Endovascular treatment of cranial venous sinus obstruction resulting in pseudotumor syndrome

Report of three cases

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It is probable that a significant number of cases of pseudotumor syndrome (PTS) occur because of cranial venous outflow obstruction, yet reports of direct treatment of the obstruction are few and inconclusive. In this study the authors report three cases of PTS with angiographically confirmed venous sinus obstruction treated by direct, endovascular procedures; urokinase infusion in two and balloon venoplasty in one. Two patients suffered transient complications that resolved satisfactorily. All three showed initial resolution of the signs and symptoms of PTS but one relapsed after 8 months and required surgical treatment. The possible role and methods of treatment of cranial venous outflow obstruction in PTS are discussed.

KEY WORDS • pseudotumor syndrome • cranial venous obstruction • endovascular therapy • urokinase

T he role of impaired cranial venous outflow, whether due to structural factors such as intraluminal thrombosis and extraluminal compression or functional factors such as raised venous pressure from high-flow arteriovenous malformations, in the causation of PTS is well recognized. Also well recognized is the variable efficacy of current treatment methods, their infrequent side effects, and their failure to correct the underlying cause of PTS, whether it is venous outflow obstruction or something else. Since the initial report by Ray and Dunbar there have been several descriptions of attempts to deal directly with venous outflow obstruction in PTS, by using anticoagulating agents, removal of compression, or vein-to-vein bypass, and, most recently, by a direct approach to intraluminal venous disorders. In the last instance the therapeutic endeavors were mentioned only briefly in two papers primarily devoted to evaluating the role of venous outflow obstruction in PTS. In this paper we report in detail on three patients treated with a direct approach to intraluminal disease by using microcatheters to deliver urokinase to the clot or to perform balloon angioplasty.

Case Reports

Case 1

History and Examination. This 49-year-old man presented with a 3-week history of right occipital headache and blurred vision. His history was unremarkable and he was not taking any medications. On examination he had moderately severe bilateral papilledema but normal visual acuity and fields. There were no focal neurological abnormalities. His CSF pressure on lumbar puncture was in excess of 300 mm H₂O and the fluid was of normal composition. Cranial CT scanning demonstrated thrombosis of the SSS and the right transverse and sigmoid sinuses (Fig. 1A and B). The left transverse sinus was hypoplastic.

Operation. In view of the degree of sinus involvement, coupled with the existing abnormality of the left transverse sinus, we decided to attempt direct treatment. A microcatheter with multiple side holes (Tracker; Boston Scientific, Target, Inc., Fremont, CA) was introduced through a guiding catheter in the right femoral vein and positioned in the SSS adjacent to the thrombosed area. After satisfactory placement was established, 100,000 U urokinase was infused, resulting in significant clearing of both the right
transverse and sigmoid sinuses. The patient underwent systemic heparinization and the urokinase infusion was continued overnight through the indwelling microcatheter at a rate of 10,000 U per hour.

Postoperative Course. By the next morning the patient’s headache had resolved. Repeat thrombolysis that evening with 900,000 U urokinase delivered to the sagittal and right transverse sinuses resulted in further, significant improvement in flow in these channels. The overnight infusion rate was increased to 50,000 U per hour. The following day an additional 500,000 U urokinase was infused into the right transverse sinus and right IJV. A final angiogram demonstrated good patency of all sinuses and the right IJV (Fig. 1E). There was some residual clot in the transverse and sigmoid sinuses and the IJV on the right. The urokinase infusion was discontinued. Heparin was administered for 10 days and anticoagulation therapy was continued with warfarin. Apart from some minor abnormalities of liver enzymes thought to be caused by heparin and since resolved, there were no complications of treatment. The patient was shown to have a moderately positive anticardiolipin antibody. His clinical course was good in that he has remained symptom free since the initial treatment, with progressive and complete resolution of his papilledema. Neurological follow up was discontinued after 15 months, at which time he was entirely well.

Case 2

History and Examination. This 32-year-old, nonobese woman was diagnosed as having PTS 3 years before the hospital admission reported here. Her disease had proven refractory to medical treatment and she had undergone placement of a lumboperitoneal shunt. This too was unsatisfactory; low pressure and CSF leakage problems ensued despite four revisions over a 1-year period. The shunt was ligated and medical treatment with acetazolamide was again tried, to no avail. Disabling headaches and photopsia persisted and she was admitted to the Royal Prince Alfred hospital for insertion of a cisternoatrial shunt. Her CSF pressure had been markedly elevated both before placement of her original shunt and after its ligation, and was typically in excess of 300 mm H2O for a range of measurements. The fluid was always of normal composition. A preoperative MR phase-contrast venogram demonstrated marked narrowing of the right transverse sinus (Fig. 2 left). Retrograde sinography with manometry demonstrated a pressure gradient across the smooth narrowing in the distal right transverse sinus with pressures of 39 mm Hg above the stenosis and 14 mm Hg in the jugular bulb. In addition, there was a prominent arachnoid granulation in the left transverse sinus, again with a pressure gradient (34 mm Hg above the granulation, 18 mm Hg below it).
The pressure in the midsagittal sinus was 37 mm Hg (Fig. 2 center).

Operation. Because of the problems she had experienced with other treatments, particularly CSF shunting, we decided to attempt direct treatment of the venous disorder rather than place a cisternoatrial shunt. Accordingly, balloon dilation of both transverse sinus lesions was performed using a Grapevine 10 microcatheter (Micro Interventional Systems, Inc., Sunnyvale, CA [now defunct]). This resulted in moderate improvement in both proximal transverse sinus pressures, which decreased to 28 mm Hg and 23 mm Hg on the right and left, respectively; flow also improved (Fig. 2 right).

Postoperative Course. The patient tolerated the procedure well and experienced significant improvement in symptoms. Acetazolamide and warfarin therapy were initiated at discharge, and at her 6-week follow-up review she reported further improvement in symptoms. Therefore, shunt insertion was postponed indefinitely. She remained well for 8 months, although she continued to take acetazolamide and anticoagulating medications, before she reported further improvement in symptoms. Thereafter, acetazolamide and warfarin therapy were initiated at discharge, and at her 6-week follow-up review she reported further improvement in symptoms. Therefore, shunt insertion was postponed indefinitely. She remained well for 8 months, although she continued to take acetazolamide and anticoagulating medications, before again developing increasingly severe headache. She was then readmitted for further examination. She had no neurological and, in particular, no papilledema or abnormalities of visual acuity or fields. Continuous intracranial pressure monitoring showed moderate intracranial hypertension with intermittent plateau waves. A cisternoatrial shunt was placed but unfortunately had to be removed due to early development of infection. She subsequently underwent surgery for bilateral subtemporal decompression and has now remained relatively well, although not without symptoms, for a further 12-month period.

Case 3

History and Examination. This 29-year-old, obese woman presented with a 2-week history of worsening left parietal headache, blurred vision, and a feeling of fullness and tenderness, together with a rushing sound, in the left ear. Her history was unremarkable; she was a nonsmoker and was taking contraceptive pills but no other medications. On examination we found severe bilateral papilledema with hemorrhages, right visual acuity of 6/6, left visual acuity of 6/60 (long-standing amblyopia), enlarged blind spots, and a venous hum on auscultation behind the left ear, which increased with compression of the right IJV and decreased with compression of the left IJV. The CSF pressure on lumbar puncture was in excess of 300 mm H2O; the fluid was of normal composition. Although results of a CT scan obtained before admission were reported to be normal, one obtained on admission showed evidence of thrombus in the vein of Galen. Both MR imaging and MR angiography demonstrated thrombosis of the left transverse sinus associated with left mastoiditis (Fig. 3A and B). The ventricular size was normal on all scans. Cerebral angiography demonstrated thrombotic occlusion of the left sigmoid sinus and stasis in the dominant left transverse sinus (Fig. 3C and D). Because of the severity of her PTS and the presumed recent development of her venous occlusion, we decided to attempt direct treatment of the latter.

Treatment and Early Posttreatment Course. After administration of antibiotic drugs and systemic anticoagulating agents, we used a Tracker single-end hole microcatheter to deliver 1.2 million U urokinase over a 40-minute period to the angiographically identified site of sinus occlusion, with restoration of patency in the left sigmoid sinus and flow in the left transverse sinus. Anticoagulation therapy was continued with heparin. Over the first few days her condition improved, with resolution of her headache and diminution in the degree of papilledema. However, 5 days after thrombolysis she again developed headaches and new fundal hemorrhages were noted. A repeat angiogram revealed thrombosis of the left IJV and left transverse and sigmoid sinuses, with extension into the hypoplastic right transverse sinus. Flow in the SSS was markedly slowed. Selective catheterization of the left IJV and left transverse sinus was performed and a total of 1.4 million U urokinase was infused, resulting in the return of patency in both transverse sinuses. Infusion of urokinase at a rate of 50,000 U per hour was continued through an indwelling microcatheter with its tip positioned in the SSS; the tip of the guiding catheter was in the left IJV.

FIG. 2. Left: Preoperative MR phase-contrast venogram showing marked narrowing of the right transverse sinus (arrowheads). Center: Retrograde sinography and manometry studies demonstrating focal obstruction of the right transverse sinus and associated intraluminal pressure gradients. The left-sided arachnoid granulation is designated “a.” Right: Repeated retrograde sinography and manometry studies obtained postdilation demonstrating improvement in flow and pressure gradients. Pressures are expressed in millimeters of mercury.
Endovascular treatment of cranial venous sinus obstruction in PTS

The patient became headache free and a follow-up angiogram obtained the following day revealed further improvement in the left transverse sinus and swifter flow in the SSS. Urokinase infusion was continued at a rate of 25,000 U per hour through each of the lumina. Some clot persistence was demonstrated on daily angiograms, and the catheters were repositioned as necessary. On the 4th day of infusion, with little further clot reduction, the patient developed heparin-induced thrombotic thrombocytopenia syndrome. The infusion of urokinase was stopped, the catheters were removed, and warfarin therapy was initiated. The patient then continued her acetazolamide and warfarin therapy for 6 months, during which time she was asymptomatic but had persistent mild bilateral papilledema with no impairment of visual function. Investigation for a possible thrombophilic tendency, both off and on anticoagulating medications, revealed no abnormalities.

Later Posttreatment Course. Eight months after discharge, after medications had been discontinued for 2 months, the patient developed recurrence of headache. On examination, we found no abnormalities besides mild blurring of the nasal margin of the left optic disc and the longstanding reduction in left visual acuity. However, her CSF pressure on lumbar puncture was again markedly elevated, at 370 mm H₂O, with normal fluid composition. Repeat cerebral angiography demonstrated no evidence of fresh thrombus but there were numerous new venous channels around the left jugular bulb (Fig. 3E). Acetazolamide therapy was restarted and it abolished the headache. She has now remained well for more than 2 years after the initial treatment, has no clinical evidence of intracranial hypertension, and is off medication.

Discussion

The association of cranial venous sinus disease with pseudotumor cerebri and its possible causative role was recognized in early descriptions of PTS, particularly in the case of chronic middle ear infection with thrombotic occlusion of the transverse sinuses, and especially in the work of Symonds,21 who coined the term “otic hydrocephalus” in 1931. Since that initial recognition several things have happened. First, although the incidence of middle ear disease in reported series of PTS has fallen markedly, a number of other forms of causative venous pathological conditions have been identified, which are broadly divisible into problems within the sinuses themselves and those causing external compression. Second, methods of demonstrating pathological conditions in the sinuses have greatly improved. Most recently, the possibility of a relatively noninvasive direct approach has emerged, with the development of agents for clot lysis and delivery of these agents to the cranial venous sinuses, as well as dilation of stenoses, through microcatheters posi-
tioned with the aid of angiography. These developments raise several questions, but the one primarily addressed in this small study is the possible therapeutic role of such methods in PTS. Is there a place for direct treatment of intrasinus disease in PTS?

To approach this question properly one must answer a number of other questions. First, how common is causative venous sinus disease in PTS? Certainly a wide variety of causes have been identified, as listed, for example, by Johnston, et al.8 Review of this list shows immediately that many of these causes, such as congenital hypoplasia, craniostenosis,3 head injury,7 primary and secondary neoplasms,13,14 and high-flow arteriovenous malformations12 are of little significance numerically. In two recent studies, however, it has been suggested that a much more significant, indeed even universal, role exists for venous pathological conditions in PTS,3,18 although this matter is still being debated. Second, how good are the methods of recognition of venous sinus disease? Both CT and routine MR studies may reveal venous sinus occlusion and a causative lesion if one is present, but certainly they cannot be relied on to exclude such abnormalities. Although MR angiography and standard digital subtraction angiography are more complete examinations, they are not infallible. The most satisfactory investigative tool is undoubtedly retrograde venography, which, when combined with intraluminal pressure measurements9 not only will give a very satisfactory anatomical demonstration of intra- or parasinus pathological conditions, but may also allow clarification of the relevance of such conditions to a CSF circulation disorder.

As for treatment itself, since the initial endeavors of Ray and Dunbar17 there have been a number of reports of direct treatment of venous sinus disease in PTS, usually by removal of an external compressing lesion16 or by vein-to-vein bypass grafting.5,6,19 However, in the overwhelming majority of patients with PTS, even those in whom sinus disease is recognized, treatment still is not directed at the underlying condition. In this context, there are two important considerations. First, although this is not a review of the treatment of PTS, we would summarize that medical methods (most commonly acetazolamide and corticosteroid treatment) have a low success rate in the first instance or a high recurrence and complication rate in the second, whereas surgical methods, in addition to the undesirability of their invasiveness, are fraught with difficulty.9 A common feature of all methods besides CSF shunting is the failure to return CSF pressure levels to normal despite amelioration of clinical symptoms. Second, there are now several reports of venous sinus thrombosis performed in patients not presenting with PTS, in whom systemic or locally delivered thrombolytic agents such as urokinase18,22 and streptokinase were used.17 Although the precise role of such treatments in sinus occlusion accompanied by focal neurological signs remains ill defined, given the potential hazards of using thrombolytic agents in situations in which there is infarction or hemorrhage, the idea of such a direct treatment for PTS is attractive. In such circumstances not only are the possible afore-mentioned contraindications absent but the treatment is directed at the presumed cause of the syndrome.

This study is a preliminary examination of such an approach. Three patients were treated, the first particularly because of the extent and presumed recent development of the sinus involvement, the second because of the manifest failure of other methods of treating PTS, and the third because of the relatively focal nature of the sinus problem, which led us to believe in the feasibility of the method. Clinically, the treatment was effective in all three cases in the short term, with resolution of symptoms and, where present, papilledema. In the longer term two of the three patients have remained well without further therapy, after follow-up periods of 15 months and 2 years, respectively, whereas the third (Case 2) has required further treatment. With regard to CSF pressure posttreatment, this was not measured in the first patient because he was entirely well, whereas in the other two it remained elevated and both experienced some return of headache. Furthermore, in one of these patients surgical treatment was necessary, whereas the other’s condition resolved with a short course of acetazolamide. In the two other reports in which direct treatment of sinus disease by the methods described here is mentioned, details are scanty but clearly, in a total of five cases, results were mixed; there was a discrepancy between radiological improvement and clinical outcome and no report of sustained resolution.3,11 The conclusions that may be drawn from this report must be seen in the context of the possibility of a significantly greater role of venous sinus disease in the origin of PTS than has been hitherto recognized, of the variable success and unsatisfactory nature of existing treatment methods of PTS, and of the increasing availability and sophistication of the direct methods described here. Our report shows, in a preliminary way, that such a direct approach to pathological conditions of the sinus in PTS is feasible and carries the prospect, at least in the short and medium term, of effective clinical resolution of the intracranial hypertension associated with this disease. Of course, this study would need to be considerably extended and linked with a particular effort to elucidate precisely the significance of causative venous sinus disease in PTS.

References


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Endovascular treatment of cranial venous sinus obstruction in PTS


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