Acute Disseminated Encephalomyelitis Following Pulmonary Tuberculosis

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Abstract

Acute disseminated encephalomyelitis (ADEM) which developed following pulmonary tuberculosis in a 50-year-old male patient is described. Tuberculosis needs to be considered among the infections leading to ADEM in countries where tuberculosis is frequent. Physicians must be aware of this specific clinical condition in patients with recently diagnosed tuberculosis, experiencing neurological disorder simultaneously.

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Introduction

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disorder of the central nervous system and is rarely diagnosed in elderly patients (1). The incidence of ADEM in the first decade of life is nearly three times higher than the incidence in the adolescent period. ADEM usually develops following an infection or vaccination (2). Measles, mumps and Influenza A or B infections are the most common infections but bacterial infections, such as *Mycoplasma pneumonia, Chlamydia and Legionella* are also rarely described as the triggering condition. Vaccination for rabies, diphtheria, tetanus, pertussis and smallpox may cause the development of ADEM in children (3).

The mechanism of ADEM remains incompletely understood despite the extraordinary richness and complexity of immunologic abnormalities, which have been extensively studied. Peptides from microbial proteins that have sufficient structural similarity with the host's self peptides can activate T-lymphocytes. CD4+ T-lymphocytes when activated infiltrate the central nervous system and recruit additional mononuclear cells to cross the blood-brain barrier, leading to inflammation and demyelization (4). CD8+ T-lymphocytes are also implicated in the pathogenesis. As the lesions become older the macrophages increase and

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lymphocytes decrease in number, resulting in fibrillary fibrosis in the adjacent brain tissue.

Systemic symptoms like fever, malaise, headache, nausea and vomiting often precede the neurological symptoms of ADEM and begin 4-21 days after the inciting event. The onset of symptoms is rapid and peak dysfunction occurs within several days (5).

In the literature, both viral and bacterial infections are described as antecedent events for ADEM, but tuberculosis is not yet shown as a trigger (3). In this report, we describe a patient with pulmonary tuberculosis who experienced severe neurological symptoms complying with ADEM starting within two weeks after the initial diagnosis.

Case Report

A 50-year-old male patient first presented with complaints of a non-productive cough which had persisted for one year, malaise and a weight loss of 4 kgs in the past 2 months. He was a current smoker with a 30 packs/year history. There was no history of fever or hemoptysis. Physical examination revealed normal findings.

The chest radiograph on admission showed a reticular density in the left upper lobe. The computed tomography of the thorax showed a parenchymal infiltration in the apico-posterior segment of the left upper lobe with minimum fibrosis. No lymphadenopaty was detected in the mediastinum and hilum. The radiological findings were reported to be suggestive for bronchogenic spread of pulmonary tuberculosis (Figure 1). Tuberculin skin test was positive with 12 mm induration. No BCG scar was detected.

The bacteriologic evaluation of the sputum for acid-fast bacilli (AFB) was negative. A fiberoptic bronchoscopy was performed. Bronchoalveolar lavage (BAL) from the apico-posterior segment of the left upper lobe was done with 120 mL of saline solution. The smear of the BAL fluid was-negative for acid fast bacilli.

Based on the radiological findings and tuberculin skin test positivity, diagnosis of active pulmonary tuberculosis was made. Anti-tuberculous treatment with four drugs (isoniazid 5 mg/kg/day, rifampin 10 mg/kg/day, etambutol 20 mg/kg/day, pyrazinamide 30 mg/kg/day) was initiated and the patient was discharged.

On the 10th day of this treatment, the patient presented with digital parestesia and fever and was readmitted. Ataxia, sudden unsteadiness, diplopia and headache developed the following day. The neurological examination showed a left internuclear ophthalmoplegia associated with a right eye abducting nistagmus. He had truncal ataxia and right side cerebellar syndrome and could not walk without assistance. The sensation of dizziness and disequilibrium persisted for two weeks. Cerebrospinal fluid examination showed no abnormality in opening pressure, glucose, chloride and protein levels. Oligoclonal band and IgG index were in the normal range. Pre and post contrast T2-weighted and FLAIR magnetic resonance imaging showed multiple lesions involving the right cerebellum and the centrum semiovale. These lesions showed contrast enhancement after gadolinium (Figure 2).

The patient was considered as a case of acute demyelinizing disease and pulse methylprednisolone (1 g/day for 3 days and 0.5 g/day for 3 days) was started. He improved rapidly and became afebrile with diminished neurological findings on the 7th day of hospitalization. The diplopia, ataxia and disequilibrium reversed completely and the patient was discharged.

On the 3rd week from the first presentation, the diagnosis of pulmonary tuberculosis was confirmed by the isolation of *Mycobac-*

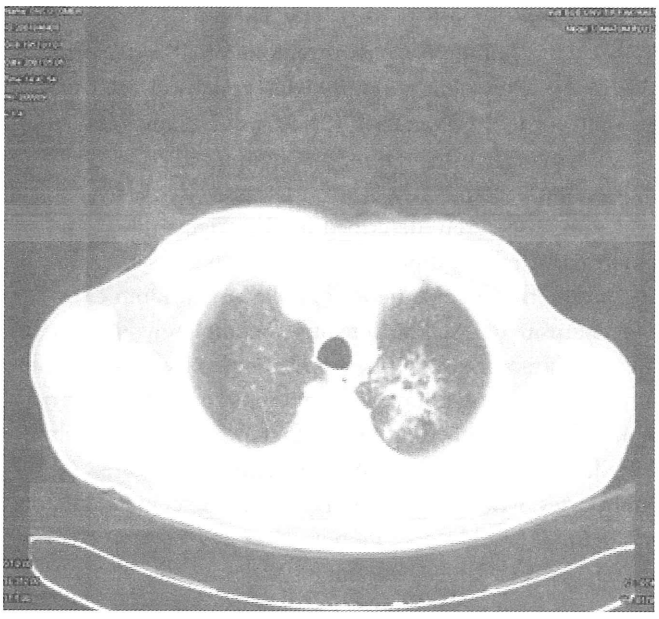

Figure 1. *Parenchymal infiltration in the left upper lobe on HRCT of thorax.*

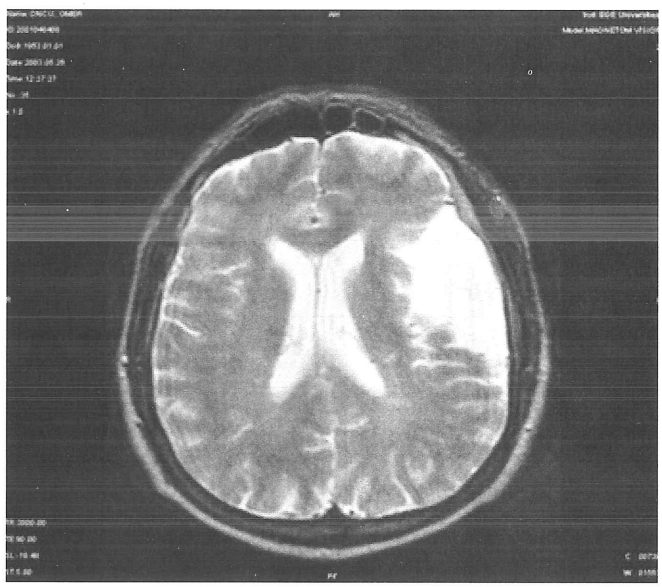

Figure 2. *T2-weighted MRI showing hyperintense signal changes in the centrum semiovale.*

terium tuberculosis in the Löwenstein-Jensen culture media. The treatment for tuberculosis was continued with two drugs (isoniazid and rifampin) after two months of initial therapy. Five months after his first admission, T1-weighted MRI showed hypointense and T2-weighted MRI hyperintense lesions in the medulla oblongata and pons without contrast enhancement, suggesting inactive lesions due to past inflammation. The patient successfully completed his six-month tuberculosis treatment. Now, 9 months after his first admission, he is completely asymptomatic. The chest radiograph is normal and the cultures are negative for acid fast bacilli.

Discussion

ADEM is frequently suspected in children with a past history of infection or vaccination. It has not been described in adult patients with active pulmonary tuberculosis. To our knowledge, this paper demonstrates for the first time a patient with simultaneous occurrence of active pulmonary tuberculosis confirmed by positive culture for *Mycobacterium tuberculosis* and ADEM confirmed by clinical and MRI findings that resolved with steroid treatment. ADEM can usually be distinguished from multiple sclerosis (MS) by 1) a history of preceding infectious illness or immunization; 2) an association with constitutional symptoms and signs such as fever; 3) a predominance of cortical signs such as mental status changes and 4) a less prominent evidence for involvement of posterior column modalities.

In typical cases of ADEM, the symptoms develop 2-20 days following an infectious illness. In our case, the time between the diagnosis of tuberculosis and the initiation of ADEM symptoms was 10 days. While the majority of ADEM cases are those following an infection or vaccination, initiation of treatment may also provoke the onset of ADEM symptoms. Cases of ADEM following administration of sulfonamides, paraaminosalysilic acid (PAS) and streptomycin have been reported (6). In our patient, the onset of the neurologic disorder occurred after the initiation of treatment for tuberculosis and this led us consider the treatment to be possibly responsible for ADEM.

Headache is reported in 45-65%, ataxia in 35-60% and meningismus in 20-30% of cases with ADEM. Among the most common abnormalities are visual, speech or mental status disturbances and psychiatric abnormalities. Weakness (50-75% of cases) is more commonly discerned than sensory defects. In the presented case, headache and ataxia were initial symptoms. The patient also experienced language disturbance, weakness and signs of depression during the course of neurological pathology.

Demyelinating lesions of ADEM are best visualized by MRI. These lesions usually exhibit no mass effect and can be seen scattered throughout the white matter of the posterior fossa and of the cerebral hemispheres. The corpus callosum is usually not involved. In order to distinguish ADEM from MS, lesions on MRI should be of the same age and no new lesion should appear on imaging studies after the first attack (7,8). In the presented case, the MRI of the central nervous system showed multiple affected areas with the same characteristics and no new lesions were detected on the follow-up MRI.

The neurological symptoms may be confused with tuberculous encephalitis. In our case, central nervous system tuberculosis was excluded by normal findings in cerebrospinal fluid examination. The affected areas in the brain also differ from tuberculosis, as tuberculosis usually causes basal lesions or tuberculoma formation (9).

In conclusion, tuberculosis may be considered as an antecedent infection for ADEM in countries where tuberculosis is frequent. Physicians must be aware of this specific clinical condition in patients with recently diagnosed tuberculosis, experiencing neurological disorder simultaneously.

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