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Case report

Tuberculous Orchiepididymitis, Meningoencephalitis and Hydrocephalus

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A B S T R A C T

Tuberculous meningoencephalitis (TBM) is a rare and serious, often fatal presentation of active tuberculosis and account for about 1% of cases. Early diagnosis and prompt treatment of TBM is essential to reduce morbidity and mortality. Here, we report a case of TBM in 60-year-old man. TBM was considered on the basis of clinical presentation, laboratory findings (hyponatraemia), cerebrospinal fluid studies, radiological findings (hydrocephalus on multi-slice computed tomography), and history of orchiepididymitis of unknown origin one year earlier, together with information that the patient originated from Kosovo where incidence of tuberculosis is still high. Mycobacterium tuberculosis was cultured from cerebrospinal fluid on Lowenstein-Jensen medium confirming diagnosis of TBM. Subsequently, acid-fast bacilli (AFB) staining on samples obtained after orchiectomy a year ago was performed, revealing AFB. Anti-tuberculosis therapy is still in course. This is the second case of tuberculous meningoencephalitis with the same disease pattern (i.e. tuberculous orchiepididymitis – meningoencephalitis) in our Department, and this fact was crucial for the presumptive diagnosis and urgent treatment of TBM. The former case was described five years ago.

Key words: *tuberculousis, orchiepididymitis, meningoencephalitis, hydrocephalus*

Introduction

Central nervous system (CNS) disease caused by *Mycobacterium tuberculosis* is an uncommon yet higly devastating manifestation of tuberculosis. CNS tuberculosis (TB) account for approximately 1% of all cases of tuberculosis, carries a high motality and a distressing lavel of neurological morbidity[1]. Early diagnosis of CNS TB is necessary for appropiate tretment to reduce this morbidity and mortality[2]. *Mycobacterium tuberculosis* infection is prevalent in more than 2 billion people worldwide, with about 15 million of these individuals with active infection[3,4]. Tuberculosis remains a worldwide burden, with a large majority of new active tuberculosis cases occurring in underdeveloped and developing countries[4]. In 80% of new tuberculosis cases, demographic factor such as poverty, crowding, malnutrition, and a compromised immune system play a major role in the worldwide epidemic, while the remaining 20% of tuberculosis cases are associated with HIV in Sub-Saharan Africa[5,6].

Here we report a case of CNS TB in an immunocompromised male.

Case Report

A 60-year male, originated from Kosovo, with dilatative cardiomiopathia and chronic liver disease, was admitted to the Nephrology unit with a slight fever, cephalea, malaise and signs of chronic renal failure. In anamnestic data, the patient mentioned orchiepidydimitis of unknown origin one year back when underwent right side orchiectomy. Laboratory on admission: CRP 83.5 mg/L, ESR 112 mm/h, RBCs 3.02×10^{12}/L, Hb 86 g/L, WBCs 6.2×10^9/L, platelets 279×10^9/L, urea 8.2 μmol/L, creatinine 191 μmol/L, Na 127 mmol/L, bilirubine 10 μmol/L, AST 37 IU/L, ALT 45 IU/L, AP 191 IU/L, GGT 274 IU/L. A chest radiogram showed some degree of miopatic and enlarged cardiac configuration but without pathological inflammation. During eight hospital days, the patient became confused, lethargic with sphincter dysfunction. Multi-slice computed tomography (MSCT) of the brain showed normotensive hydrocephalus (Figure 1). Physical examination revealed a stiff neck and urgent lumbal puncture was performed. Cerebrospinal fluid (CSF) revealed: L 59×10^6/L (neutrophils 87, lymphocytes 7, monocytes 4 and basophiles 2%), glucose level 1.6 mmol/L, a

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total proteini 0.56 g/L, lactate 3.47 mmol/L, chloride 102 mmol/L.

On the basis of clinical presentation, epidemiological data, past medical history of orchiepididymitis, CSF findings, hyponatraemia and hydrocephalus, the diagnosis of tuberculous meningoencephalitis was considered. Prompt treatment with four first-line anti-tuberculosis drugs was initiated. *Mycobacterium tuberculosis* was cultured from cerebrospinal fluid on Lowenstein-Jensen medium confirming diagnosis of TB CNS. Subsequently, acid-fast bacilli (AFB) staining on samples obtained after orchiectomy a year ago was performed, revealing AFB. Clinical course thereafter showed gradual but constant improvement in clinical, laboratory and CSF parameters. Anti-tuberculosis therapy is still in course.

Discussion

Central nervous system disease caused by *Mycobacterium tuberculosis* is an uncommon manifestation of tuberculosis, which was universally fatal in the era before anti-tuberculosis therapy. Due to its relative rarity and the protean nature of the symptoms, tuberculosis of the CNS remains a formidable diagnostic challenge[7]. In the largest prospective epidemiological study on CNS tuberculosis, the chance of developing CNS tuberculosis was 1.0% among 82.764 tuberculosis cases from 1970 to 2001 in a Canadian cohort[8]. In Kosovo, the incidence of TB was decreased but is still high[9,10]. Both children and HIV-coinfected patients are at high risk for developing CNS tuberculosis[11,12]. Other risk factors include malnutrition and recent measles in children, alcoholism, malignancies, and use of immunosuppressive agents in adults[13–15]. TB meningitis is the most common cause of chronic meningitis, with clinical presentation often consisting of a subacute febrile illness with generalized neurological syndrome. CNS TBC has the highest mortality rate (20% to 50%) among all forms of TB, and it is associated with more serious complications and sequelae.

The pathogenesis involves establishment of tuberculous foci in the brain or meninges, usually from primary infection or reactivation infection. The foci progress and rupture into the subarachnoid space, thus seeding infection into the central nervous system[17]. The haematogenous seeding of *M. tuberculosis* occurs most frequently in regions of the body that are highly oxygenated, including the brain[18].

Clinical signs of patients presenting with TB meningitis can be easily assessed for severity based on modifications of the Medical Research Council staging system which has been shown in numerous series to have considerable prognostic value[19]. The classical staging system is as follows: stage I is fully conscious and no focal deficit; stage II is conscious but with inattention, confusion, lethargy, and focal neurological signs such as cranial nerve palsies; and stage III is stuporous or comatose, multiple cranial nerve palsies, or complete hemiparesis or paralysis. A more contemporary modification of the staging system defines grade I as alert and oriented without focal neurological deficits, grade II as a Glasgow coma score of 11 to 14 or 15 with focal neurological deficits, and grade III as a Glasgow coma score of 10 or less with or without focal neurological deficits[20,21].

Consequence of TB meningitis are hydrocephalus and development of vasculitis in the vessels of the circle of Willis, the vertebrobasilar system, and the perforation branches of the middle cerebral artery, resulting in infarctions[2,7]. Common findings on imaging are abnormal meningeal enhancement in the basal cisterns, hydrocephalus, and vascular complications[2]. Hydrocephalus may occur in the early or latent stage of the disease even after commencement of anti-TB drugs, and its management may influence prognosis. Hydrocephalus encountered in TB meningitis can be broadly divided into two types: communicating type, which is common, secondary to an obstruction of the basal cisterns by inflammatory exudates and obstructive type, which is less common and either secondary to a focal parenchymal lesion causing mass effect or due to the entrapment of a part of the ventricle by granulomatous ependymitis[2].

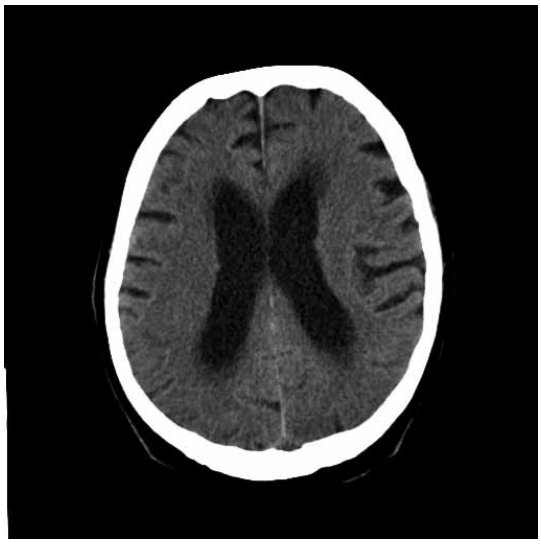

Fig. 1. Normotensive hydrocephalus on multi-slice computed tomography.

The typical analysis of cerebrospinal fluid with CNS TB demonstrates a moderate lymphocytosis, moderately elevated protein levels, and hypoglycorrachia. As such, the CNS profile of CNS TB mimics the profiles of a large list of both infectious and noninfectious processes that affect the CNS. The predominance of neutrofils in some cases likely represents an earlier stage of infection, which, over the course of days to weeks, will convert to a predominantly lymphocitic profile[22,23]. CSF can also demonstrate the presence of acid-fast bacilli. *Mycobacterium tuberculosis* complex can be identified specifically by DNA probe or by nucleic acid amplification test[24,25]. Non-invasive imaging modalities, such as computed tomography scan and magnetic resonance imaging are routinely used in the diagnosis of neurotuberculosis.

Treatment for all forms of CNS TBC should consist of 4 drugs (isoniasid, rifampicin, pyrasinamid, ethambutol) for 2 mouths followed by 2 drugs (isoniasid, rifampicin) for at least 10 months[26]. Studies show that adjunctive corticosteroids decreases mortality[27].

Tuberculous meningoencephalitis in presented patient was considered on the basis of clinical presentation, laboratory findings (hyponatraemia) cerebrospinal fluid studies, radiological findings (hydrocephalus on MSCT and MRI of the brain), and history of orchiepididymitis of unknown origin one year earlier, together with information that the patient originated from Kosovo where incidence of tuberculosis is still high. Subsequently, acid-fast bacilli (AFB) staining on samples obtained after orchiectomy a year ago was performed, revealing AFB. Anti-tuberculosis therapy is still in course. This is the second case of tuberculous meningoencephalitis with the same disease pattern (i.e. tuberculous orchiepididymitis – meningoencephalitis) in our Department, and this fact was crucial for the presumptive diagnosis and urgent treatment of TB CNS. The former case was described five years ago[28]. We point out that in case of meningoencephalitis, hydrocephalus and orchiepididymitis, tuberculosis must be taken into consideration.

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TUBERKULOZNI ORHIEPIDIDIMITIS, MENINGOENCEFALITIS I HDROCEFALUS

SAŽETAK

Tuberkulozni je meningoencefalitis (TBM) rijedak, no ozbiljan, često fatalan oblik aktivne tuberkuloze i na njega otpada oko 1% svih slučajeva tuberkuloze. Rana dijagnoza i liječenje ključni su u smanjenju pobola i smrtnosti. Prikazan je slučaj TBM-a u šezdesetogodišnjaka. Na TBM se posumnjalo na temelju kliničke slike, laboratorijskih nalaza (hiponatremija), analize cerebrospinalnog likvora, radiografskih nalaza (hidrocefalus na višeslojnoj spiralnoj kompjuteriziranoj tomografiji mozga) te podatka o preboljelom orhiepididimitisu nepoznate etiologije godinu dana ranije, a uzevši u obzir da je bolesnik podrijetlom s Kosova gdje je učestalost tuberkuloze još uvijek visoka. *Mycobacterium tuberculosis* je izoliran iz cerebrospinalnog likvora na Lowenstein-Jensenovoj podlozi potvrdivši dijagnozu TBM-a. Naknadno su i u uzorcima tkiva dobivenima nakon orhiektomije godinu dana ranije nađeni acidorezistentni bacili. Antituberkulozna terapija je u tijeku. Ovo je drugi slučaj tuberkuloznog meningoencefalitisa s jednakim obrascem bolesti (tj. tuberkulozni epididimitis-meningoencefalitis) u našoj Klinici što je bilo ključno u postavljanju radne dijagnoze i započinjanju hitnog liječenja. Prvi je slučaj opisan prije pet godina.