

## CASE REPORTS

## Benign intracranial hypertension during prednisolone treatment for inflammatory bowel disease

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### Abstract

**Benign intracranial hypertension (BIH, pseudotumour cerebri) is a rare condition with unknown aetiology although hormonal influences have been implicated. It occurs spontaneously, particularly in young obese women, and is associated with several drug treatments including corticosteroids. Two young adult women are described in whom headache and papilloedema in association with raised intracranial pressure occurred during prednisolone treatment for inflammatory bowel disease. This provides further evidence of the risk of BIH during corticosteroid treatment and has not been described before in adults with this condition. Advice is given to gastroenterologists to use corticosteroids with caution in adults, particularly young, fertile female patients. The treatment of a severe relapse of colitis in a patient who has had one episode of steroid related BIH remains a dilemma.**

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Benign intracranial hypertension (BIH or pseudotumour cerebri) is a rare condition causing headache, vomiting, and papilloedema in the absence of a space occupying intracranial lesion or hydrocephalus. Although the exact incidence is unknown it is certainly more common in women from the ages of 15 to 40 years. It is rarely familial. The cause is unknown although it would be reasonable to assume that one of the determinants of cerebrospinal fluid pressure is disordered. Donaldson<sup>1</sup> has suggested that any of the four determinants of cerebrospinal fluid pressure (increased venous pressure, increased arachnoidal resistance, cerebrospinal fluid hypersecretion, and increased elastance of the cerebrospinal fluid) may be interrupted in BIH. It has long been suggested that hormonal imbalance plays a part. Raised concentrations of oestrone in the cerebrospinal fluid have been noted in patients with BIH.<sup>2,3</sup> This may have a role in stimulating cerebrospinal fluid formation. Extraovarian production of oestrone from androstenedione occurs largely in adipocytes and may have a significant part to play in the occurrence of BIH obese women. Oestrone or other oestrogen related compounds during pregnancy and present in oral contraceptives could also stimulate cerebrospinal fluid formation in

the choroid plexuses. BIH is most commonly associated with obesity<sup>4</sup>; its association with other clinical conditions, for example, chronic middle ear disease probably secondary to dural sinus thrombosis, pregnancy,<sup>5</sup> deficiency states such as hypovitaminosis A and iron deficiency, and Cushing's syndrome<sup>6</sup> is rare. The 'empty sella syndrome' or incompetence of the diaphragma sella with associated raised intracranial pressure has implicated BIH in the cause of this rare condition.

Drug induced BIH occurs rarely and has been reported with the use of oral contraceptives, nalidixic acid, nitrofurantoin, tetracycline, etretinate,<sup>7</sup> and corticosteroids. Most reports of BIH with corticosteroid treatment have concerned young children<sup>8</sup> although there have been some reports in adults. The onset of BIH usually occurs on withdrawal of corticosteroids after prolonged treatment. In disorders such as asthma,<sup>9,10</sup> nephrotic syndrome,<sup>11,12</sup> psoriatic arthritis,<sup>13</sup> polyarthritis, the adrenogenital syndrome, and topical treatment for eczema and psoriasis,<sup>14,15</sup> BIH during the use of corticosteroids has been described. It has not been described in the context of corticosteroid treatment in inflammatory bowel disease in adults. We describe two young adult women in whom headache and papilloedema in association with raised intracranial pressure occurred during prednisolone treatment for acute inflammatory bowel disease.

### Case reports

#### CASE 1

A 27 year old women presented four months after the birth of her first child with a four week history of diarrhoea, abdominal pain, and weight loss of two and a half stone. She was a non-smoker and had had no previous medical history. She was taking no drugs. There was no family history of note. On examination she was not obese but was pyrexial and tachycardiac with lower abdominal tenderness. Neurological examination was normal. Investigations, including colonoscopy with multiple biopsy specimens showed acute Crohn's colitis. She was given intravenous hydrocortisone 100 mg four times daily. After four days she was changed to oral prednisolone 40 mg daily. On day 7 she began to

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complain of generalised headache. Examination, including fundoscopy, was normal. Prednisolone was reduced to 30 mg daily. On day 8 she was discharged home with instructions to reduce the dose of prednisolone to 15 mg daily over the next three weeks. One month after starting steroids she was reviewed in outpatients. Her diarrhoea had settled but the headaches had become worse. She was also complaining of double vision and blurred vision. On examination she was slightly cushingoid but normotensive with no abnormal neurological findings. One week later, however, examination showed a convergent strabismus and bilateral papilloedema. There were no other abnormal neurological findings. Prednisolone treatment was gradually stopped. Computed tomography of the head was normal but a lumbar puncture showed a cerebrospinal fluid pressure  $>30$  cm H<sub>2</sub>O with normal protein, glucose, and cell count thus confirming the diagnosis of benign intracranial hypertension. Fifteen ml of cerebrospinal fluid were drained. On review two weeks later there was minimal headache but papilloedema persisted. Repeat lumbar puncture two months later showed a cerebrospinal fluid pressure of 25 cm H<sub>2</sub>O and 12 ml of cerebrospinal fluid were drained (postprocedure pressure 12 cm H<sub>2</sub>O). The BIH and Crohn's disease remain in remission 15 months later.

#### CASE 2

A 29 year old woman presented in March 1984 with a two year history of tenesmus, urgency, and rectal bleeding. She was a non-obese, non-smoker but was taking an oral contraceptive. Her sister had ulcerative colitis. At sigmoidoscopy inflammation to 20 cm was found with normal mucosa above; biopsy specimens showed ulcerative proctitis. A barium enema was normal. Treatment with sulphasalazine was started. Over the next four years she was maintained on sulphasalazine orally with occasional hydrocortisone foam enemas for exacerbations of the proctitis. She had a successful pregnancy in 1987 although she had a troublesome flare up of the proctitis at 17 weeks. In 1988 a further exacerbation failed to settle on sulphasalazine and hydrocortisone foam enema so oral prednisolone (20 mg daily) was given for the first time. She could gradually stop the prednisolone after six months but six months later had a further severe exacerbation of her proctitis requiring reintroduction of oral prednisolone. The symptoms were so severe that briefly she had 60 mg per day. One month after starting oral prednisolone she developed headache, vomiting, blurred vision and paraesthesia in the left arm and leg. She was not taking oral contraceptives. Examination showed bilateral papilloedema but no other neurological signs. Computed tomography was normal but a lumbar puncture showed a cerebrospinal fluid pressure of 25.5 cm of water with normal protein, glucose, and cell content. The diagnosis of benign intracranial hypertension was made. The severity of the bowel symptoms necessitated the continuation of the prednisolone although the sulphasalazine was stopped. Coamilofruse (frusemide and

amiloride) and later spironolactone were tried for the intracranial hypertension without much benefit. She had nine cerebrospinal fluid taps over the following four months during which the headaches and papilloedema slowly settled. Prednisolone was finally stopped three months after it was started and sulphasalazine was not restarted. Three years later she is now well without bowel or neurological symptoms and is not receiving any treatment.

#### Discussion

These cases provide further evidence of the risk of BIH during corticosteroid treatment. The temporal relation of steroid treatment to the onset of symptoms in both cases cannot be ignored. It is also of interest to note that the onset of symptoms was before the beginning of reduction in dose, although the signs of raised intracranial pressure became evident later. Other drugs have been implicated in the pathogenesis of BIH but there is no evidence of ingestion of any of these. Our second patient did have additional drug treatment but we have no reason to believe that sulphasalazine is associated with the onset of BIH. In neither case was the patient taking the contraceptive pill at the onset of the BIH. Both patients had had a pregnancy within the preceding 12 months although again there was no close temporal relation to the onset of BIH. BIH has, however, been noted to occur both during and after pregnancy.

The treatment of corticosteroid induced BIH is similar to other forms of BIH. Lumbar puncture and cerebrospinal fluid drainage remains the basic treatment and both our cases settled after lumbar punctures and have not recurred. Acetazolamide and other diuretics may also be tried.<sup>16,17</sup> Weight reduction alone in obese patients has been shown to be of benefit.<sup>18</sup> Corticosteroids themselves have also been used in the treatment of BIH<sup>17</sup> and it has been the response to this treatment in the past that has led to the suggested role of hormonal imbalance in the cause of BIH. In those patients with corticosteroid induced BIH increasing the dose again often leads to the resolution of symptoms and signs. Further slow and careful reduction in steroid dose can then be continued without recurrence. In resistant cases cerebrospinal fluid shunting may be necessary to relieve the progressive visual loss that can accompany this condition. It is in fact the loss of vision that should dictate the need for treatment rather than the cerebrospinal fluid pressure.

The prognosis of BIH is excellent although the term 'benign' can be misleading as associated visual loss can be severe and in some cases permanent.<sup>4,19</sup> There have, however, been no reported fatalities from BIH.

Advice about the risk of development of BIH has already been given on the use of steroids in children.<sup>20</sup> We believe that this advice should also extend to adults, and gastroenterologists must be aware of the risk of BIH in adults with inflammatory bowel disease receiving corticosteroid treatment especially young, fertile, female patients. The patient receiving a reducing dose of steroids who complains of persistent headache

with or without visual symptoms should be examined carefully with this in mind.

The treatment of a severe relapse of colitis in a patient who has had one episode of steroid related BIH remains a dilemma. There is no evidence that any one corticosteroid carries less risk of inducing BIH than any other and the risk of developing a second episode of BIH after further steroid treatment is unknown. Fortunately neither patient has required further steroid treatment of their colitis to date.

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