



# Benign intracranial hypertension and chronic renal failure

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■ Benign intracranial hypertension (also called pseudotumor cerebri, otitic hydrocephalus, or meningeal hydrops) is a syndrome of markedly elevated intracranial pressure in the absence of intracranial mass, inflammation, or obstruction. Numerous disease processes and medications have been associated with it. However, renal failure has not been documented as an associated condition. In this report, the case of a 27-year-old Native American man with chronic renal failure of unknown etiology is described, with new-onset headache, papilledema, and elevated intracranial pressure. After normal cerebrospinal fluid, computed tomography, and magnetic resonance imaging studies, a diagnosis of benign intracranial hypertension was made. Despite repeated lumbar punctures with cerebrospinal fluid removal, the patient's headaches persisted, and intracranial pressures remained in the 200 to 400 mm H<sub>2</sub>O range. After initiation of hemodialysis due to progressive deterioration of renal function, the patient's headaches became less severe and eventually disappeared. This case represents a unique association of chronic renal failure with benign intracranial hypertension.

□ KIDNEY FAILURE, CHRONIC; INTRACRANIAL PRESSURE; PSEUDOTUMOR CEREBRI □ CLEVE CLIN J MED 1992; 59:419-422

**B**ENIGN INTRACRANIAL hypertension (BIH)—also called pseudotumor cerebri, otitic hydrocephalus, or meningeal hydrops—is a syndrome of markedly elevated intracranial pressure in the absence of an intracranial mass, inflammation, or obstruction. Numerous disease processes and medications have been associated with it. Renal failure, however, has not been listed among the associated conditions. In this report, we describe the case of a 27-year-old Native American man with chronic renal failure of unknown etiology, new-onset headache, papilledema, and intracranial hypertension.

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## BACKGROUND

BIH was first described by Quinke et al<sup>1</sup> in 1893. The most common group of patients reported in the literature with BIH have been young, obese females during their reproductive years<sup>2</sup>; however, other associations have included hypoparathyroidism, anemia, sarcoidosis, systemic lupus erythematosus, vitamin A intoxication and deficiency, and the use of tetracyclines, nalidixic acid, and sulfa drugs.<sup>3-8</sup>

The pathophysiology behind the development of idiopathic BIH is not well understood although some investigators have theorized abnormalities in cerebrospinal fluid (CSF) absorption as the primary underlying problem.<sup>9,10</sup> Detailed studies using continuous intracranial pressure monitoring and radioisotope tracing have shown reduced absorption of CSF in these patients. Nevertheless, consistent pressure abnormalities in selected study groups have not

been demonstrated, and consequently many features of this syndrome remain unexplained.

Although BIH has been reported in specific medical conditions that have been known to produce renal disease, we have found only one other report of elevated intracranial pressure in a patient with renal failure: Lal et al<sup>11</sup> described a case of BIH in a patient on chronic hemodialysis. However, the patient's course was complicated by the development of an iatrogenic arteriovenous fistula which affected cerebral venous drainage.

#### CASE REPORT

A 27-year-old Native American man presented to his primary care physician with a 2- to 3-day history of right flank pain, visual blurring, and headaches. The patient had no history of fever, chills, dysuria, polyuria, hematuria, oliguria, or other complaints. The patient denied any history of alcohol abuse, drug abuse, or unusual toxic exposures. There was no history of nephrolithiasis or trauma.

His past medical history was significant for a hospitalization 3 years prior to this admission for the workup of new-onset glucose intolerance, in addition to a new finding of proteinuria. Physical exam at the time 3 years prior showed no evidence of retinopathy or neuropathy. A 24-hour urine collection showed 15 g protein and a creatinine clearance of 63 mL/min/1.73 m<sup>2</sup>. Renal ultrasound revealed an absent left kidney and a normal-appearing right kidney without evidence of obstruction. A renal biopsy was not performed due to the presence of only one functional kidney. The patient underwent an empiric trial of prednisone 60 mg a day for 5 months, as well as oral cyclophosphamide 100 mg a day for 3 months without improvement in his proteinuria. This therapy was subsequently tapered and discontinued. Further endocrine evaluation revealed no evidence of overt diabetes.

Physical exam at the time of admission revealed an obese Native American man in mild distress due to headache. Blood pressure was 180/110 mm Hg, and the patient was afebrile. A head-ear-eye-nose-throat exam was remarkable for bilateral retinal hemorrhages and papilledema. Lungs were clear, and the cardiac exam revealed a regular rate and rhythm with a 2/6 systolic ejection murmur. The abdomen was soft without tenderness, hepatosplenomegaly, or bruits. There was mild right costovertebral tenderness. The extremities revealed no peripheral edema. Neurologically, the patient was alert, oriented, and without focal deficits.

Laboratory studies revealed normal electrolytes and a creatinine of 9.3 mg/dL (822 μmol/L). The serum calcium was depressed at 5.7 mg/dL (1.4 mmol/L), and the serum phosphate was elevated at 7.7 mg/dL (2.5 mmol/L). The hematocrit was 33% with normal indices, and the white blood cell count and differential were normal. Urinalysis showed 4+ protein, as well as numerous white cells and red blood cells without casts. Electrocardiographic and chest roentgenographic studies were unremarkable.

The patient was hospitalized and ampicillin therapy was started for presumed pyelonephritis. All cultures were negative, and the patient's flank pain resolved. A renal ultrasound was done and revealed a normal right kidney, but with evidence of mild hydronephrosis. Further urological evaluation did not show any anatomic abnormality responsible for the obstruction, and follow-up ultrasound was normal. A 24-hour urine collection revealed a creatinine clearance of 11 mL/min/1.73 m<sup>2</sup> and protein excretion of 14.0 g. Blood pressure was easily lowered and maintained in the 120/80 to 140/90 mm Hg range with oral nifedipine 10 mg po tid and nadolol 40 mg/day. Ophthalmologic evaluation confirmed the presence of flame hemorrhages, arteriovenous constriction, dilated ophthalmic veins, and bilateral papilledema. Computed tomography (CT) of the head showed no masses or edema, and the ventricles were normal in size. Magnetic resonance imaging (MRI) of the head confirmed the normal findings of the CT scan, with particular attention paid to the cerebral sinuses. A lumbar puncture was performed shortly after admission in the lateral decubitus position under normal respiration, and an opening pressure of 320 mm H<sub>2</sub>O was recorded. The fluid was clear without pleocytosis or protein elevation, and subsequent cultures were negative. A neurological consultation was obtained, and repeat lumbar punctures with CSF drainage was recommended.

The patient was discharged in stable neurologic condition and with a serum creatinine of 10.6 mg/dL (937 μmol/L). Despite resolution of the retinal findings after 2 months, the patient continued to complain of severe intermittent headaches. Repeat lumbar punctures and drainage were performed, but intracranial pressures remained elevated in the 200 to 400 mm H<sub>2</sub>O range. The patient's weight remained stable and he remained free of peripheral edema. Deterioration of renal function continued, and he was subsequently started on hemodialysis (approximately 4 months after onset of initial symptoms). After the initiation of his hemodialysis, the patient's headaches became less

severe and eventually disappeared over the next 12 months. His ophthalmologic exam remained benign. Unfortunately, he refused further lumbar punctures. Approximately 1.5 years after the initiation of hemodialysis, the patient underwent a successful cadaveric renal transplant. His post-transplant follow-up has been unremarkable, and he has remained free of recurrent signs and symptoms of intracranial hypertension.

#### DISCUSSION

As mentioned before, conditions that have been associated with benign intracranial hypertension are numerous in the medical literature. Unfortunately, many of these associations are the result of the indistinct definition of BIH. In order to establish a more uniform definition of this neurologic syndrome, Johnston and Paterson in 1974,<sup>12</sup> and later Ahlskog et al in 1982,<sup>2</sup> identified specific criteria necessary for the diagnosis of BIH. Ahlskog required the following conditions to be documented before the diagnosis be made: 1) cerebrospinal fluid pressures above 200 mm H<sub>2</sub>O in the supine position under normal respiration; 2) normal CSF fluid composition; 3) signs and symptoms related to elevated CSF pressures alone (headache, papilledema); and 4) normal CT and/or MRI findings. Applying these more rigid diagnostic criteria to an extensive list of prior case reports of BIH, investigators identified only 11 different associated conditions. Renal failure was not noted to be one of these 11 conditions.

Other accepted conditions associated with BIH do not seem to be present in the case described above. It is unlikely that medications were responsible for this patient's elevated intracranial pressure. The remote use of corticosteroids and their subsequent discontinuation more than 2 years prior to the development of symptoms makes their relationship unlikely. There was no other antibiotic use other than ampicillin. History, physical exam, and laboratory studies showed no evidence of iron deficiency anemia or systemic illness such as systemic lupus erythematosus or sarcoidosis. Although elevated intracranial pressures can be seen with malignant hypertension,<sup>13</sup> the ease of blood pres-

sure control and the prolonged elevation of intracranial pressure in this case did not support this diagnosis. Although the resolution of the ophthalmologic disturbances may lag behind the decrease in elevated blood pressure after treatment for malignant hypertension, the intracranial pressure has been shown to follow the systemic pressure more closely.<sup>14</sup> As opposed to the case report of Lal et al,<sup>11</sup> this patient had never undergone central venous catheter placement, and consequently the likelihood of an arteriovenous fistula with secondary elevation of cerebral venous pressure is unlikely.

In summary, this unfortunate patient with chronic renal failure satisfied all the necessary criteria for the diagnosis of BIH as defined by Ahlskog et al.<sup>2</sup> Since no other cause for BIH could be identified as previously described, the unique association of BIH and chronic renal failure is suggested. The poorly understood pathophysiology of BIH and its apparent rarity in the presence of renal failure make it difficult to determine whether this was a case of coincidence or true association. Was benign intracranial hypertension the first sign of uremia in this patient? While most experts believe that patients with end-stage renal failure have normal to slightly elevated intracranial pressures,<sup>15,16</sup> these assumptions are based on animal and older pathological studies.<sup>17-19</sup> The significance of elevated intracranial pressure with regards to the disequilibrium syndrome in hemodialysis has been elucidated in the literature; however, it has not been felt to be a factor in the complicated pathophysiology of uremic encephalopathy.<sup>20</sup> The symptoms of headache and visual blurring are not common complaints related to uremia. On the other hand, CSF pleocytosis and elevations in CSF protein have been reported in uremia, but their importance is not well understood. In addition to the pathophysiologic unknowns surrounding BIH, the absence of potentially helpful patient data also complicated the analysis of this particular case. Specifically, sodium and water balance, repeat CSF pressure monitoring, and post-dialysis studies may have provided additional helpful information. Nevertheless, this patient's classic presentation of BIH represents an interesting and heretofore unreported association with chronic renal failure.

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