Unusual presentation of more common disease/injury

Tuberculous meningitis, an unusual presentation in a young lady

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Summary

A 37-year-old Persian-speaking woman presented with epigastric pain, vomiting and non-specific frontal headache. Examination was unremarkable except for an isolated sixth nerve palsy found a few days after admission. Blood results were normal, as was the chest radiograph and the CT scan of the head. Initial cerebrospinal fluid (CSF) analysis revealed a significantly elevated protein level with reduced glucose, as well as CSF lymphocytosis. Tuberculosis (TB) meningitis was considered and she was commenced on anti-TB treatment before confirmation of the diagnosis. A full contact tracing was performed with regular follow-up with TB nurses. When she was seen in the clinic a month later, her symptoms had subsided completely.

BACKGROUND

The resurgence of tuberculosis (TB) in some parts of the UK has been associated with changing patterns in its epidemiology. Over the last 50 years, it has moved from a disease that occurred across all parts of the population to one occurring predominantly in specific population subgroups. Rates are higher in certain communities, mainly by virtue of their connections to higher-prevalence areas of the world. Endemic factors such as homelessness and alcohol misuse are important factors.

This patient presented initially, with non-specific symptoms and no telltale signs of TB meningitis (TBM).

Lumbar puncture led us to the final diagnosis. We all recognise the significance of history taking in clinical diagnosis. This case highlights the importance of a thorough history particularly when faced with language difficulties.

Most of the cases of TB in UK are pulmonary in nature but it is important to be familiar with non-pulmonary sites of TB infection such as central nervous system, gastrointestinal system or bones.

CASE PRESENTATION

A 37-year-old Persian-speaking woman who had emigrated from Afghanistan to the UK, presented to our Acute Medical Unit (AMU) with a 1 week history of epigastric pain radiating to the back. She had associated vomiting and non-specific frontal/occipital headache. This was preceded by a 2 week history of general malaise with persistent headaches.

There was no previous history of any headaches or abdominal problems. Furthermore, there was no history of recent travel, surgery, trauma and had not used contraceptive pills. She did not have shortness of breath, a cough or weight loss.

On initial assessment, there was no focal neurology with a normal mental status and examination of the other

systems was normal. Her vital signs were within normal range and she was afebrile throughout her admission.

However, on day 4 of admission, left sixth nerve palsy was observed. There were no abnormalities detected on funduscopy.

INVESTIGATIONS

On admission, blood results were predominantly normal except a mildly elevated d-dimer at 1036 and erythrocyte sedimentation rate at 48 mm/h. Subsequent blood tests showed a similar picture.

A chest radiograph and an ultrasound scan of abdomen were reported as normal.

In view of the headaches a CT head (without contrast) was carried out and was unremarkable.

After gathering further history from the husband (who acted as an interpreter), it came to light that the patient had emigrated from Afghanistan less than 12 months ago. This key factor prompted us to carry out a lumbar puncture in order to rule out TB meningitis, despite her having no known contacts. This showed slightly cloudy fluid with a raised opening pressure of 36 mm H₂O (7–18), white blood cell count of 93/mm³ mainly lymphocytes 90%, polymorphs 10% (<5 mononuclear cells/mm³), markedly raised protein 2.8 g/l (0.2–0.4), low glucose at 1.1 mmol/l with plasma glucose 5.6 mmol/l (2/3 to 1/2 of blood glucose), red blood cells 13/mm³ probably trauma-related. Gram stain was negative. Cerebrospinal fluid (CSF) microscopy including auramine and Ziehl–Neelsen stains were negative. At this stage, anti-TB medications and dexamethasone were commenced after discussion with the microbiology and neurology colleagues.

The PCR test for TB on CSF was negative but the serum T-Spot test, an interferon γ release assay (IGRA) test was positive for TB (a Mantoux skin test was not conducted, as a result for the T-Spot test was available more quickly). *Mycobacterium tuberculosis* was isolated from CSF culture 20

Stage	Clinical Picture
1 (Early)	Nonspecific (e.g. generalized malaise, fever, anorexia)
2 (Intermediate)	Lethargy Meningism Moderate focal neurological deficits (e.g. cranial nerve palsies)
3 (Advanced)	Seizures Severe neurological deficits (e.g. paresis) Stupor or coma

Figure 1 The Medical Research Council staging system for the clinical classification of tuberculosis meningitis.

days after the sample was sent and was sensitive to first line anti-TB medications.

The bronchial washing taken from the bronchoscopy was negative for AAFB. In addition, the patient was also HIV antibody negative.

These results showed a clear picture of TBM. High resolution CT scan of the thorax ruled out miliary TB.

DIFFERENTIAL DIAGNOSIS

1. Viral illness with headache
2. Viral meningitis
3. Fungal meningitis
4. Sarcoidosis
5. Carcinomatous/lymphomatous meningitis
6. Cerebral venous sinus thrombosis
7. Intracranial space occupying lesion.

TREATMENT

She was started on isoniazid, rifampicin, pyrazinamide, ethambutol for the first 2 months. Isoniazid and rifampicin were continued thereafter. In view of high CSF protein and abducens nerve palsy she was given a short course of steroids. There was regular follow-up by TB nurses for review of her symptoms and to aid in medication compliance and side effects. Contact tracing was carried out with screening for her husband and children. One of her children was T-Spot positive (blood sample) and was given chemoprophylaxis.

OUTCOME AND FOLLOW-UP

When we saw her in AMU clinic, her symptoms had improved markedly. She was continuing to improve following advice from the TB nurses and was followed up at the regional infectious disease centre. She is now more aware of her health and continues to observe her children for any symptoms.

DISCUSSION

TB is one of the major global causes of morbidity and mortality and the majority of these deaths are in the developing countries (WHO report 2010).

The number of TB cases observed in the UK continues to rise. The rate of disease in the UK in 2009 was 14.6 per 100 000, 4% higher than in 2008 and 28% higher than in 2000. The majority of patients continue to be young adults aged 15 to 44 years (60%) and non-UK born (73%). Rates of disease in the non-UK-born are 20-fold higher (around 86 per 100 000) than for those born in the UK (around 4 per 100 000). The majority of non-UK born patients (79%)

Variable	Score
Age	
≥ 36	2
< 36	0
Blood WBC Count (10 / ml)	
≥ 15000	4
< 15000	0
History of illness (days)	
≥ 6	-5
< 6	0
CSF total WBC count (10 / ml)	
≥ 900	3
< 900	0
CSF % Neutrophils	
≥ 75	4
< 75	0

Figure 2 The Vietnam Algorithm for the diagnosis of tuberculosis meningitis.

were diagnosed 2 or more years after arrival in the UK.¹ There is proven strong association between HIV and TB. A patient with HIV is estimated to have 20 to 37-fold increase in risk of developing any form of TB. Around 13% of new TB cases occur in patients with HIV.² TBM makes up 2% of all TB cases in the UK.

TBM is a life-threatening and most severe form of extrapulmonary TB which is associated with increased mortality and morbidity in developing countries. The worst outcome of TBM is mainly due to delay in diagnosis because of variable clinical presentation and poor sensitivity and specificity of available diagnostic tests.³

The Medical Research Council (MRC) has developed a three tier staging system for the clinical classification of TBM⁴ (figure 1)

Atypical presentations include a slow onset course affecting cognition or a rapid onset course mimicking acute bacterial meningitis or even a subarachnoid haemorrhage.

Patients with TBM always have a focus of infection elsewhere, which can often be difficult to find. In >50% of cases, there is an acute miliary TB.⁵

The British Infection Society Guidelines⁶ suggest that TBM is best diagnosed with lumbar puncture and examination of the CSF. CSF leucocytosis (predominantly lymphocytes), a rise in CSF protein, and a CSF: plasma glucose ratio of <50% is highly suggestive of the disease.

Imaging is key for the diagnosis of cerebral tuberculoma although does not provide diagnostic confirmation. Results from IGRA tests such as T-Spot are available within 48 h while waiting for TB culture results. This test is valuable where the negative PCR test result on CSF is less reliable. T-Spot test may remain positive after successful TB treatment.⁷

The Vietnam diagnostic algorithm⁸ (figure 2) is often used to guide clinical diagnosis of TBM compared to non-TBM. The parameters of this algorithm include age; duration of symptoms, blood white cell count, CSF total white cell and neutrophil cell counts. The applicability of The

Vietnam diagnostic algorithm is currently being retrospectively evaluated to aid in the diagnosis of TBM in the UK population. Although this tool was not used as part of the patient's clinical assessment at the time, in retrospect, the score in our patient supported TBM diagnosis. This score indicates that a diagnosis of TBM is more likely in comparison to any other form of meningitis such as acute bacterial meningitis.

Treatment for all forms of central nervous system TB should consist of four drugs (isoniazid, rifampicin, pyrazinamide, ethambutol) for 2 months followed by two drugs (isoniazid, rifampicin) for at least 10 months. Adjunctive corticosteroids (either dexamethasone or prednisolone) should be given to all patients with TBM, regardless of disease severity. Treatment delay is strongly associated with death and empirical anti-TB therapy should be started promptly in all patients in whom the diagnosis of TBM is suspected. Do not wait for microbiological or molecular diagnostic confirmation.⁶

A case series, which evaluated 43 TBM cases admitted in Neurology Department⁹ found that the most frequent presentations were malaise (93%), anorexia (88%), headache (81%), meningism (81.4%), fever (65.1%), vomiting (51%) and cranial nerve palsies (46.5%)-multiple cranial nerve palsies in 46.5% and sixth nerve palsy 32.6%. 53.5% of the evaluated patients presented at stage II on the MRC classification. Similar presentations were noted in a case series conducted by Christensen *et al.*¹⁰ This series also commented that 33% of patients made a full recovery whereas 48% had sequelae.

One case report¹¹ describes a 19-year-old lady who presented with a cough, productive of yellow sputum and a severe headache. Once her headaches subsided, she was discharged after a normal chest x-ray and white cell count. She was later readmitted with recurrence of the headache, vomiting and had a generalised tonic-clonic seizure. This lady was diagnosed by CSF PCR; CSF culture and CT head were all normal. She made a full recovery with no adverse neurological sequelae.

A second case report¹² describes a 19-year-old man who developed a subacute headache and fever for 2 weeks, followed by a focal seizure and left hemiparesis. Initial CSF studies showed a polymorphonuclear pleocytosis, mildly elevated protein level and normal glucose. An MRI showed focal meningoencephalitis. Repeated CSF cultures did not isolate any bacteria, although the patient was started on anti-TB medication. Four weeks later, a positive CSF culture gave the diagnosis of TBM.

Learning points

- ▶ TBM can present non-specifically. Differentiating it from viral meningitis on clinical grounds alone is difficult, thus the lumbar puncture is essential for diagnosis.
- ▶ TBM should be considered in patients coming from endemic areas, presenting with non-specific symptoms and headaches.
- ▶ One should always keep TB infection in mind when faced with at-risk individuals.
- ▶ A thorough history and examination are always key and every effort must be taken to arrange interpretation in non-English speaking patients.
- ▶ Our case report and other case studies highlight that the CSF culture results may not be reported positive until after a few weeks. Therefore it is important to start treatment on the basis of clinical suspicion.

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Competing interests None.

Patient consent Obtained.

REFERENCES

1. Anderson L, Moore J, Kruijsaar M, *et al.* Tuberculosis in the UK: Report on tuberculosis surveillance in the UK 2010. *Health Protection Agency* 2010.
2. Gibson PG. *Evidence-based Respiratory Medicine*. Oxford: Blackwell Publishing 2005:325.
3. Iype T, Chacko S, Raghavan S, *et al.* Preliminary report of directly observed treatment, short course in tuberculous meningitis. *Ann Indian Acad Neurol* 2010;**13**:57–60.
4. Rajshekhar V. Management of hydrocephalus in patients with tuberculous meningitis. *Neurology India* 2009;**57**:368–75.
5. Goering R, Dockrell H, Zuckerman M, *et al.* *Mims' Medical Microbiology*. Third Edition. Philadelphia, PA: Mosby-Year Book Europe 2008.
6. Thwaites G, Fisher M, Hemingway C, *et al.* British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. *J Infect* 2009;**59**:167–87.
7. Dinnes J, Deeks J, Kunst H, *et al.* A systematic review of rapid diagnostic tests for the detection of tuberculosis infection. *Health Technol Assess* 2007;**11**:1–196.
8. Thwaites GE, Lan NT, Dung NH, *et al.* Tuberculous meningitis: many questions, too few answers. *Lancet* 2005;**366**:70–70.
9. Zafar A, Irfan M. Lateral rectus palsy: an important sign in diagnosing tuberculous meningitis. *KUST Med J* 2011;**3**:10–14.
10. Christensen AS, Andersen AB, Thomsen VO, *et al.* Tuberculous meningitis in Denmark: a review of 50 cases. *BMC Infect Dis* 2011;**11**:47.
11. D'Souza R, Franklin D, Simpson J, *et al.* Atypical presentation of tuberculous meningitis: a case report. *Scott Med J* 2002;**47**:14–15.
12. Wang PY, Hsieh FY, Cheng TY. Atypical presentations of tuberculous meningitis—a case report. *Zhonghua Yi Xue Za Zhi (Taipei)* 1991;**48**:153–7.

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