Intracranial hypertension (IH) is a common clinical issue in neurology and neurosurgery. The pathognomonic signs consist of headache, vomiting, and papilledema. IH may be caused by obstruction of venous drainage. The most frequent causes of obstruction are venous sinus lesions, including acute and chronic thrombosis; damage or ligation after trauma; meningeal inflammation; metabolic disturbances; meningeal metastases; and benign tumors. Some studies have demonstrated that the stenosis of sinuses is associated with idiopathic intracranial hypertension (IIH). However, the abnormal imaging findings in IIH are nonspecific and can also be found in patients with raised intracranial pressure (ICP) due to cerebral venous thrombosis. Compression caused by a small lesion or invasion of the venous sinus may lead to stenosis of the local region. Despite major improvements in MRI examination over the past decade, misinterpretation of brain MRI and/or CT findings may lead to a delayed diagnosis in patients presenting with raised ICP. Results of noninvasive imaging techniques are often unclear with regard to identification of the underlying pathology, and the definitive diagnosis is frequently determined during surgery. In some patients, small venous sinus lesions may be misdiagnosed as IIH due to the absence of imaging findings. Consequently, a majority of these patients receive conventional medical therapy for several months with an unfavorable clinical outcome. Therefore, early diagnosis of sinus lesions with pathological confirmation is crucial for an effective treatment plan.

In this study, we investigated a new method using percutaneous endovascular biopsy (PEB) for diagnosis in IH patients with venous sinus lesions. Patient clinical profiles, procedure technical success and safety, and clinical success were evaluated. On the basis of a comprehensive literature search, we believe that this is the first patient cohort in which the feasibility and safety of this method has been demonstrated.

Methods

From June 2016 to August 2017, 9 patients with IH underwent PEB for confirmation of the presence of an intrasinus lesion and assessment of its anatomical relationship.
with nearby structures. In all 9 patients, diagnosis of acute intracranial venous sinus thrombosis was excluded by use of a contrast-enhanced magnetic resonance black-blood thrombus imaging (MRBTTI) technique before the procedure.²⁵

All patients provided informed consent for PEB after being informed about the procedure and its benefits and potential complications. All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional committee.

Description of Technique

All patients were placed in the supine position under local anesthesia with full heparinization and neurological monitoring. Screening coagulation tests were ordered routinely. Both femoral arterial and venous access were obtained in all 9 patients. Consequently, manual compression at the site of the vascular puncture was performed over a period of 10 minutes in order to achieve hemostasis. In 6 patients, a 70-cm 8-Fr vascular introducer sheath (Cook) was used to provide better support. In the other 3 patients, an 11-cm 8-Fr vascular introducer sheath (Cardis) was used. Before PEB, the lesion in the venous sinus was confirmed with an angiogram. ICP manometry was performed with a PROGREAT microcatheter (Terumo) attached to the pressure transducer. An 8-Fr ENVOY guiding catheter (Codman) and a 6-Fr naïve catheter (ev3) were cautiously positioned proximal to the lesion in 8 patients. A 1.8-mm biopsy forceps device (Micro-Tech) was gently advanced upward with both stainless-steel hinged cutting jaws in the closed position. The biopsy device was advanced under fluoroscopic guidance. In 1 patient, a 2.3-mm biopsy forceps device (Micro-Tech) was gently advanced in a 70-cm 8-Fr vascular introducer sheath, which was placed in the left jugular foramen. An introducer tip with hinged jaws was guided in the open position and gently placed into the lesion, anchoring the jaws in the lesion, and then the hinged jaws were maneuvered into the closed position. The naïve catheter was pushed to a fixed position, followed by withdrawal of the biopsy forceps device. Two to 4 tissue samples of the lesion were obtained. For the 1.8-mm device the theoretical specimen volume was 5 mm³. However, in some cases the specimen obtained was larger than the volume of the jaws. After the operation, we used protamine to reverse the effects of heparin. The specimens were fixed in both normal saline and formalin solutions and evaluated pathologically.

Results

A cohort of 9 patients, comprising 3 men and 6 women with a mean ± SD age of 46 ± 9 years, was reviewed. A summary of patient characteristics and pathological results is presented in Table 1. Four patients presented with headache and 4 patients presented with papilledema. One patient presented with both headache and papilledema. Lumbar puncture analysis results showed high CSF pressure in all 9 patients (range 330–510 mm H₂O). Five intrasinus lesions were located in the transverse sinus, 3 in the sigmoid sinus, and 1 in the jugular foramen. One patient (case 9) presented with left sigmoid sinus stenosis complicated by dural arteriovenous fistula (DAVF).

Technical success in obtaining a biopsy specimen was achieved in 6/9 patients (66.7%). A total of 7 intravascular lesions were observed and evaluated, 1 lesion in each of 5 patients and 2 lesions in 1 patient. A mean of 3 samples was obtained per biopsy procedure (range 2–5). Some patients experienced a transient headache and recovered completely after the procedure. No intra- or postprocedural complications occurred. The confirmed lesions were meningoima in 2 patients and fibrous thrombus in 4 patients. In one patient (case 1), a fibrous thrombus was observed in the first procedure and meningoima was confirmed in the second attempt. Five patients underwent venous sinus stenting, 1 patient underwent tumor resection, 1 patient received a ventriculoperitoneal shunt, 1 patient received anticoagulation therapy, and 1 patient underwent embolization of DAVF.

Illustrative Cases

Case 1

A 37-year-old woman had a 3-month history of progressive visual deterioration. The fundus examination exhibited bilateral stage 2 papilledema. The lumbar puncture showed high CSF pressure (340–360 mm H₂O). Enhanced MR images revealed a lesion located in the left

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Presentation</th>
<th>ICP (mm H₂O)</th>
<th>Lesion Location</th>
<th>Lesion Type</th>
<th>Pathology</th>
<th>Treatment</th>
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<tr>
<td>1</td>
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<td>46</td>
<td>Papilledema</td>
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<td>Stenosis</td>
<td>—</td>
<td>Stenting</td>
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<tr>
<td>2</td>
<td>M</td>
<td>50</td>
<td>Papilledema</td>
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<td>Left sigmoid sinus</td>
<td>Stenosis</td>
<td>Fibrous thrombus</td>
<td>Stenting</td>
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<tr>
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<td>37</td>
<td>Papilledema</td>
<td>354</td>
<td>Left jugular foramen</td>
<td>Occlusion</td>
<td>Fibrous thrombus (1st PEB); meningoima (2nd PEB)</td>
<td>CSF shunting</td>
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<tr>
<td>4</td>
<td>F</td>
<td>66</td>
<td>Headache</td>
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<td>Occlusion</td>
<td>Meningioma</td>
<td>Resection</td>
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<td>—</td>
<td>Stenting</td>
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<tr>
<td>6</td>
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<td>Papilledema</td>
<td>502</td>
<td>Right transverse sinus</td>
<td>Stenosis</td>
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<tr>
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<td>F</td>
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<td>Headache, vomiting</td>
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<td>Stenosis</td>
<td>Fibrous thrombus</td>
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<tr>
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<td>F</td>
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<td>Headache, papilledema</td>
<td>402</td>
<td>Right transverse sinus</td>
<td>Stenosis</td>
<td>—</td>
<td>Stenting</td>
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<tr>
<td>9</td>
<td>M</td>
<td>46</td>
<td>Headache</td>
<td>358</td>
<td>Left sigmoid sinus</td>
<td>Stenosis</td>
<td>Fibrous thrombus</td>
<td>DAVF embolization</td>
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</tbody>
</table>

TABLE 1. Summary of patient characteristics and pathological results
jugular foramen (Fig. 1A and B). A digital subtraction angiogram revealed an occlusion of the left sigmoid sinus (Fig. 1C and D). The PROGREAT microcatheter recorded a mean pressure of 354 mm H₂O in the confluence of the sinus. During the patient’s first procedure, a 1.8-mm biopsy forceps device was advanced upward in an 8-Fr ENVOY guiding catheter that was placed in the left jugular foramen. Five samples were obtained, and pathological analysis revealed a thrombus. After 8 months of oral anticoagulant therapy, the patient’s symptoms did not improve significantly and she received further treatment. At this time a second enhanced MR image showed that the lesion was not changed. In the second procedure after 8 months, a 2.3-mm biopsy forceps device was gently advanced upward in a 70-cm 8-Fr vascular introducer sheath that was placed in the left jugular foramen (Fig. 1E). Three samples were obtained, and pathological analysis revealed meningioma (Fig. 1F). This patient underwent a CSF diversion procedure, and the papilledema had improved at the 3-month follow-up examination.

Case 2

A 40-year-old woman had a 50-day history of progressive visual deterioration. Bilateral papilledema was confirmed by fundus photography. Lumbar puncture showed a high CSF pressure (500 mm H₂O). With the use of magnetic resonance venography (MRV), this patient was initially diagnosed as having IIH with right transverse sinus stenosis (Fig. 2A). Subsequently, an enhanced MR image revealed a small lesion located in the right transverse sinus (Fig. 2B). A digital subtraction angiogram revealed stenosis of the right transverse sinus (Fig. 2C). The PROGREAT microcatheter recorded a mean pressure of 502 mm H₂O in the superior sagittal sinus. A 1.8-mm biopsy forceps device was gently advanced upward in an 8-Fr ENVOY guiding catheter that was placed in the right sigmoid sinus (Fig. 2D). Three samples were obtained and fixed in formalin solutions (Fig. 2E and F). This patient underwent stent placement (Fig. 2G). Pathological analysis revealed a fibrous thrombus (Fig. 2H). Lumbar puncture showed low CSF pressure (90–100 mm H₂O) 3 days after the procedure. The papilledema had improved after 6 months of follow-up.

Discussion

IH caused by venous sinus stenosis or occlusion has been studied for decades. Any lesion that obstructs
the venous pathway from the granulations to the right heart is a potential biological cause of IH. With recent progress in imaging technology, we have been able to use the MRBTI technique to find small intrasinus lesions in some patients with IH in whom it was difficult to diagnose and distinguish the lesion from the patient’s clinical history, especially in patients with atypical symptoms. These patients are at risk for being misdiagnosed with IIH. In such cases, if the pathological results can be obtained accurately, subsequent treatment can be guided more effectively. However, obtaining the pathological specimens of sinus lesions using a minimally invasive approach is challenging.

Specimens from patients with hypertrophic pachymeningitis or meningioma can be obtained by standard meningeal biopsy or resection. However, this procedure may cause relatively severe surgical trauma. Thrombus specimens from patients with cerebral venous sinus thrombosis can be obtained by mechanical thrombectomy. PEB has been described as “a safe and efficient procedure providing the most effective technique to obtain a tissue sample of high diagnostic quality,” and can be used for early diagnosis in patients with nonspecific lesions. To our knowledge, no previous studies have demonstrated the feasibility of PEB for early diagnosis in patients with venous sinus lesions.

Stenosis of the sinuses appears as smooth narrowing of the venous sinus (extraluminal type) or an abrupt filling defect (intraluminal type). In the current cohort, the angiographic images of 7 stenosis cases demonstrated the intraluminal type and were in accordance with the results of enhanced MRI. Specimens from 3 patients revealed fibrous thrombus, which is the putative cause of venous sinus stenosis and a secondary cause of IH. We speculated that some IIH patients experienced venous sinus thrombosis, without onset of acute symptoms, and residual fibrous thrombosis caused chronic obstruction of the venous sinus.

In recent years, transvenous dural venous sinus stent (DVSS) insertion has emerged as a potential therapy for resistant IH cases. More than 20% of DVSS patients developed restenosis in their medium- or long-term follow-up. It is currently unclear which types of lesions are prone to restenosis. If these lesions can be identified by using biopsy specimens, the surgeon may tailor treatment, such as shunting, according to the patient’s pathological result.

Technically, assisted by the guiding or naive catheter, the PEB device exhibited the advantages of being flexible and able to follow even the most tortuous vascular paths up to the lesions. Fluoroscopic imaging enabled us to evaluate the precise position of the biopsy device in real time to avoid sampling a nontargeted biopsy site, particularly the normal vessel wall. In order to achieve a biopsy material of optimal quality, the introducer sheath required positioning toward the surface of the lesion, which was stabilized when the biopsy device was advanced to the target lesion. Owing to the rigidity of the device, the ideal positioning was not always feasible, especially in the lesser curvature of the sigmoid sinus where the trajectory of the introducer included multiple curvatures. Because of the unsatisfactory flexibility of the head, lesions at the lower and inner wall were challenging to obtain compared to lesions of the upper and lateral wall. The lesions of 3 patients could not be located at the lower wall of the transverse sinus or inner wall of the sigmoid sinus.
Because of the rarity of this disease, one major limitation of the study is the small number of enrolled patients. This technique may be improved for use in additional procedures for which a flexible type of biopsy forceps device is essential.

Conclusions
Percutaneous endovascular biopsy of venous sinus lesions is a safe and efficient alternative procedure. This technique may help the surgeons to obtain an early diagnosis and choose appropriate treatment in patients with IH.

References

Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Quan. Acquisition of data: Quan. Analysis and interpretation of data: Quan. Drafting the article: Quan. Critically revising the article: Xu. Reviewed submitted version of manuscript: Quan. Administrative/technical/material support: Quan, X Li, Xu, Lin, Liu, D Li. Study supervision: Quan.

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