

*Teaching Point*  
(Section Editor: A. Meyrier)

## Reversible bilateral optic disc swelling in a renal patient treated with nitrofurantoin

Edward Pringle, Henrietta Ho, Eoin O’Sullivan and Charles Soper

Ophthalmology and Renal Departments, Mayday University Hospital, CR7 7YE, UK

**Keywords:** intracranial hypertension; nitrofurantoin; optic disc; papilloedema

### Introduction

There are many causes of optic disc swelling in patients with chronic renal impairment. Broadly these fall into two groups. In the first group, optic nerve function is impaired from the onset of disease. These are usually (but not always) unocular. These optic neuropathies are caused by the same underlying disease responsible for the renal impairment (vascular disease, vasculitis or more rarely a neoplastic process) or as a result of the renal impairment. In the second group, nerve function may be preserved in the early stages of the disease. This includes raised intracranial pressure and hypertensive optic neuropathy. Typically bilateral optic disc swelling occurs in this group. In our case the investigation and management was complicated by the patients’ multiple co-morbidities.

### Case

An 81-year-old gentleman with inactive disabling rheumatoid arthritis with pancytopenia due to Felty’s Syndrome and recurrent urinary sepsis had an abdominal aortic aneurysm repaired with a metal endovascular stent. He had chronic renal impairment, serum creatinine 184  $\mu\text{mol/l}$ , eGFR 33 ml/min and suffered chronic pain from vertebral collapse. He was receiving a combination of ramipril, amlodipine, paracetamol, alphacalcidol and nitrofurantoin for prophylaxis against multi-resistant *E. Coli* urinary tract infections from January to September 2006.

His vision gradually started failing. On examination the right eye acuity was 6/36 and left eye 6/12. Both eyes had dense cataracts but normal fundi. Following bilateral

cataract surgery, his vision improved to right 6/9 and left 6/6; however, he was noted to have swollen discs in both eyes, but no headache. His visual fields were full; there was no relative afferent pupillary defect. His blood pressure was well controlled. It was thought that the disc swelling was due to raised intracranial pressure rather than a bilateral optic neuropathy in view of his preserved optic nerve function.

Investigation was frustrated by his metal stent that prevented magnetic resonance imaging of his brain, sagittal sinus and optic nerves. A CT scan, however, did not demonstrate any intracranial space occupying lesions. A lumbar puncture was not performed in view of his thrombocytopenia.

His nitrofurantoin was stopped, and over the subsequent year his optic disc swelling subsided markedly. Optic nerve function remained normal. A presumptive diagnosis of nitrofurantoin-induced intracranial hypertension was made.

### Discussion

This case presented with bilateral optic disc swelling and well-controlled hypertension. None of the typical symptoms of raised intracranial pressure were present such as early morning headaches, visual obscurations (transient episodes of binocular visual loss lasting seconds), double vision (due to sixth cranial nerve palsy), or transient ‘whooshing’ type of tinnitus. So-called asymptomatic intracranial hypertension is well recognized; in a recent paediatric case series 31% of the cases were asymptomatic [1].

Nitrofurantoin has been repeatedly implicated in the pathogenesis of raised intracranial hypertension [2–4]. The underlying mechanism is still not fully understood but presumably a mismatch develops between cerebrospinal fluid production by the choroid plexus and its absorption by the arachnoid granulations. Several case reports and case series have repeatedly implicated other drugs as a contributory factor in intracranial hypertension including minocycline [5], tetracycline [6], nalidixic acid [7], danazol [8],

Correspondence and offprint requests to: Charles Soper, Renal Department, Mayday University Hospital, CR7 7YE, UK. E-mail: charles.soper@mayday.nhs.uk

ciprofloxacin [9], vitamin A [10], isotretinoin [11], corticosteroids [12] and sulphasalazine [13].

In this case of presumed intracranial hypertension we were unable to confirm an elevated CSF pressure because of the patient's thrombocytopenia; furthermore, we were unable to exclude sagittal sinus thrombosis because a magnetic resonance venogram was not possible due to his endovascular stent. A rechallenge with nitrofurantoin may have confirmed that this was indeed a true case of drug-induced intracranial hypertension; however, as is highlighted in the case reports above, this is not ethically acceptable practice. Documenting the presence of full visual fields and the lack of a relative afferent papillary defect was crucial to the diagnosis: it was unlikely that we were confronted with a bilateral simultaneous optic neuropathy due to vascular disease or vasculitis.

Nitrofurantoin is usually best avoided in renal patients, both because of a higher incidence of side effects and impaired efficacy through poor urinary concentration. Our patient had multiple resistant urinary tract infections with sensitivity only to nitrofurantoin amongst oral agents, and was reluctant to stop the agent, even after it was suspected of causing side effects. Of the four previous reports known to us, one patient had a GFR of 20 ml/min and was also apparently receiving the drug prophylactically [2]. In one retrospective study [3], 4.4% of children following renal transplantation were noted to develop intracranial hypertension. In this study nitrofurantoin, minocycline and weight gain were noted to be risk factors. Resolution has been usually reported within weeks, but visual loss may be irreversible.

### Teaching Points

1. Nitrofurantoin is a recognized cause of intracranial hypertension. It is usually avoided in moderate chronic renal impairment. If its prolonged use is necessary, examination of the optic disc for swelling by the attending physician, optometrist or ophthalmologist seems advisable.

2. The management of swollen discs depends on the underlying aetiology. It is important to distinguish between raised intracranial pressure and other optic neuropathies based on optic nerve function.
3. Chronic raised intracranial pressure, of any aetiology, is a potentially blinding condition, though in the early phases patients maybe asymptomatic.

*Conflict of interest statement.* None declared.

### References

1. Bassan H, Berkner L, Stolovitch C *et al.* Asymptomatic idiopathic intracranial hypertension in children. *Acta Neurol Scand* 2008 Mar 12 [Epub ahead of print]
2. Korzets A, Rathaus M, Chen B *et al.* Pseudotumor cerebri and nitrofurantoin. *Drug Intell Clin Pharm* 1988; 22: 345
3. Francis PJ, Haywood S, Rigden S *et al.* Benign intracranial hypertension in children following renal transplantation. *Pediatr Nephrol* 2003; 18: 1265–1269
4. Sharma DB, James A. Letter: Benign intracranial hypertension associated with nitrofurantoin therapy. *Br Med J* 1974; 28 4: 771
5. Chiu AM, Chuenkongkaew WL, Cornblath WT *et al.* Minocycline treatment and pseudotumor cerebri syndrome. *Am J Ophthalmol* 1998; 126: 116–121
6. Walters BN, Gubbay SS. Tetracycline and benign intracranial hypertension: report of five cases. *Br Med J (Clin Res Ed)* 1981; 282: 19–20
7. Cohen DN. Intracranial hypertension and papilledema associated with nalidixic acid therapy. *Am J Ophthalmol* 1973; 76: 680–682
8. Hamed LM, Glaser JS, Schatz NJ *et al.* Pseudotumor cerebri induced by danazol. *Am J Ophthalmol* 1989; 107: 105–110
9. Winrow AP, Supramaniam G. Benign intracranial hypertension after ciprofloxacin administration. *Arch Dis Child* 1990; 65: 1165–1166
10. Gangemi M, Maiuri F, Di Martino L *et al.* Intracranial hypertension due to acute vitamin A intoxication. *Acta Neurol (Napoli)* 1985; 7: 27–31
11. Roytman M, Frumkin A, Bohn TG. Pseudotumor cerebri caused by isotretinoin. *Cutis* 1988; 42: 399–400
12. Walker AE, Adamkiewicz JJ. Pseudotumor cerebri associated with prolonged corticosteroid therapy: report of four cases. *JAMA* 1964; 188: 779–784
13. Sevgi E, Yalcin G, Kansu T *et al.* Drug induced intracranial hypertension associated with sulphasalazine treatment. *Headache* 2008; 48: 296–298

*Received for publication:* 13.2.08

*Accepted in revised form:* 3.4.08