS in coccidiodomycosis.

Antibodies to \textit{Histoplasma} by complement fixation or immunodiffusion were negative in our Case 1, as they have been in others. Characteristic granulomatous inflammation was found on histopathological examination of tissue from carpal tunnel debridement in our case. Yeast-like organisms were visualized on silver staining. Fungal cultures were not obtained, but are usually positive.

All cases of CTS caused by \textit{Histoplasma capsulatum} received surgical decompression of the carpal tunnel space. \textit{Histoplasma}-induced CTS may reflect generalized infection or recur locally after surgery. Consequently, all patients reviewed, including ours, received amphotericin B until a cumulative dose of 1.0 to 3.5 gm was reached.

Mycobacterial agents that most frequently produce median nerve compression in the carpal tunnel are \textit{Mycobacterium tuberculosis} and \textit{M. bovis}, usually without pulmonary involvement, although atypical mycobacterial CTS has been reported. Carpal tunnel syndrome caused by atypical \textit{Mycobacteria} is often associated with a puncture wound near the ipsilateral wrist occurring 4 to 6 weeks prior to the onset of symptoms. \textit{Mycobacterium fortuitum} is a rapidly growing organism found ubiquitously in nature; infections are almost always associated with contaminated trauma. Our case of CTS caused by \textit{M. fortuitum} was a farmer who denied major trauma or puncture wound.

The purified protein derivative (PPD) skin test is usually positive in \textit{M. tuberculosis}-induced CTS. Negative or weakly positive skin reactions to standard tuberculin protein are seen in patients with atypical mycobacterial infections. Three of four patients with \textit{M. fortuitum} infections, including our Case 2, had negative skin tests with PPD-intermediate strength. Acid-fast bacilli may be seen on smears of tissue debrided from the carpal tunnel, but definitive diagnosis is made by culture, as it was in this report.

The recommended treatment for CTS caused by \textit{Mycobacteria} is decompression and debridement of the carpal tunnel space plus antituberculous medication. For CTS caused by atypical \textit{Mycobacteria}, Gunther recommends isoniazid and ethambutol or rifampin for a period of 18 to 24 months.

Medical therapy was not employed in this case of \textit{M. fortuitum}-induced CTS because of the resolution with surgery and lack of systemic symptoms. Infections with this organism may resolve with surgery alone. Dalovisio and Pankey recommended doxycycline or amikacin in chronic progressive cases of \textit{M. fortuitum}, although the appropriate dosages and duration of treatment have not been established.

Granulomatous inflammation was noted on histopathological examination of tissue in both of our
Infection-induced carpal tunnel syndrome cases, and when found on frozen section should lead to complete microbiological studies including stains and cultures for mycobacteria, fungi, and bacteria.

References

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