Spindle cell pseudotumor of the brain associated with *Mycobacterium haemophilum* and *Mycobacterium simiae* mixed infection in a patient with AIDS: the first case report

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**Introduction**

Spindle cell pseudotumors may occur due to mycobacterial infection, especially in immunocompromised hosts including those with AIDS. They have been reported from many body sites; the lymph nodes are predominantly involved, most frequently associated with *Mycobacterium avium* complex infection. To the best of our knowledge, Mycobacterium-associated spindle cell pseudotumors have not been previously described in the brain stem and in association with mixed mycobacterial infection.

**Case report:** We describe a man with AIDS who presented with right hemiparesis and truncal ataxia. Magnetic resonance imaging revealed enhancing nodular lesions at the cerebral peduncle and medulla. A mycobacterial spindle cell pseudotumor was diagnosed on surgical specimens. Blood and brain tissue cultures grew *Mycobacterium haemophilum* and *Mycobacterium simiae*. 

**Conclusions:** To our knowledge, this is the first case of spindle cell pseudotumor of the brain associated with *M. haemophilum* and *M. simiae* mixed infection.
many body sites including the lymph nodes, skin and soft tissue, bone marrow, spleen, retroperitoneum, lungs, and brain. The lymph nodes are predominantly involved, most frequently associated with Mycobacterium avium complex (MAC) infection. To the best of our knowledge, Mycobacterium-associated spindle cell pseudotumors have not been previously described in the brain stem and in association with mixed mycobacterial infection. We report the first case of spindle cell pseudotumor involving the brain associated with Mycobacterium haemophilum and Mycobacterium simiae mixed infection in a patient with AIDS.

Case report

A 40-year-old British diabetic man was admitted to King Chulalongkorn Memorial Hospital, Bangkok, Thailand due to right hemiparesis, progressive truncal ataxia, and vertigo for one month. Three years prior to admission he had been diagnosed with AIDS and pulmonary tuberculosis. A Ziehl—Neelsen staining of his sputum had revealed numerous acid-fast bacilli (AFB), but mycobacterial culture had not been performed. He had received a complete 6-month course of anti-tuberculous treatment (isoniazid, rifampin, pyrazinamide, and ethambutol for the first two months; isoniazid and rifampin for the last four months). He had taken fluconazole and trimethoprim/sulfamethoxazole as primary prophylaxis for cryptococcosis and Pneumocystis jirovecii pneumonia, respectively. He had been well, without receiving anti-retroviral treatment, until one month prior to this admission when he had developed right hemiparesis, progressive truncal ataxia, vertigo, and horizontal binocular diplopia. He also noted a low-grade fever and weight loss of 5 kg. Physical examination revealed a cachectic patient with generalized papular cutaneous eruptions and oral hairy leukoplakia. Neurological examination revealed hemiparesis and decreased pinprick sensation of the right side, truncal ataxia, right facial palsy of the upper-motor neuron type, decreased gag reflex of both sides, deviated tongue to the left, and impaired finger-to-nose test of the right hand.

A complete blood count showed a hematocrit of 40%, a white blood cell (WBC) count of $6 \times 10^9$ cells/l (80% neutrophils, 15% lymphocytes, and 5% monocytes), and a platelet count of $150 \times 10^9$ cells/l. Blood chemistries and chest radiogram were normal. His CD4 cell count was 26 cells/$\mu$m$^3$. Cranial magnetic resonance imaging (MRI) revealed generalized cerebral atrophy with multiple enhancing isointense (on T1-weighted image) nodular lesions at the left cerebral peduncle and medulla (more at the left lateral medulla) (Figure 1). All lesions involved the leptomeninges adjacent to the cisterns. Lumbar puncture revealed normal cerebrospinal fluid (CSF) pressure, 10 mononuclear cells/$\mu$l, glucose of 72 mg/dl, protein of 49 mg/dl, negative tumor cells and cryptococcal antigen, and negative polymerase chain reaction (PCR) for Mycobacterium tuberculosis and cytomegalovirus. Serum immunoglobulin G for Toxoplasma gondii was positive.

Figure 1 Cranial magnetic resonance imaging revealed generalized cerebral atrophy, with multiple enhancing isointense (on T1-weighted image) nodular lesions at the left cerebral peduncle and medulla (more at the left lateral medulla). All lesions involved the adjacent leptomeninges.
During hospitalization, he developed acute urinary retention, paraparesis, and hyporeflexia of both legs. Cauda equina syndrome due to arachnoiditis was suspected, and thus lumbar puncture was performed again and revealed normal opening pressure, 20 mononuclear cells/μL, glucose of 47 mg/dL (blood glucose of 303 mg/dL), and protein of 135 mg/dL. Partial surgical removal of the lesion at the left medulla was performed, and histopathological examination showed a dense proliferation of predominantly spindle cells arranged in fascicles, in association with epithelioid histiocytes, lymphocytes, and mononuclear cells (Figure 2). A Ziehl–Neelsen staining revealed numerous AFB within these spindle cells and in the interstitium. Auramine staining was not performed. PCR for *M. tuberculosis* from the biopsy tissue was negative. He was then empirically treated with isoniazid, rifampin, pyrazinamide, ethambutol, and clarithromycin.

Automated mycobacterial blood cultures subsequently grew *M. haemophilum*. However, the brain tissue grew *M. simiae*. Confirmation of both species was made by the amplification of 16S ribosomal RNA using the real-time nested PCR (Perkin Elmer Cetus, Norwalk, USA) and sequencing using the automated sequencing ABI-prism 310 (Foster City, CA, USA).  

His general condition gradually improved with the continuation of all five anti-mycobacterial agents, except some residual neurological deficits. One month after hospitalization, he commenced anti-retroviral treatment including zidovudine, lamivudine, and efavirenz. He was discharged home, and was seen for the last time three months after the operation.

**Discussion**

Non-tuberculous mycobacterial infections have been increasingly reported in many organs both in immunocompetent and immunocompromised patients. Localized infections are frequently described in immunocompetent hosts, in contrast to the higher rates of disseminated infections in those with immunocompromised status. The species distribution of mycobacterial clinical isolates from patients with AIDS varies widely among many studies depending on geographic area and the microbiological methods utilized. MAC is among the most frequently isolated pathogens, followed by *Mycobacterium kansasi*, *Mycobacterium fortuitum*, *Mycobacterium chelonae*, *Mycobacterium xenopi*, *Mycobacterium gordonae*, and *Mycobacterium flavescens*.  

*M. haemophilum* and *M. simiae* are rarely described in the literature. *M. haemophilum* was first described in 1978 in Israel in a patient with Hodgkin’s disease who presented with subcutaneous lesions.  

It is a fastidious growing Mycobacterium, requiring hemin or ferric ammonium citrate and an optimal temperature for growth of between 30 and 32 °C. However, some strains of *M. haemophilum* are capable of growth at 37 °C on Middlebrook 7H10 agar medium containing hemin. The hemin requirement distinguishes *M. haemophilum* from a group of isoniazid-resistant isolates of *M. tuberculosis*. *M. haemophilum* can cause a wide variety of human infections ranging from localized to disseminated infections.

*M. simiae* was first isolated from *Macacus rhesus* monkeys in 1965. It is a slow growing photochromogenic Mycobacterium and shares many features with members of MAC and *Mycobacterium scrofulaceum*. *M. simiae* is unique among mycobacteria in that part of its 16S ribosomal RNA gene sequence is similar to those sequences shared by slowly growing mycobacteria, while another portion resembles sequences shared among rapidly growing mycobacteria and can be correctly classified by molecular methods. *M. simiae* can cause a wide variety of infections from localized to disseminated infections.  

Our patient had positive blood and brain tissue cultures for *M. haemophilum* and *M. simiae*, respectively. The negative cultures of the brain tissue for *M. haemophilum* were probably due to no hemin or ferric ammonium citrate, essential for growth of this organism. In addition, our patient may have had disseminated and localized brain infections caused by *M. haemophilum* and *M. simiae*, respectively. To our knowledge, no mixed infection with *M. haemophilum* and *M. simiae* has been described in the literature. Only one case of a mixed disseminated infection with *M. simiae* and MAC has been reported in a patient with AIDS. Our case may be the first report of a mixed disseminated infection with *M. simiae* and *M. haemophilum*, even though the microbiology results did not confirm the fact.
Histopathological appearances associated with mycobacterial infection in patients with AIDS include caseous, non-caseous, or poorly granulomatous inflammation, suppurrative inflammation, necrotizing inflammation, or non-specific inflammation. Spindle cell pseudotumors have been reported to be rare complications of mycobacterial infections in immunocompromised patients. 1–8 To our knowledge, only one case of spindle cell pseudotumor of the brain caused by MAC has been reported, in a patient without HIV infection. 2 Thus, our case is the first report of spindle cell pseudotumor of the brain stem associated with mycobacterial infection.

In conclusion, there should be awareness that mycobacterial infections may be associated with spindle cell pseudotumors, especially in patients with AIDS. This condition should be included in the differential diagnosis because the clinical impact of distinguishing between mesenchymal tumors and mycobacterial pseudotumors is significant. Conflict of interest: No conflict of interest to declare.

References


