Digoxin toxicity presenting as encephalopathy

JR Greenaway, B Abuaisha, MG Bramble

Summary
We describe two cases of digoxin toxicity presenting with clinical and electroencephalographic evidence of encephalopathy without other features of digoxin toxicity.

Keywords: digoxin toxicity, electroencephalography

Digoxin toxicity often presents with gastrointestinal side-effects such as anorexia, nausea or vomiting. Other side-effects include cardiac dysrhythmias, visual disturbance and drowsiness.

Case 1
A 68-year-old woman was admitted to hospital with a one-week history of profound somnolence. She had been non-specifically unwell in the preceding month and had fallen twice without any history of head injury. There was no history of anorexia, nausea, vomiting or visual disturbance. Her past medical history consisted of ischaemic heart disease, congestive cardiac failure, atrial fibrillation, cerebrovascular disease and chronic airflow limitation. Medication comprised frusenide 120 mg, spironolactone 100 mg, prednisolone 5 mg, ranitidine 150 mg, digoxin 250 µg, all daily, with isosorbide mononitrate 20 mg and nifedipine SR 10 mg both twice daily.

Clinical examination revealed no focal neurological signs but confirmed extreme drowsiness. Investigations revealed no abnormality of full blood count, urea and electrolytes, liver function tests, blood glucose, thyroid function tests or B12 and folate. Blood cultures and VDRL were negative. Chest X-ray was normal and electrocardiogram showed sinus rhythm with lateral ST depression. Computed tomography (CT) scan of brain revealed no abnormality and lumbar puncture resulted in clear, colourless cerebrospinal fluid with no growth, normal glucose and mildly raised protein at 0.63 g/l (normal < 0.4 g/l). Electroencephalogram (EEG) showed focal right anterior quadrant delta slowing consistent with Herpes encephalitis. However, following a telephone conversation with her general practitioner it transpired that her digoxin dose had been doubled to 250 µg daily approximately one month prior to admission. Her digoxin level when checked was > 5 µg/l. Digoxin was withheld and the patient gradually woke up. One week later she was back to normal (digoxin level 0.3 µg/l).

Case 2
A 66-year-old woman with a previous history of rheumatic valvular heart disease (mitral and aortic valve replacements), atrial fibrillation, chronic congestive cardiac failure and angio-...

Box 1

Digoxin: CNS side-effects
- lethargy and fatigue
- weakness
- headache
- visual disturbances (colour perception problems (including xanthopsia), reduced visual acuity, visual field defects, pain on eye movement)
- depression
- psychosis
- drowsiness
- confusion
- delirium
- encephalopathy
- hallucinations
- epileptic seizures
- choreiform movements
- dysphoria
- dysthagia
- trigeminal neuralgia
Tests in the elderly confused patient

<table>
<thead>
<tr>
<th>Blood</th>
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<tr>
<td>• full blood count</td>
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<tr>
<td>• plasma viscosity/ESR</td>
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<td>• creatinine, urea, electrolytes</td>
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<td>• liver function tests</td>
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<td>• glucose</td>
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<td>• thyroid function tests</td>
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<td>• vitamin B₁₂ levels</td>
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<td>• drug and alcohol levels</td>
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<th>Radiology</th>
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<tr>
<td>• chest X-ray</td>
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<td>• CT scan of brain</td>
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<th>Culture</th>
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<tr>
<td>• urine</td>
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<td>• blood</td>
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<td>• CSF</td>
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Dysplasia was noted to be extremely drowsy and confused prior to an elective blood transfusion. There was no history of anorexia, nausea, vomiting or visual disturbance. Her medication consisted of digoxin 250 μg daily, captopril 25 mg tid, frusemide 250 mg bid, and warfarin 4 mg daily.

Examination was normal apart from a known right homonymous hemianopia (previous embolus). Investigations revealed no abnormality apart from anaemia but, in view of Case 1, the digoxin level was checked and found to be 4.2 μg/l. EEG showed marked generalised changes, again consistent with a metabolic or drug-inducedencephalopathy. The cause of her digoxin toxicity was attributed to increasing age as there had been no change in her drug treatment and renal function tests were normal.

Learning points

- consider digoxin toxicity in the differential diagnosis of all patients with altered mental state
- CNS side-effects can occur in the absence of cardiac or gastrointestinal disturbance
- elderly patients are at increased risk of side-effects
- toxicity may occur in the absence of a change in digoxin dosage or additional drug prescriptions

Box 2

The digoxin was stopped for three days by which time the patient was fully back to normal with a digoxin level of 0.7 μg/l.

Discussion

A variety of neurological disturbances have been described in association with digoxin toxicity (box 1). Epileptiform seizures and chorea occur infrequently. Extreme fatigue or drowsiness is common and may be attributed to severe cardiac failure if digoxin toxicity is not considered in the differential diagnosis. The problem of recognition is compounded by the fact that digoxin is commonly prescribed for elderly patients with heart failure or cardiac dysrhythmias in whom the increased likelihood of digoxin toxicity is well established. It is therefore important for clinicians to recognise that the neurological manifestations of digoxin toxicity can occur without the usual gastrointestinal or cardiac side-effects. The spectrum of altered mental status from lethargy through to coma is possible. A serum digoxin level should be checked in any elderly patient presenting with abnormal cerebral function, irrespective of whether or not the dose of digoxin has been changed.

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