Bacterial meningitis- surely not

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Word count 1405
Case Report

A 62-year-old retired woman was admitted to hospital via her GP for investigation of a four-week history of vomiting and malaise associated with hyponatraemia. She had initially been diagnosed as suffering from a viral gastroenteritis. However, the vomiting had persisted and had become associated with a mild frontal headache. There was no history of diarrhoea or abdominal pain. She had an unremarkable past medical history, never smoked, with no recent foreign travel and was not taking any regular medication.

On examination, in hospital, she appeared clinically dehydrated but was otherwise well, alert and orientated. She was afebrile with a blood pressure of 130/76 mmHg. She had a sinus tachycardia of 104/minute, but normal heart sounds. Neurological examination was unremarkable. There was no rash, photophobia, neck stiffness or stigmata of endocarditis.

Investigations revealed a plasma sodium of 127 mmol/l (135-145 mmol/l), potassium of 3.4 mmol/l (3.5- 5.0 mmol/l), urea 4.8mmol/l and creatinine of 68 mmol/l. There was no evidence of syndrome of inappropriate antidiuretic hormone (SIADH) production (serum osmolality 261mmols/kg; urine osmolality 71 mmols/Kg; urine sodium < 10mmol/L). Serum complement and plasma immunoglobulin levels were within the normal range as were a full autoimmune profile and thyroid function. Random cortisol level was mildly elevated at 799 nmol/L (normal 140 –700nmol/L) consistent with a stress response.
Her initial white cell count (WCC) was mildly elevated at 13.0 x 10^9/L (normal 4–11 x 10^9/L) of which neutrophils were 10 x 10^9/L (normal 2-7.5 x 10^9/L). Her ECG and chest X-ray were normal. C-reactive protein was slightly elevated at 10 mg/L (normal <5 mg/L) and erythrocyte sedimentation rate (ESR) was normal at 5 mm/hour. Her Chest X-ray was normal.

Initial microbiological investigations (blood cultures, urine analysis and culture) were normal.

Early management consisted of slow intravenous rehydration with normal saline and antiemetic therapy, which led to a mild symptomatic improvement. Upper gastrointestinal endoscopy revealed mild oesophagitis.

During the next two weeks laboratory investigations remained stable (CRP normal; ESR normal; sodium 127-131 mmol/L; WCC 11-13 x 10^9/L). On day 4 of admission she developed a mild fever 37.5ºC which persisted (<38ºC). A CT scan of the head revealed periventricular patchy white matter changes but no features of raised intracranial pressure or space occupying lesion. She became slowly more lethargic, withdrawn, and depressed. By day 17 of admission she was uncooperative and although alert and orientated her conversation was occasionally confused. Her symptoms of intermittent nausea and vomiting with occasional frontal headache continued.

On day 18 she underwent a lumbar puncture (LP) as she had become withdrawn, temperature 37.5ºC, and WCC of 11 x 10^9/L (neutrophils 9.3 x 10^9/L). Her nausea and vomiting had failed to fully settle with supportive treatment. The LP results were as follows: cerebrospinal fluid (CSF) appearance was pale yellow and clear; protein = 5.69 g/L (0.15-0.4 g/L); CSF glucose 1.7 mmol/L versus plasma glucose 5.7 mmol/L (ratio =
30%, normal > 50%); CSF WCC = 106/mL (normal <5 WCC/mL) - 99% lymphocytes. Gram stain revealed evidence of the presence of gram-negative coccobacilli; acid–fast bacilli were not seen. She was commenced on intravenous ceftriaxone.

Contrast MRI brain revealed sub-acute infarction of the right frontal cortex but with no evidence of meningeal enhancement. EEG demonstrated slow wave activity consistent with meningo-encephalitis.

Within 48 hours of intravenous antibiotics she was more alert, orientated, with increased mobility. CSF culture grew a gram-negative cocci, which was identified as *Neisseria meningitidis* group B, type NT, subtype NT P1.16/nt. She underwent contact tracing and completed a 10-day course of intravenous ceftriaxone. She continued to make a slow but progressive recovery. After a period of rehabilitation and intense physiotherapy she was discharged home 40 days after admission, with mild residual gait ataxia.

**Discussion**

We present a case of chronic meningococcal meningitis presenting in the older (<65 years) adult. The diagnosis was delayed due to the atypical clinical presentation. This case report presents two important clinical concepts: bacterial meningitis in the older adult and presentation of chronic meningitis.

Chronic meningitis is defined as symptoms and signs of meningeal inflammation and persisting cerebrospinal fluid (CSF) abnormalities such as elevated protein level and pleocytosis for at least one month. It affects only 10% of meningitis sufferers, and is linked to a large variety of causes (both infective and non infective). There are several
features that may help to differentiate it from acute meningitis (table 1). However, whilst there are numerous published individual case reports on chronic meningitis, there is a definite paucity of large case series in the literature.

Bacterial meningitis is usually a rapidly progressive and highly lethal disease in older adults. Rapid diagnosis is vital as the prognosis worsens with diagnostic delay leading to a high rate of sustained neurological deficit in this age group. Despite the widespread use of antibiotics the overall case mortality rate remains unchanged and is far higher (37-44%) compared with that seen in younger adults (10-25%) with significant long-term morbidity (up to 70% of infected patients) in survivors.

*Neisseria meningitides* is the leading overall cause of bacterial meningitis in the Western World and predominates in young adults. *N. meningitides* is a gram-negative, aerobic diplococcus. They are classified into serogroups (eg A,B,C etc) according to the immunological reactivity of their polysaccharides. The most prevalent serogroups implicated in clinical meningococcal meningitis are serogroup B (62%, our patient) and the more virulent serogroup C (22%). The relatively reduced virulence of serogroup B may partly explain the chronicity of presentation and reduced inflammatory response seen in our patient. Serogroups B and C have a seasonal variation occurring more commonly in the first quarter of the year (our patient presented in February). The infection is more common in blacks and lower socioeconomic classes and is linked to both active and passive smoking.

Given the success of childhood immunization and an aging population the proportion of older adults presenting with bacterial meningitis is increasing. There are several additional factors, which make the older adult more prone to bacterial and
occasionally chronic meningitis. Older adults often have underlying acute and chronic
diseases (eg diabetes, renal or hepatic failure) with immunescence (decline in immune
function).\textsuperscript{1} This can lead to symptoms which can be confused with those of meningitis
and at the same time increase the propensity to infection.\textsuperscript{1,16} The role of immunescence in
predisposing patients to bacterial meningitis is not clearly defined, but appears to relate to
defects in innate, specific cellular and humoral immunity leading to an attenuated
immune response.\textsuperscript{1,17-19} Persons who lack or are deficient of antibody-dependent,
complement-mediated lysis (bacteriocidal activity) are most susceptible to
meningococcal disease.\textsuperscript{13} Our patient had an unremarkable past medical history with
normal complement and immunoglobulin levels with no evidence of
immunosuppression.\textsuperscript{20-22}

The clinical presentation of bacterial meningitis is more variable in the older as
compared with the younger adult (table 2), with fewer patients manifesting fever, neck
stiffness, and headache than among younger adults.\textsuperscript{1} It has been suggested that 1 of 3
findings (fever, neck stiffness, altered mental state) is present in virtually all patients with
meningitis and that the absence of these features virtually excludes meningitis with a high
negative predictive value (table 1).\textsuperscript{1} Our patient had none of these features on
presentation and had been unwell for four weeks prior to presentation, but did develop a
mild fever (<38ºC) and cognitive dysfunction during her inpatient stay.

Diagnosis was made more difficult due to the lack of inflammatory response
observed in laboratory tests. Although there was a persistent mild neutrophilia both the
CRP and ESR were normal throughout the course of the disease, which is unusual but has
been reported in chronic meningitis (table 2).\textsuperscript{23-25} Also in this case there was a blunted febrile response, which is often seen in older adults in general.\textsuperscript{26}

Our patient’s CSF showed a lymphocytosis, raised protein, and low glucose ratio, which is seen in only 10\% of bacterial meningitis and would normally suggest infection with \textit{Listeria monocytogenes} meningitis and alternative causes such as tuberculous and fungal infection.\textsuperscript{27,28} The finding of hyponatraemia without SIADH as in our patient, whilst uncommon, has previously been documented and is more commonly associated with chronic than acute menigitis.\textsuperscript{25,29}

This case highlights the diagnostic challenge associated with the older patient presenting with bacterial meningitis. The diagnosis requires thorough investigation during the inpatient stay. Early lumbar puncture is to be encouraged as it is essential to confirm the diagnosis. Despite a delayed diagnosis appropriate antibiotic therapy can still lead to a good outcome.
References

1. Choi C: **Bacterial meningitis in aging adults.** *Clin Infect Dis* 2001, **33**:1380-1385.

2. Ellner JJ, Bennett JE: **Chronic meningitis.** *Medicine (Baltimore)* 1976, **55**:341-369.


25. Anderson NE, Willoughby EW: **Chronic meningitis without predisposing illness--a review of 83 cases.** *Q J Med* 1987, **63**:283-295.


Table 1. Features distinguishing bacterial meningitis in the young compared with the older (>65 years) adult

<table>
<thead>
<tr>
<th>Description</th>
<th>Young adult</th>
<th>Older adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying chronic disease</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Immune function</td>
<td>Often normal</td>
<td>Often reduced (immunescence)</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Usually typical</td>
<td>Often atypical</td>
</tr>
<tr>
<td>Most commonly identified pathogen</td>
<td>Neisseria meningitides</td>
<td>Streptococcus pneumonia</td>
</tr>
<tr>
<td>Fever</td>
<td>Common</td>
<td>May be blunted or absent</td>
</tr>
<tr>
<td>Average case mortality %</td>
<td>10-25%</td>
<td>37-44%</td>
</tr>
<tr>
<td>Rash</td>
<td>Relatively common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Description</td>
<td>Acute meningitis</td>
<td>Chronic meningitis</td>
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<tr>
<td>----------------------</td>
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<tr>
<td>Fever</td>
<td>Common</td>
<td>May be absent or low grade</td>
</tr>
<tr>
<td><strong>Inflammatory markers</strong> (eg CRP, ESR)</td>
<td>Elevated</td>
<td>May be minimally elevated and rarely normal</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Usually typical</td>
<td>Atypical</td>
</tr>
<tr>
<td>Most common aetiology</td>
<td>Neisseria meningitides</td>
<td>Variable (eg tuberculous and malignant meningitis)</td>
</tr>
<tr>
<td>Hyponatraemia</td>
<td>Uncommon</td>
<td>Relatively common</td>
</tr>
<tr>
<td>Age</td>
<td>Most commonly young adults</td>
<td>Highly variable, includes elderly in view of diagnostic difficulty</td>
</tr>
</tbody>
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