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Safety and Clinical Outcomes after Transverse Venous Sinus Stenting for Treatment of Refractory Idiopathic Intracranial Hypertension: Single Center Experience

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Abstract

Background—Idiopathic intracranial hypertension (IIH) is a syndrome of elevated intracranial pressure of unknown etiology. Unilateral or bilateral transverse sinus (TS) or transverse-sigmoid junction stenosis is present in about 30%–93% of these patients. There is an ongoing debate on whether venous sinus stenosis is the cause of IIH or a result of it. The subset of IIH patients who continue to have clinical deterioration despite maximum medical therapy is termed as "refractory IIH." Traditionally, cerebrospinal fluid diversion surgeries (ventriculoperitoneal shunt and lumboperitoneal shunt) and optic nerve sheath fenestration (ONSF) were the mainstays of treatment for refractory IIH. In the last decade, venous sinus stenting (VSS) has emerged as a safe and effective option for treating refractory IIH patients with venous sinus stenosis. Through this study, we want to share our experience with venous stenting in refractory IIH patients with venous sinus stenosis associated with a significant pressure gradient (≥10 mm Hg).

Methods—Retrospective chart review of all the patients diagnosed with refractory IIH who underwent VSS or angioplasty at our comprehensive stroke center from November 2016 to March 2019.

Results—A total of seven refractory IIH patients underwent VSS or angioplasty within the specified period. The mean age was 39 years. Eighty-five percent of the patients were women (n = 6). The mean body mass index (BMI) was 37 kg/m^2. Headache was the most common symptom (85%, n = 6) followed by transient visual obscurations (71%, n = 5) and pulsatile tinnitus (57%; n = 4). All patients had papilledema. Fifty-seven percent of patients (n = 4) had impaired visual field. Mean lumbar opening pressure was 40.6 cm H_2O (SD = 9.66; 95% CI = 33.5—47.7). All patients were on maximum doses of acetazolamide ± furosemide. Six patients (85%) had dominant right transverse-sigmoid sinus. Fifty-seven percent of the patients had severe right transverse ± sigmoid sinus stenosis (n = 4) and the rest (43%) had bilateral TS stenosis (n = 3). Presenting mean trans-stenosis pressure gradient was 18 mm Hg (SD = 6.16; 95% CI = 13.43–22.57). Six patients (85%) were treated with TS stenting and one (15%) with only angioplasty. Post-stenting mean trans-stenosis pressure gradient was 4.8 mm Hg (SD = 6.6; 95% CI = −0.1–9.7). All patients were able to come off their medications with significant improvement in neurological and ophthalmological signs and symptoms. No procedure-related complications occurred.

Conclusion—TS stenting ± angioplasty is a safe and effective means of treating refractory IIH with venous sinus stenosis associated with a significant pressure gradient (≥10 mm Hg).

Keywords

Idiopathic intracranial hypertension; venous stenosis; stenting; angioplasty; pressure gradient

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INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a relatively uncommon, poorly understood syndrome of elevated intracranial pressure (ICP) of unknown etiology [1,2]. The overall prevalence of IIH in North America is approximately 0.9–1.07/100,000 but rises to 15–19/100,000 among women aged 20–44 years who were overweight (≥20% above their ideal bodyweight) [3]. The diagnostic criteria involve symptoms and signs of increased ICP in the absence of a space-occupying or obstructive lesion. In addition, there must be a documented elevation of ICP and normal cerebrospinal fluid (CSF) composition [4].

Female sex and obesity are the only proven associations with IIH. Multiple diseases and medications have been implicated, but any definitive association has never been conclusively proven [5]. Many pathophysiologic mechanisms have been proposed, including parenchymal edema, increased cerebral blood volume, venous outflow obstruction, and obesity-related increased central venous pressure, but no consensus on the pathophysiological causes currently exists [6]. Recently, a study proposed a strong genetic association with IIH. The strongest associations observed were for rs2234671 on chromosome 2 (P = 4.93 × 10-07), rs79642714 on chromosome 6 (P = 2.12 × 10-07), and rs200288366 on chromosome 12 (P = 6.23 × 10-07) [7].

The most common symptoms include headaches, transient visual obscurations mainly associated with Valsalva, pulsatile tinnitus, and diplopia. Commonly associated signs include arcuate visual field defects, papilledema, increased retinal fiber layer thickness, and abducens nerve palsy.

Management of IIH is targeted at the protection of optic nerve function and control of symptoms. In the mild cases of IIH (absence of severe, rapidly progressive vision loss), a stepwise approach is typically implemented as first-line treatment. This includes lifestyle modifications, such as diet and weight loss when clinically appropriate, and medical management, including stopping offending agents or starting acetazolamide ± furosemide. Unfortunately, recurrence rates with medication have reached 40%. Patients who do not respond to maximum conservative therapy are termed as refractory cases and may require surgical intervention in the form of CSF diversion or optic nerve sheath fenestration (ONSF) [8].

Although IIH is a diagnosis of exclusion, 30%–93% of patients were found to have cerebral sinus stenosis [9]. It is an ongoing debate on whether stenosis is the cause of IIH or the result of elevated ICP as a secondary disease process. Other than the traditional surgical options described earlier, venous stent placement, as a treatment option for refractory IIH, is a relatively new treatment modality introduced in 2002. A metaanalysis of the 19 case reports and case series on venous stenting for refractory IIH by Teleb *et al.* [10] included 207 patients of which 181 (87%) showed improvement or complete resolution of symptoms, 27 (13%) reported no change of symptoms, and 1 reported worsening of symptoms. The recent and first prospective study by Liu *et al.* [11] concluded that patients with refractory IIH were found to have venous sinus stenosis with an elevated trans-stenosis pressure gradient and ICP; venous sinus stenting (VSS) results in immediate abolition of the pressure gradient, reduction in ICP, and functional, neurological, and ophthalmological improvement. There were no major peri- or postprocedural complications, except 20% of the patients (n = 2) developed stent adjacent stenosis on a 3-month follow-up angiogram which was clinically significant and required restenting [11].

In this study, we share our experience with venous stenting in patients with refractory IIH who had transverse sinus (TS) stenosis associated with a significant pressure gradient (≥10 mm Hg).

METHODS

A retrospective chart review of all the patients diagnosed with refractory IIH who underwent VSS or angioplasty was carried out at our comprehensive stroke center from November 2016 to March 2019. The study protocol was approved by our local institutional review board (JFK Health system IRB).

Patient selection and characteristics

Patients were considered eligible for stenting based on the following criteria: (1) refractory IIH; (2) papilledema confirmed by an ophthalmologist; and (3) dural venous sinus stenosis of the dominant venous outflow system with a gradient of ≥10 mm Hg. This cut-off pressure was selected because a gradient of 5–6 mm Hg from the superior sagittal sinus (SSS) to the internal jugular bulb is present in normal controls [12,13].

Demographic features [e.g., age, gender, and body mass index (BMI)], presenting clinical features, CSF opening pressures, neuroophthalmologic evaluation, prestenting medical treatments, radiographic (MRV/CTV) results, procedural details including trans-stenosis pressure gra-

TABLE 1.

Case	Age (years)	Sex	BMI (kg/m2)	Presenting symptoms	CSF pressure (cm H_2O)	Ophthalmological findings	Pre-op meds	Radiographic findings	Clinical outcomes
1	54	F	35	headaches blurry vision	38	VF: OD -Superior field defect Severe bilateral papilledema RNFLT: OD-160 µm; OS-196 µm	Acetazolamide	Dominant right sinus Bilateral TS stenosis	headaches resolved; Off meds; VF normal; RNFLT—OU 89 µm; Papilledema resolved
2	31	F	31	headaches vision loss	37	VF: Superior field cut Severe bilateral papilledema RNFLT : OD 141 µm; OS 142 µm	Acetazolamide	Dominant right sinus Right TS and sigmoid sinus stenosis	headache resolved; off meds; stable superior field defect; Papilledema resolved RNFLT —OD 79 µm OS 81 µm
3	43	F	38	headaches visual obscurations	43	VF : normal Moderate bilateral papilledema RNFLT: OD 159 µm; OS 145 µm	Acetazolamide Furosemide	Dominant right sinus Bilateral TS and sigmoid stenosis	headache resolved; off meds; normal VF; papilledema resolved; RNFLT—OD 107 µm OS 115 µm
4	55	M	47	headaches pulsatile tinnitus, Visual obscurations	33	Bilateral infranasal field defect Bilateral mild papilledema	Acetazolamide	Dominant right sinus Right TS stenosis	headache resolved, visual fields and papilledema unchanged
5	35	F	55	headaches pulsatile tinnitus	30	normal visual fields bilateral mild papilledema RNFLT: OD 162 µm; OS 186 µm	Acetazolamide	Dominant right sinus Right TS stenosis	headaches and tinnitus resolved; papilledema improved; RNFLT—OU 85 µm
6	16	F	27	headaches, tinnitus, Double vision, blurry vision	62	VF: OD – Inferior field cut; OS – Superior field cut, Left 6th palsy, bilateral mild papilledema, RNFLT: OD 180 µm; OS – 200 µm.	Acetazolamide	Dominant left sinus Bilateral TS & sigmoid sinus stenosis	headaches and tinnitus resolved normal visual fields, resolved 6th nerve palsy, papilledema resolved RNFLT- OD 120 µm; OS 115 µm.
7	32	F	36	pulsatile tinnitus	41	Normal visual fields Mild papilledema RNFLT: OU -115 µm	Acetazolamide	Right transverse-sigmoid junction severe stenosis; hypoplastic left transverse sinus	Tinnitus resolved

TABLE 2.

Case	Procedure	Prestenting pressure gradient	Poststenting pressure gradient	Stent used	Balloon used	Follow-up MRV/CTV
1	Right transverse sinus angioplasty	22	18	Unsuccessful Wall stent (10 × 37)	Sterling(5.5 × 40)	No radiographic follow up. 6 month neuro-opth.exam was stable.
2	Right transverse sinus stenting	22	1	Successful Wall stent (10 × 40) Unsuccessful Epic stent (10 × 40)	none	Patent stent
3	Right transverse sinus stenting	20	12	Successful Protégé stent (10 × 20) Unsuccessful second Protégé (10 × 20/40) Unsuccessful Wall stent (10 × 20)	none	Patent stent
4	Right transverse sinus stenting	10	0	Successful Protégé stent (10 × 40)	none	Patent stent
5	Right transverse sinus stenting	27	1	Successful Protégé stent (10 × 40)	none	Patent stent
6	Left transverse sinus stenting	16	1	Successful Zilver stent (10 × 40)	none	Patent stent
7	Right transverse sinus stenting	10	1	Successful Zilver stent (10 × 40)	none	Patent stent

dient and clinical outcomes, were obtained by the retrospective chart review.

Procedure

Patients diagnosed with refractory IIH, who had either unilateral dominant or bilateral venous sinus stenosis, were scheduled for diagnostic angiography and venous manometry prior to stenting ± angioplasty.

The femoral artery (5F cordis sheath) and venous access (8F 90-cm cook shuttle) were obtained at the start of the case, and a diagnostic angiogram was done through a 4F Vert diagnostic catheter placed in a right internal cere-

bral artery. An 8F Shuttle (Cook) was advanced into the right jugular bulb. A 4F 150-cm Bernstein hydrophilic glide catheter was advanced across the stenotic right TS, torcula, and into the SSS over the 0.035 glide wire (Terumo Inc.). The glide wire was removed, and a standard arterial pressure transducer was calibrated and connected to the Bernstein catheter. Venous manometry was then performed, with recording of mean venous pressures in the SSS, torcula, proximal and distal segments of TS stenosis, sigmoid sinus, and jugular vein. A difference of ≥10 mm Hg across the stenosis was required to proceed with stenting. The Bernstein catheter was again navigated to SSS over the 0.035 glide wire. It was then exchanged with a 0.035 extra stiff Amplatz wire. A 10 mm × 40 mm Zilver (Cook), 10 mm × 20/40 mm Protégé (Covidien), or a 10 mm × 20 mm Wall stent (Boston Scientific) was then advanced over the Amplatz wire and deployed across the TS stenosis. Other stents including 10 mm × 37 mm wall stent (Boston Scientific) and 10 mm × 40 mm epic stent (Boston Scientific) were tried but were unsuccessful in navigating across the stenosis. No angioplasty was required except in one case where we were not able to advance the stent across the stenosis. Poststent deployment, arteriograms were obtained to analyze the changes in hemispheric venous drainage patterns. Poststent venous manometry was done to verify the efficacy of the stenting procedure and the elimination of the trans-stenosis pressure gradient. The arteriotomy site was then closed with an Angioseal device (St. Jude Medical), and the venotomy site was closed with manual pressure. Intravenous heparin was given during the stent procedure to increase the activated clotting time to 250–300 sec. Poststent deployment, intra-arterial eptifibatide bolus was administered and Eptifibatide IV drip was started, which was switched to dual antiplatelet therapy after 20 hours. Dual antiplatelet therapy was continued for 6 months, and aspirin indefinitely thereafter.

Several technical considerations contribute to successful stenting. Due to the inherent tortuosity in the sigmoid sinus–TS system and the stiffness of the stent, a robust support system is required for adequate access and to navigate bigger stents. Wider (10 mm) and longer (40/80 mm) stents are better to prevent restenosis and stent adjacent stenosis.

Angiographic follow-up and outcome assessment

Neurointervention clinical follow-up was scheduled within 2 weeks after the procedure to evaluate for any procedure-related complications. Neuroophthalmological follow-up was scheduled around 4–6 weeks poststent placement. Ophthalmological evaluations included visual acuity testing, visual field testing (Humphrey), fundoscopy, and optical coherence tomography (OCT). Radiographic follow-up was performed with noninvasive imaging (MRV/CTV) at 6 months after the stenting procedure.

RESULTS

A total of seven patients were referred to the neurointervention clinic at our comprehensive stroke center by a neuroophthalmologist with the diagnosis of refractory IIH and cerebral venous sinus stenosis from November 2016 to March 2019. The mean age was 39 years. Eighty-five percent of the patients were women (n = 6). The mean BMI was 37 kg/m^2. Headache was the most common symptom (85%, n = 6) followed by transient visual obscurations (71%, n = 5) and pulsatile tinnitus (57%; n = 4). All patients had papilledema and increased retinal fiber layer thickness which were diagnosed by a neuroophthalmologist. Fifty-seven percent of the patients (n = 4) had impaired visual field. The mean lumbar opening pressure was 40.6 cm H_2O (SD = 9.66; 95% CI = 33.5–47.7). All patients had failed medical treatment with a maximum dose of acetazolamide; in addition, furosemide was administered to one patient (15%). Six patients (85%) had a dominant right transverse-sigmoid sinus. Fifty-seven percent of the patients had severe right transverse ± sigmoid sinus stenosis (n = 4) and the rest (43%) had bilateral TS stenosis (n = 3) (Table 1). Prestenting mean trans-stenosis pressure gradient was 18 mm Hg (SD = 6.16; 95% CI = 13.43–22.57). Poststenting mean trans-stenosis pressure gradient was 4.8 mm Hg (SD = 6.6; 95% CI = −0.1–9.7). Six patients (85%) were treated with TS stenting and one (15%) with angioplasty. Stents used successfully were Zilver 10 mm × 40 mm (n = 2), Protégé 10 mm × 40 mm (n = 2), Protégé 10 mm × 20 mm (n = 1), and Wall 10 mm × 20 mm (n = 1). Other stents that were tried but unsuccessful are Wall 10 mm × 20 mm (n = 1), Wall 10 mm × 37 mm (n = 1), Epic 10 mm × 40 mm (n = 1), Protégé 10 mm × 20 mm (n = 1), and Protégé 10 mm × 40 mm (n = 1). Sterling 5.5 mm × 40 mm balloon was used in the solo angioplasty case. Technical success was achieved in all patients except one where the stent could not be advanced through the stenotic sinus despite preceding angioplasty. This patient was treated with primary angioplasty only (procedural details are shown in Table 2, and preangiographic and postangiographic images are shown in Figure 1). No major or minor periprocedural complications occurred. All patients were followed up in the neuroophthalmological clinic within 4–6 weeks of stenting. All patients had a complete or

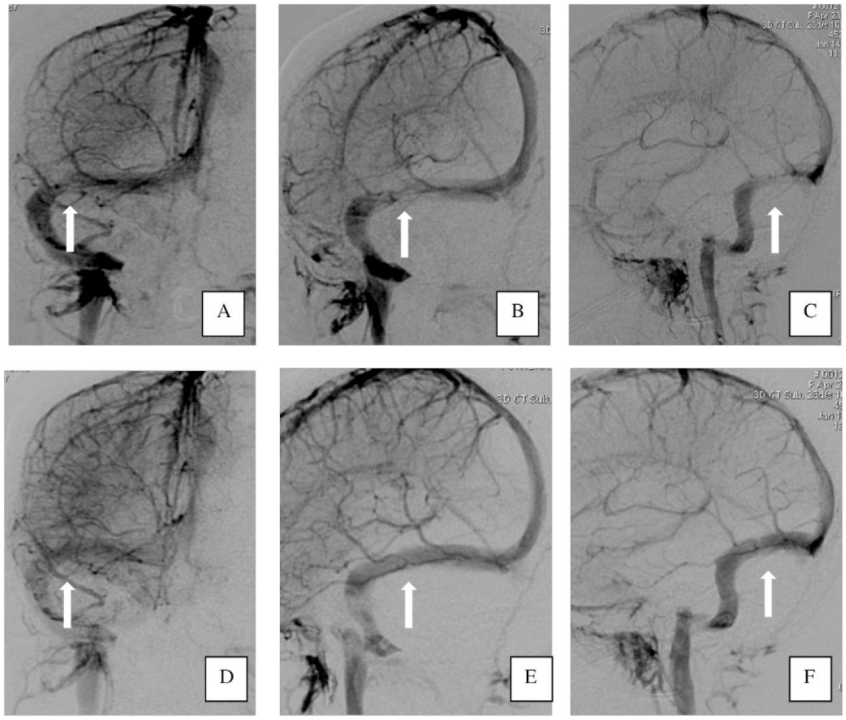

Figure 1. Prestenting and poststenting conventional angiogram images of a 37-year-old woman with refractory IIH. (A)–(C) Anterioposterior, oblique, lateral, and reformatted views showing severe stenosis of dominant right transverse venous sinus. (D)–(F) Anterioposterior, oblique, lateral, and reformatted views showing complete resolution of right transverse sinus stenosis.

near-complete resolution of papilledema (Figure 2) and a significant decrement of retinal fiber layer thickness. Of the four patients who presented with visual field defect, two improved (50%) and two remain unchanged (50%) (Figure 3). Headache and tinnitus were resolved in all the patients who presented with these symptoms. All patients were able to come off acetazolamide and furosemide. Six patients (85%) had a 6-month follow-up MRV or CTV that confirmed patent stent, and one patient (15%) never had a 6-month radiographic follow-up but had a 6-month neuroophthalmological evaluation which was better from the preintervention examination.

DISCUSSION

CSF diversion surgeries [ventriculoperitoneal shunt (VPS) and lumboperitoneal shunt (LPS)] and optic nerve sheath fenestration (ONSF) are the traditional surgical options available for treating medically refractory IIH, but, unfortunately, these procedures have significant limitations. Clinical outcomes with CSF diversion vary considerably depending on the series. Stabilization or improvement in vision has been reported to occur in as few as 62% of patients undergoing VPS or LPS and headaches to improve or resolve in as few as 45%, with frequent recurrences over time. Shunt revisions are required in 38%–63% of the patients. Furthermore, although rare, serious complications (including a 0.5% risk of in-hospital death) have been reported [14]. Similarly, ONSF is associated with substantial treatment failure rates (worsening in vision after a period of stabilization in 34% of patients at 1 year and 45% at 3 years) and failure to improve headache in one-third to one-half [14].

Over the last decade, multiple case reports and series have shown VSS as a very safe and effective surgical option for treating patients with refractory IIH who have dural sinus stenosis with significant trans-stenosis pressure gradient. Although it is an ongoing debate on whether venous sinus stenosis is the cause of IIH or a result of it, given the high success rate of venous stenting in this subset of patients, venous sinus stenosis is proposed as a possible pathophysiological mechanism of refractory IIH [13]. A metaanalysis of the 19 case reports and series by Teleb *et al.* [10] included a total of 207 patients with refractory IIH who underwent venous stenting, 181 patients (87%) showed improvement or

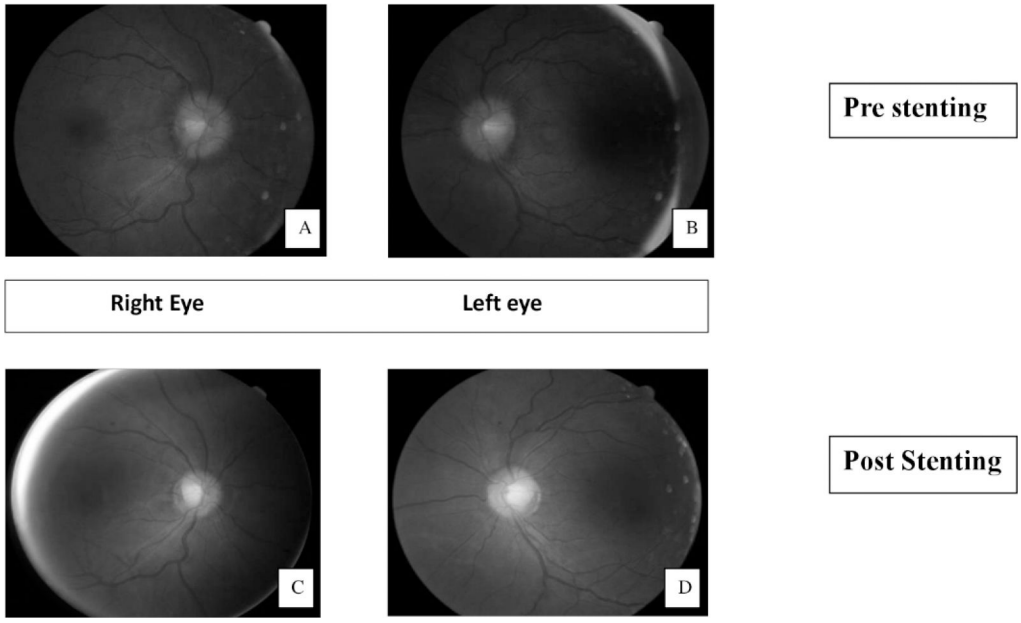

Figure 2. Fundoscopic examination (A) and (B) prior to stenting showing optic disc edema with obscuration of the optic disc margins, elevation of the optic disk, and tortuosity of retinal veins and (C) and (D) 4 weeks after stenting showing resolution of optic disc edema and improved vascular tortuosity.

complete resolution of symptoms, 27(13%) reported no change of symptoms, and 1 reported worsening of symptoms. Headaches resolved or improved in 81% of the patients. Papilledema improved in 90% of the cases (172 of 189 patients). Sinus pressure decreased from an average of 30.3 to 15 mm Hg. Sinus pressure gradient decreased from 18.5 mm Hg (n = 185) to 3.2 mm Hg (n = 172). Only three major complications related to the procedure were identified [10]. A recent and first prospective study by Liu *et al.* [11] concluded that in patients with refractory IIH who are found to have venous sinus stenosis with an elevated trans-stenosis pressure gradient and ICP, VSS results in immediate abolition of the pressure gradient, reduction in ICP, and functional, neurological, and ophthalmological improvement. There were no major periprocedural or postprocedural complications, except in 20% patients (n = 2) who developed stent adjacent stenosis on a 3-month follow-up angiogram which was clinically significant and required restenting [11].

Our study results strongly support the conclusions drawn by previous studies. Of the seven patients treated, all patients had a resolution of presenting symptoms, all patients had a complete or near-complete resolution of papilledema and significant decrement of retinal fiber layer thickness, all patients had improvement or stabilization of vision, and all patients were able to come off acetazolamide. No major or minor periprocedural complications were reported. Based on the previous studies and our own experience, we strongly believe that VSS is a safe and effective treatment in the refractory IIH patients with venous sinus stenosis associated with a significant pressure gradient (≥10 mm Hg). The major limitations of our study are underpowered and retrospective nature.

CONCLUSION

TS stenting is a safe and effective means of treating refractory IIH with venous sinus stenosis associated with a significant pressure gradient (≥10 mm Hg). In light of excellent clinical outcomes documented in our study as well as in the literature, further investigation with a multi-center randomized clinical trial would be beneficial in facilitating the transition of VSS into the realm of the standard of care in refractory IIH.

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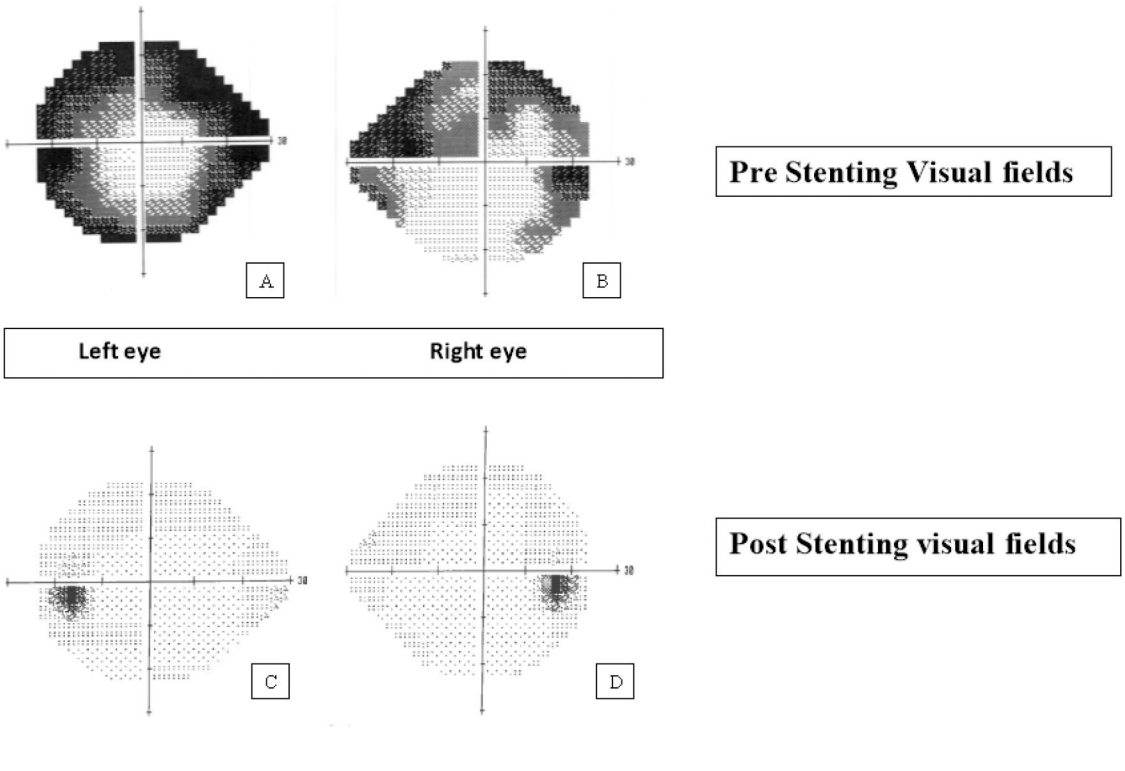

Figure 3. Prestenting and poststenting visual fields in a patient with refractory IIH. (A) and (B) Significant bilateral visual field defect. (C) and (D) Bilateral normal visual fields.

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