Pseudotumor Cerebri: a New Door Opens for Treatment

R. CROSA, O. MARABOTTO, G. MEEHROFF, C. LEGNANI, J. BOSCHI, A. NEGROTTA, K.G. TERBRUGGE*, P. LASJAUNIAS**

Department of Neurosurgery (Drs. Crosa R, Negrotto A), Neurology (Dr Legnani C), Ophthalmology (Dr Meehroff G), Radiology (Drs. Marabotto O, Boschi J.), Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay.

*Department of Medical Imaging, University of Toronto, ON, Canada.

**Service de Neuroradiologie Diagnostique et Thérapeutique, Centre Hospitalier Universitaire de Bicêtre, Paris, France.

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Summary

Pseudotumor cerebri remains a scarcely known pathology. We present the experience of a multidisciplinary working group which studied this disorder focusing on the venous alterations of the dural sinuses.

Seventeen cases were studied, diagnosed, controlled and treated by our team. In one of the cases, we placed a stent in the left lateral sinus with good result.

In all the patients we observed various degrees of stenosis in the brain venous sinuses quantified by pressure measurement. Nevertheless, to determine the exact cause of this pathology, more studies are necessary.

Introduction

Although there have been references to this disease for over a century¹, little is known about the etiopathogenesis of pseudotumor cerebri. Therefore, multiple hypotheses on the cause of this pathology have been formulated over the years. As a consequence of the various pathophysiological layouts, diverse types of treatment have been applied, achieving different results in each particular case.

Based upon recent studies², we have focused on the diagnosis and treatment of pseudotumor cerebri from the point of view of the alterations in the venous drainage of the brain.

Historical Background

The first physician to describe patients with intracranial pressure increase (ICP), normal cerebrospinal fluid (CSF) and no intracranial tumor was Taylor in 1880. In 1904, Nonne named it "pseudotumor cerebri". Diagnostic protocols were prepared by Davidoff and Dyke (in the 1920s) and then by Dandy in 1937. More recently (in 1955), Foley³ suggested the term "benign endocranial hypertension" for this disease. In 1965, the adjective "benign" was severely questioned - with good reason - by Bucheit, based upon the patients' clinical evolution.

Definition

Pseudotumour cerebri is a rare disease characterized by an increase in intracranial pressure with no pathological findings disclosed by conventional imaging studies.

Clinical Features

Pseudotumour cerebri more frequently affects women (although this is not true when it happens at an early age) who are obese, with an incidence peak between 20 and 50 years. It is not unusual to see a background of mild to moderate hypertension in these patients.

The clinical signs of pseudotumor cerebri –

headache and papilledema - associated or not with different degrees of visual deficit (even blindness) - are a consequence of the increase in ICP.

Pathogenesis

The origin and pathophysiological mechanisms causing pseudotumor cerebri have remained controversial. Several hypotheses have included as the cause of this disease brain edema, CSF overproduction, alterations in the drainage of CSF as well as in the brain blood volume along with endocrinological disorders⁴. Despite all these theories, the mechanisms of this pathology remain unsettled.

Diagnostic criteria

The diagnostic characteristics of the pseudotumor cerebri syndrome were first described by Dandy in 1937 and then reformulated by Smith in 1985^{5,6,7,8}. These criteria have been recently revised to adapt them to the latest technical advances in neuroimaging⁹:

• CURRENT DIAGNOSTIC CRITERIA for pseudotumor cerebri:

1. If there are symptoms, they must be caused by endocranial hypertension or papilledema.
2. If there are signs, they should only be secondary to endocranial hypertension or papilledema.
3. Record of CSF hypertension measured by manometer performed on left side decubitus.
4. Normal composition of CSF.
5. Absence of hydrocephalus, lesions with effect on intracranial mass, intracranial vascular lesions shown on NMR or CT with intravenous contrast agents in typical patients* and NMR and resonance venography in atypical patients.
6. No other proven cause of endocranial hypertension.

By typical patients we understand obese females whose age ranges between 20 and 50 years.

Given the need for a multidisciplinary approach to this pathology, three years ago we formed a group of specialists (neurosurgeons, neuroradiologists, neurologists, hematologists

and ophthalmologists) interested in pseudotumor cerebri. We selected and made a follow-up of all the patients with this diagnosis admitted to our hospital. There clearly are no unanimous criteria when facing a definition of the causes or planning the treatment of this disorder. This leads to the employment of various treatment techniques based upon different criteria which do not lead to a better understanding of the disease or improve the patient's quality of life.

Our objective was to demonstrate that PC is related to changes in brain venous drainage by studying patients by direct retrograde venography and pressure measurement in the sinus.

Material and Methods

To date we have selected 17 patients with a diagnosis of PC based on the diagnostic criteria listed above. Their ages range from nine to 52 years, all of them are females. In all the cases, there was a strict weekly follow-up by an ophthalmologist in the first two months and every two weeks in the following months. A standard eye examination and HRT were performed at all ophthalmologic appointments. All the patients underwent a direct retrograde venography through selective microcatheterism of all the brain venous sinuses using a femoral approach. Pressure recordings were performed in all cases by means of a transducer connected to a microcatheter. All the patients were checked during at least a two-year period by the neurologists and neurosurgeons of the PC group. In all the cases, the medical treatment included a diet and acetazolamide (the latter for not more than five months).

Patients

Clinical Case Report

Patient: 38-years-old, obese. Mild arterial hypertension. She was admitted to the Neurology and Neurosurgery Service of Hospital de Clínicas having suffered from headache for two months. A bilateral papilledema was found during the physical examination. A brain CT with and without contrast, NMR and venographic resonance studies were performed and no pathological alterations were found. Rachimetry showed a CSF pressure of 35 cm of H₂O (25.8 mmHg). Medical treatment started upon the diagnosis of pseudotumor cerebri, with ace-

tozalamide and furosemide and she was discharged. She was readmitted a month later, with an increase in the headache intensity and episodes of visual darkening becoming more and more frequent. An increase in papilledema and a marked decrease in bilateral visual acuity were observed. A new rachimetry showed a CSF of 42 cm of H₂O (30.8 mmHg). A new study by means of a direct retrograde venography was decided (figures 1, 2 and 3); the following records were obtained:

Initial pressure records obtained through the right jugular:

PSSS	PT	PSTP	PSTD	PSSg	PY
30 mmHg	33 mmHg	26 mmHg	24 mmHg	12 mmHg	11 mmHg

Initial pressure records obtained through the left jugular:

PSSS	PT	PSTP	PSTD	PSSg	PY
30 mmHg	33 mmHg	34 mmHg	29 mmHg	13 mmHg	11 mmHg

PSSS: superior sagittal sinus pressure; PT: screw pressure (Herofilo press); PSTP and D: pressure of proximal and distal transverse sinus respectively; PSSg: pressure of the sigmoid sinus; PY: jugular pressure

Besides the severe hypertension in the venous sinuses, we were able to clearly determine a right and left pressure gradient with the following values:

- a 12 mmHg gradient between the right transverse sinus and the beginning of the ipsilateral sigmoid sinus;
- a 16 mmHg gradient between the left transverse sinus and the ipsilateral sigmoid sinus.

It was decided to make the dilatation of the stenosis of the left lateral sinus by the placement of a self expandable stent (figure 4).

The pressure records obtained from the left after the placement of the stent are the following:

PSSS	PT	PSTP	PSTD	PSSg	PY
22 mmHg	19 mmHg	17 mmHg	16 mmHg	14 mmHg	11 mmHg

Figure 1 Direct retrograde venography to the right showing a distal stenosis to the final end of the transverse sinus (circle). It also shows the pressure measures at those ends (arrows), with a clear gradient in relation to the stenosis.

Figure 2 Direct retrograde venography to the left showing a stenosis of the proximal part of the sigmoid sinus (circle); the arrows show the pressure measures in mmHg obtained at the ends, with a clear pressure gradient between both of them.

Figure 3 Cerebral angiography (frontal projection) in venous phase, showing with arrows the different pressure values in mmHg obtained in each sector of the venous system during the study.

Figure 4 Selfexpandable stent deployed in the lateral sinus (lateral view). Proximal to the jugular bulb, a balloon is inflated in order to dilate this portion. The microguide is seen distal in the lateral sinus.

Figure 5 Venous phase of cerebral angiography in frontal view, before the treatment. By the circle, the localization of the stenosis is showed. The numbers (in mmHg) are the values of the pressure measurements in both sides of this stenosis.

As can be seen, we were able to reduce the pressures in the venous sinuses to almost normal values. The disappearance of the previously recorded pressure gradient and the elimination of the stenosis are also observed in the venographic sequences (figures 5 and 6).

Figure 6 similar venous phase to the previous figure, but after the treatment. It is also showed by the circle the localization of the stenosis, and by the numbers the values of the pressure. It can be seen that the difference of the values in both sides of the stenosis has lowered. The symptoms of the patient gradually began to disappear.

After the placement of the stent in the venous sinuses, the symptoms gradually began to disappear. The patient's ophthalmologic records clearly show the improvement of the papilledema (figures 7 to 12).

Discussion

In this paper, we have presented the experience of a multidisciplinary working group on pseudotumor cerebri. We have submitted 17 cases, diagnosed, controlled and treated by our team. In one of the cases, we placed a stent in the left lateral sinus and the venous drainage of a patient improved after her symptoms had worsened in spite of the intensive medical treatment prescribed. All the patients were studied, and various degrees of stenosis in the brain venous sinuses were observed and quantified through pressure measurement.

As was also described in other studies^{2,25}, we found that stenosis of the brain venous sinuses may be found related to this pathology.

There are many theories that postulate the mechanism through which stenosis is related to pseudotumor cerebri (and therefore endocranial pressure). For example one says that it is the consequence of an alteration in the reabsorption of CSF by arachnoid granulations, which is mainly ruled by the pressure in the SSS¹⁰⁻¹⁷. It was also proposed that this increase

Figures 7, 8 On the left side there is the patient's ophthalmologic record of the right eye carried out on 07/07/03, before the treatment. On the right side the same record carried out 20 days after the placement of the stent in the venous sinus, on 08/01/04. It is possible to see the improvement of the papilledema.

Figures 9, 10 Similar ophthalmologic records to the previous figures, but of the left eye. On the left side, study carried out the 07/7/03 before the treatment. On the right side, record 20 days after the placement of the stent in the venous sinus, on 08/01/04. This eye also improved.

in pressure would slowly stretch and collapse the dural walls of the transverse sinuses and eventually create a flow limiting stenosis and a pressure gradient²⁵. Another hypothesis² considered the possibility of a small encephalic hernia in the sinus, adhesions of unknown ori-

gin in the sinuses which would progressively slow down the venous flow until it appears like a real stenosis¹⁸⁻²¹, or hypertrophy of the arachnoid granulations.

In any case, it is not clear if the stenosis is the cause or the consequence of the rise in in-

Figure 11 Papillary edema evolution of the left eye by 3D reconstruction before and after stent placement.

tracranial pressure and we have not been able to determine the cause of the stenosis. Even though many causes can be implicated in the genesis of this disorder, an anatomopathological study to prove the anatomical substratum of stenosis would be necessary to this end.

We deem that the irrefutable proof of stenosis in the venous sinuses in patients with pseudotumour cerebri, opens a new door to the study of this pathology. As we have previously explained, this syndrome has undergone many treatment strategies and techniques, due to the confusion when faced with an explanation of its etiopathogenesis^{22,23,24}.

Direct venography is a useful tool to study the status of the venous sinuses in pseudotu-

mour cerebri. Nevertheless, it has been taken into consideration that other authors noted that auto-trigger elliptic-centric-order three-dimensional gadolinium enhanced MR venography (ATECO-MRV)²⁵ has very good specificity and sensibility in the diagnosis of dural sinuses stenosis.

Using the ATECO MRV technique, they have shown that these stenoses are seen consistently in more than 90% of IIH patients²⁵.

We consider that direct venography done by a frequently used access and with low risk performed by trained neurointerventional doctors allows the measurement of the pressure on both sides of the stenosis which is important in this kind of pathology

Figure 12 Papillary edema evolution of the right eye by 3D reconstruction before and after stent placement.

As to the placement of stents in the venous sinuses, we believe that it could be an option in those cases where one or more stenoses are shown and in which there is no response to the usual medical treatment or a quick rapid of visual acuity.

Conclusions

Stenosis of the brain venous sinuses is very common in pseudotumor cerebri. Direct retro-

grade venography along with pressure measurement in the brain venous sinuses is a good option to study these cases once the syndromic diagnosis has been made.

More studies are necessary to determine the exact cause of this pathology. Regardless of whether the stenoses are or are not the cause, the placement of stents in the transverse sinuses to improve venous flow seems to be a useful and effective way to treat pseudotumor cerebri when there is no other option.

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Dr Roberto Crosa
Department of Neurosurgery
Hospital de Clínicas
Facultad de Medicina
Universidad
de la República, Montevideo
Uruguay
E-mail: Rocrossa@adinet.com.uy