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Tegmen Attenuation in Patients With Idiopathic Intracranial Hypertension Is Progressive

Ophir Handzel, MD; Adi Brenner-Ullman, MD; Dana Niry, MD; Uri Neuman, MD; Oren Cavel, MD; Oron Yahav, MD; Dan M. Fliss, MD; Omer J. Ungar, MD

Objectives: To prove that temporal bone tegmen attenuation in patients with idiopathic intracranial hypertension (IIH) is progressive.

Study Design: Retrospective blind study at a tertiary academic medical center.

Methods: Enrolled were medical records of patients with IIH that included at least two sequential computed tomography (CT) scans. The vertical distances between the floor of the middle fossa to the superior and lateral semicircular canals (SSC and LSC, respectively), the scutum and minimal squama thickness were measured. The same measurements were made in scans of control subjects. The impact of demographics and metabolic variables including opening lumbar puncture (LP) pressure were evaluated.

Results: Twenty medical records were enrolled. Median age at diagnosis was 21 years; 16 were females. The median body mass index (BMI) was 32 kg/m². Initial LP pressure was 195 mm cerebrospinal fluid (CSF). The median time interval between CT scans was 58 months. A median attenuation of 0.35 mm and 0.25 mm over the right and left LSC and of 0.5 mm and 0.3 mm over the right and left scutum, was found, respectively. The thicknesses of the SSC and squama remained stable. No attenuation was present in controls. The opening pressure on initial LP (median 195 mm CSF), was positively correlated with the degree of tegmen attenuation, but the age at diagnosis and BMI were not.

Conclusions: Tegmen attenuation may be progressive in patients with idiopathic increased intracranial pressure and correlated with the opening pressure on LP. Tegmen defects and CSF leak should be looked for in these patients.

Key Words: Idiopathic intracranial hypertension, cerebrospinal fluid leak, tegmen defect.

Level of Evidence: 4

INTRODUCTION

The bony floor of the middle fossa separates the intracranial contents from the middle and inner ears. Dehiscence of the tegmen tympani (TD) may result in conductive hearing loss, meningoecephalocoele, cerebrospinal fluid (CSF) leak, and otogenic meningitis. Dehiscence of the upper most area of the otic capsule results in superior semicircular canal dehiscence, with its associated autophony, aural fullness, bone hyperacusis, and sound- and pressure-evoked dizziness.

Idiopathic intracranial hypertension (IIH), also referred to as pseudotumor cerebri, or benign intracranial hypertension, is a syndrome defined by symptomatic increased intracranial pressure (ICP) in the absence of identifiable causes. The incidence and burden of IIH are growing. Several studies suggested a congenital cause, whereas others suggested acquired ones. Although the exact pathogenesis is unproven, IIH is strongly associated with elevated BMI and female gender, most prevalent in the fourth to fifth decade of life. Elevated body mass index (BMI) is a risk factor for both IIH and TD.

Although the pathogenesis of TD and spontaneous CSF leaks has not been completely elucidated, it is postulated that the hydrostatic pulsatile forces of elevated CSF pressure are exerted throughout the skull base and seek the path of least resistance. Sites of inherent structural weakness in the skull base include the cribiform plate, sphenoid sinus lateral wall, and tegmen tympani and mastoideum. Mechanisms that have been proposed for the pathogenesis of IIH include the alteration of CSF physiology as a result of resistance to absorption, abnormal pressure, and/or pulsation. It was recently proposed that vascular factors may also contribute to the underlying pathology, especially abnormalities of arterial inflow and venous outflow.

It is thought that elevated BMI increases venous pressure, reducing venous evacuation of blood from the contained intracranial vault resulting in elevated pressures. Absorption of CSF at the arachnoid villi is dependent on a pressure gradient to the dural sinuses. When the pressure in the sinus is elevated the absorption of CSF may decrease.

The relationship of an empty sella with IIH can serve as a model for the pathogenesis leading to CSF leak...
in IIH. It is thought that the exertion of chronically elevated CSF pressure or pulsatility on the diaphragm sellae causes empty sella syndrome (ESS), by CSF herniation into the sella through an opening in the diaphragm sellae, and over time causing widening and enlargement of the sella turcica and of the pituitary gland, leading to the typical appearance of the empty sella.13,14 The association between ESS and IIH is so close, that ESS may serve as a noninvasive radiographic indicator of elevated ICP, as a reversible empty sella has been reported in cases of documented intracranial hypertension after successful reduction of elevated ICP with diuretics or shunting. The sella status should not replace definitive measurement of ICP when this information will affect clinical management.15 The same CSF expending force that produces ESS is responsible for the increased CSF content of the dural sleeve of the optic nerves.

Once IIH is present, the hydrostatic pulsatile forces are exerted throughout the skull base. Sites of inherent structural weakness in the normal skull base include locations such as perforations in the cribiform plate, the fascia of the sellar diaphragm, and other areas with significant pneumatization (the temporal bones and paranasal sinuses) and subsequent thinning of the bony skull base. These sites form potential locations for development of skull base defects and CSF leak.

It is unknown, however, whether TD and CSF leak are the result of progressive tegmen attenuation or a congenital static condition in patients with IIH.16–20 It is possible that over time, the chronically elevated ICP and pulsatile CSF may erode the bone of the floor of the middle or anterior fossae, allowing herniation of the meninges and eventually leading to CSF leaks. One of the implications of this discrimination is that if tegmen attenuation is progressive, some of its life- and function-threatening complications may be preventable with treatment.

The aim of this study was to prove that tegmen thinning is progressive in patients with IIH utilizing sequential computed tomography (CT) scans.

MATERIALS AND METHODS

After approval by the institutional ethics committee, a retrospective analysis of medical records from 1992 to 2018 of patients diagnosed with IIH was performed. The updated diagnostic criteria for IIH that are used for routine patient management and research purposes4 were used to identify all IIH patients treated during this time period. Enrolled were medical records that included at least two sequential CT scans directed to the head or ears, which were of sufficient quality to allow reliable tegmen thickness measurement. Medical records that included at least two CT scans of healthy control patients were used as a comparison. The reason for repeated CT among the control group was not related to any cranial abnormality.

All CT scans taken had bone window images that were used for this study; the slice thickness in all scans taken was between 0.9 mm and 1.5 mm. Due to the retrospective nature of the study and ethics, rescanning patients with higher-definition scans was impossible. Each axial CT scan was reconstructed in the coronal plane, utilizing the Advantage workstation (GE Healthcare, Chicago, IL), based on the plain bisecting the internal acoustic canal and the lateral semicircular canal (LSC).

After reconstruction was performed, a neuroradiologist, blind to the clinical data and all CT examination details, measured independently the vertical distance between floor of the middle cranial fossa to the following three middle and inner ear structures using the reconstructed coronal plain (Fig. 1A,B): 1) the superior most portion of the superior semicircular canal (SSC), 2) the lateral most point of the LSC, and 3) the medial most point of the scutum.

The rationale was to find extracranial ancillary measurement points that were unlikely to shift in the subjects’ body between scans. Hence, the distance between such a point to one directly vertical to it at the skull base should not change unless there is a true change in the location of the point at the skull base. Minimal squama thickness served as a non-tegmen skull attenuation indicator. Each focus was measured four times per patient: on the right and left temporal bones and on two CT scans. The neuroradiologist was blinded to the date/order of the scan and to clinical data. Patients with previous craniotomy, intracranial space-occupying lesions, middle ear cleft surgery or pathology (e.g., cholesteatoma), or radiotherapy were excluded. Demographics and metabolic parameters were collected.

The distance changes between the first and second CT scans from our referral points to the floor of the middle cranial fossa and the squama thickness were compared between the study and the control groups.

To evaluate the intraobserver reliability, 10 CT scans were evaluated twice in random order. In this case, the first measurement served as the measurement for future data analysis, whereas the second one served for reliability calculation only.

Fig. 1. Technique for measuring changes in the bone of the skull base at the middle fossa. (A) Computed tomography (CT), coronal reconstruction, left ear. The arrow shows the vertical distance measured from the scutum to the floor of the skull base. (B) CT, coronal reconstruction, left ear. The white arrow depicts the vertical distance measured from the lateral most part of the lateral semicircular canal to the floor of the skull base. The black arrow depicts the vertical distance measured from the lateral most part of the lateral semicircular canal to the floor of the skull base.
Statistical Analysis

Categorical variables were described as number and percentage, and continuous variables as median and interquartile range (IQR). The interclass correlation coefficient was used to evaluate the intraobserver agreement. Differences between the first and second measurements were performed using a Wilcoxon test. The Spearman correlation coefficient was used to evaluate the association between the continuous variables. All the statistical analyses were two-tailed. A P value < .05 was considered statistically significant. SPSS (IBM SPSS Statistics for Windows, version 22.0; IBM, Armonk, NY) was used for all the statistical analyses.

RESULTS

Twenty-three medical records of patients with IIH were enrolled to the study, out of which, three medical records were excluded due to insufficient data or low-quality CT scans, leaving 20 paired scans for analysis. There were 16 (80%) females and four (20%) males. The median (IQR) age was 34 years (28–43 years), and the median (IQR) age at diagnosis was 21 years (17–27 years). The median (IQR) BMI was 32 kg/m² (29–36 kg/m²). The reason for the first CT was to exclude intracranial space-occupying lesions before lumbar puncture (LP) in all cases. The indication for a second CT in the study group was uncontrolled exacerbation, manifested as headache, before repeated LP (16 cases), sinusitis (two cases), suspected pharyngeal foreign body, and moderate head trauma (one case each). The median (IQR) time interval between the first and second CT scans was 58 months (48–104 months).

All IIH patients were treated with acetazolamide. Selected patients with BMI > 30 kg/m² were treated with a supervised diet. One patient underwent a bariatric surgery for weight reduction.

TABLE I. Intraobserver Variability.

<table>
<thead>
<tr>
<th>Locus</th>
<th>Side</th>
<th>ICC</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior semicircular</td>
<td>R</td>
<td>0.995</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.995</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lateral semicircular</td>
<td>R</td>
<td>0.997</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.999</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Scutum</td>
<td>R</td>
<td>0.99</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.996</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Squama</td>
<td>R</td>
<td>0.858</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.97</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

 ICC = interclass correlation coefficient; L = center; R = right.

TABLE II. Median Vertical Distance From Middle Fossa Dura to the Given Anatomical Structures (Centimeters).

<table>
<thead>
<tr>
<th>Locus</th>
<th>Side</th>
<th>First CT scan</th>
<th>Second CT scan</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior semicircular</td>
<td>R</td>
<td>0.95</td>
<td>0.95</td>
<td>0</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.95</td>
<td>0.9</td>
<td>0</td>
<td>.075</td>
</tr>
<tr>
<td>Lateral semicircular</td>
<td>R</td>
<td>5.15</td>
<td>4.8</td>
<td>−0.35</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>5.35</td>
<td>4.95</td>
<td>−0.25</td>
<td>.003</td>
</tr>
<tr>
<td>Scutum</td>
<td>R</td>
<td>7.35</td>
<td>7.1</td>
<td>−0.5</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>7.4</td>
<td>6.9</td>
<td>−0.3</td>
<td>.001</td>
</tr>
<tr>
<td>Squama</td>
<td>R</td>
<td>1.1</td>
<td>1.05</td>
<td>0</td>
<td>.052</td>
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<tr>
<td></td>
<td>L</td>
<td>1.2</td>
<td>1.05</td>
<td>0</td>
<td>.508</td>
</tr>
</tbody>
</table>

 CT = computed tomography; L = center; R = right.

![Fig. 2](image-url) The change in measured distances between computed tomography (CT) scans. Each box represents one measurement. The empty space stands for no tegmen thickness dynamics. Some patients showed tegmen or squamal thickening, representing a measurement inaccuracy. The solid lines delineate the error range of the measurements. Gray bar = right temporal bone, dotted bar = left temporal bone.
The control group was composed of seven age- and
gender-matched individuals. The indication for CT scans
was paranasal sinus disease (six), blunt trauma (four),
benign tumor of the head and neck (three), and epistaxis
(one). The time interval between CT scans was not signi-
ficantly different from the IIH group ($P > .05$). The median
BMI was $22 \text{ kg/m}^2$ and was found to be significantly lower
than the IIH group ($P < .001$). The intraobserver variability
for all the loci used for measurement was 0.858 or higher
($P < .001$), representing excellent reliability (Table I). Based
on these data, the tegmen and squamal thickness was mea-
ured for the entire cohort.

The median vertical distance from each of the loci
listed to the floor of the middle fossa and minimal squama
thickness per CT scan is found in Table II, in addition to
the distance change ($\Delta$) and degree of statistical signi-
ficance. In the IIH group, from the first to the second CT
scan, a significant attenuation of this distance, superior to
the lateral SSC and the scutum (loci 2 and 3), was found: a
median attenuation of 0.35 mm and 0.25 mm over the right

<table>
<thead>
<tr>
<th>Subject</th>
<th>Superior Semicircular Canal</th>
<th>Lateral Semicircular Canal</th>
<th>Scutum</th>
<th>Squama</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>1</td>
<td>$-0.02$</td>
<td>$0.01$</td>
<td>$-0.01$</td>
<td>$0.01$</td>
</tr>
<tr>
<td>2</td>
<td>$0$</td>
<td>$0.01$</td>
<td>$-0.02$</td>
<td>$0$</td>
</tr>
<tr>
<td>3</td>
<td>$0.02$</td>
<td>$0$</td>
<td>$-0.01$</td>
<td>$0.01$</td>
</tr>
<tr>
<td>4</td>
<td>$0$</td>
<td>$0$</td>
<td>$0.01$</td>
<td>$0$</td>
</tr>
<tr>
<td>5</td>
<td>$0.01$</td>
<td>$-0.01$</td>
<td>$0$</td>
<td>$0$</td>
</tr>
<tr>
<td>6</td>
<td>$0$</td>
<td>$0.02$</td>
<td>$0.01$</td>
<td>$0$</td>
</tr>
<tr>
<td>7</td>
<td>$0.01$</td>
<td>$-0.02$</td>
<td>$0.01$</td>
<td>$0$</td>
</tr>
</tbody>
</table>

**TABLE III.**
Vertical Distance Change (Centimeters) From Middle Fossa Dura to the Given Anatomical Structures of Healthy Controls.

![Graph showing tegmen and squamal attenuation as a function of lumbar puncture (LP) opening pressure. The higher the opening pressure, the more significant tegmen attenuation was measured. CSF = cerebrospinal fluid; LSC = lateral semicircular canal.](image-url)
and left lateral SSC and of 0.5 mm and 0.3 mm over the right and left scutum, respectively. The tegmen above the superior SSC (locus 1) and minimal squama thickness attenuation did not reach statistical significance. The tegmen and squamal thickness distributed near normally. In the control group, no significant attenuation was measured in all loci during the time interval between the scans.

Some of the differences in measurements of skull base and squama were positive, up to 0.2 mm. Because thickening of the bone is implausible, this implies the thickening is likely to be a measurement-accuracy limitation or the measuring tool resolution (Fig. 2). The correlation between the change in tegmen thickness and the time interval between the first and second CT scans was not statistically significant. The association between opening pressure on initial LP and tegmen attenuation rate was examined (Fig. 3). The median LP opening pressure was 195 mm CSF, ranging from 15 mm to 400 mm CSF. Spearman $\rho$ correlation coefficient revealed significant positive correlations between the opening pressure and the degree of tegmen attenuation above the scutum and LSC seen on subsequent scans; $R^2$ was 0.2215 and 0.4547 for the right and left scutum, and 0.1747 and 0.0326 for the right and left LSC, respectively. The age at diagnosis of IIH and BMI were not significantly correlated to the degree of tegmen attenuation.

Tegmen attenuation in the control group was not observed, and the differences in tegmen thickness between the CT scans were within the error limit ($\pm 0.2$ mm; Table III). The differences between the attenuation at the scutum and LSC of the study and control groups was statistically significant ($P < .001$).

**DISCUSSION**

In patients with IIH, the tegmen directly above the LSC and scutum attenuated during the inter-CT scans period. Both loci border air spaces; hence, TDs in these locations may abnormally communicate the central nervous system with the respiratory tract, allowing for the potential spread of infections intracranially. Meningitis, encephalitis, and brain abscess are among the types of infection potentially encountered in these circumstances, and they may result in significant morbidity and even death. BMI is correlated with intracranial venous pressure. This is a probable mechanism for the known association between obesity and IIH, although other mechanisms, such as hormonal, have been suggested. Obesity is a known risk factor for TD.

The degree of tegmen attenuation was positively correlated with the opening pressure on LP, obtained as part of the initial workup of IIH. This supports the notion that TD is a progressive and acquired pathology associated with increased ICP. It is known that CSF pressure at diagnosis of IIH is often above 300 mm CSF. The first years from diagnosis are characterized by relatively poor ICP control. Later, treatment may better control ICP, reflected by the reduced rates of subsequent tegmen thickness attenuation.

To span the wide range of issue associated with IIH, patients require the attention of multiple medical and surgical specialties including, but not limited to, ophthalmology, neurology, otolaryngology, and neurosurgery. Treatment options for IIH include weight loss, carbonic anhydrase inhibitor to reduce CSF production, CSF diversion and shunting, and optic nerve fenestration.

The new finding that tegmen attenuation is progressive may open a window of opportunity for treatment in preventing the creation of CSF leaking TD. Patients are commonly diagnosed with IIH based on headaches or visual symptoms. In all patients with IIH, careful thought should be paid to the status of the middle and anterior skull base overlying the airspaces in the temporal bones and sinuses. A randomized trial has shown the efficacy of combining medical treatment with weight loss as compared to weight loss in controlling mild vision loss and an associated improvement in ICP. Recently published guidelines have supported the use of acetazolamide (or alternatively topiramate) for IIH. None of these studies have looked at TD or CSF leaks as an endpoint. However, it is reasonable to assume—although yet to be proven—that strategies succeeding in reducing ICP may lessen the risk for the eventual development of CSF leaks. Given the progressive nature of TD, patients should be strongly encouraged to lose weight. The decision to add medical treatment for IIH in the absence of ocular and visual pathologies is left to the physician and patient but is a reasonable choice.

No changes in the bone overlying the SSC were captured. The pathogenesis of SSC dehiscence has not been established. Kuo et al. have found no association between IIH and the presence of SSC dehiscence. The stability of the bone of the SSC in the current study could be due to limitations in the study and not necessarily true absolute stability of the otic capsule. Given the retrospective nature of the study, some of the scans were of less than optimal quality for acquisition of data regarding the thickness of the bone of the SSC. Demonstrating these changes requires repeated high-quality thin-slice CT scans that were not available. The observation that the tegmen of the ear attenuates progressively indirectly supports the theory that SSC dehiscence is acquired. That being said, the bone overlying the SSC is part of the otic capsule, a bone with unique metabolism that may respond differently from the rest of the tegmen to the pressure of IIH.

Treatment of IIH with acetazolamide lowers intracranial pressure. Because the assumption is that elevated pressure is the force driving the skull base attenuation, and all patients were treated with acetazolamide, it is logical to ask how attenuation of the skull base was recorded. First, acetazolamide reduces, but usually does not normalize intracranial pressure or the effect of IIH (e.g., changes seen by magnetic resonance imaging). Second, most of the cohort’s patients were not treated to the full extent of the time of the observation and notably with significantly lower doses than those used in some recent publications. Smith and Friedman reported the safety and tolerability of the use of doses of up to 4 g daily. None of the study patients received these high doses. Patients commonly receive doses of 1 g/d and rarely more than 2 g/d. It is possible that some of these patients were undertreated, or that more emphasis should be given to other treatment.
modalities; weight loss could be a pivotal one. The study cohort reflects older treatment protocols.

The retrospective nature of the study makes it difficult to correlate radiographic findings with clinical correlates such as symptoms and signs commonly associated with TD. The quality of the scans studied is less than ideal. In the future, a prospective effort should include high-resolution CT scans possibly showing the true effect on the otic capsule overlying the SSC.

The first limitation derives from the small cohort size. The reason for this small number (n = 20) of patients enrolled is derived from the need to find patients who had two CT scans of sufficient quality imaging with time elapsing between the pair. Obtaining CT scans for the sole purpose of research is unethical in most circumstances, making this cohort of hard to come by. The 20 patients included, were allocated from approximately 300 patients with IIH cared for at the medical center. Additionally, the necessity of high-resolution head CT scans dictates a certain selection bias of the control. Healthy volunteers would not have two consecutive CT scans. The control group is unlikely to overlap with the study group. Most CT scans of neurosurgical patients are excluded due to presence of intracranial space-occupying lesion. The possibility that a control patient had undiagnosed IIH is possible, but the incidence of the disease in the healthy population is low (0.2–2.85 in 100,000 in nonobese male and female, respectively, resulting in total prevalence of 10.9:100,000).° One of the known risk factors for IIH is high BMI. Because the median control group BMI was 22 kg/m² and was found to be significantly lower than the IIH group (P < .001), and none of the control group was obese, the mentioned prevalence is valid to our control group. Two technical study limitations are worth mentioning. The first is the resolution limit of each CT scan, which in combination of voxel averaging can result in inaccurate tegmen thickness measurements. This issue was supported by our measurements; a few controls and IIH patients showed tegmen pseudothickening up to 0.02 cm. Based on this observation, we set our measurement tool limits to be 0.02 cm and took into account only measurements above this range. The second limitation is the difficulty to ensure identical loci and plain of measurements from one CT to the other in the same patient. We overcame this issue by setting rigid reconstruction methods (see Materials and Methods). An effort was made to present the data in their raw form to allow the reader to fully understand the limitation of the study technique. This is reflected in some of the measurements falsely depicting a thickening skull base. We believe that given the clear results and the biological and radiographic stability of the measurement points (i.e., the edge of the LSC) the results reflect a true trend in attenuation of the skull base, even if the study may not reflect the true size of the change.

The correlation between the change in tegmen thickness and the time interval between the first and second CT scans was not statistically significant. One possible explanation for this finding is that only two CT scans were analyzed per patient. The baseline scans were most commonly obtained in the initial diagnostic workup for IIH. Hence, it was impossible to calculate the annual tegmen attenuation rate because subjects with a short time interval between the scans suffered similar attenuation than longer time interval from first to second CT scan.

CONCLUSION

Tegmen attenuation may be progressive in patients with IIH. The degree of attenuation is correlated with the opening pressure on LP. Breaches in the tegmen of the temporal bone and signs of CSF leak should be looked for during the initial workup and follow-up of patients with IIH. Because the attenuation is progressive, further research is needed to verify its potential mitigation by treatment lowering IIH.

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