SPHENOID SINUS EXPANSION: A RADIOGRAPHIC SIGN OF INTRACRANIAL HYPOTENSION AND THE SUNKEN EYES, SAGGING BRAIN SYNDROME (AN AMERICAN OPHTHALMOLOGICAL SOCIETY THESIS)

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ABSTRACT

Purpose: To test the hypothesis that in patient with sunken eyes, sagging brain syndrome, bone remodeling is not limited to the orbits. Volumetric analysis of the sphenoid sinus is performed in this study.

Methods: In this university-based retrospective case-control study, the dimensions of the sphenoid sinus were measured in four patients (2 males, 2 females; mean age 26.3 years, range 16-38 years) out of five individuals identified with sunken eyes, sagging brain syndrome. Three measurements were taken: the distance between the orbital apices, the posterior extension of the sphenoid sinus posterior to the orbital apices, and the maximal horizontal width. The mean of each was determined and compared to that of the control group (5 males, 5 females; mean age 35.6 years, range 23-45 years).

Results: Posterior extension and width of the sphenoid sinus were markedly larger in the enophthalmic patients than in the control group: posterior extension (26.3±4.1 mm vs 13.4±6.3 mm, *P*=.0015, Student's *t* test), width (39.2±8.7 mm vs 25.1±6.9 mm, *P*=.0035, Student's *t* test). Mean distance between the orbital apices was slightly greater (36.3±1.7 mm vs 34.1±2.1 mm, *P*=.047, Student's *t* test).

Conclusions: Skull remodeling occurring in association with intracranial hypotension after ventriculoperitoneal shunting is not limited to the orbits. In this study we have demonstrated expansion of the sphenoid sinus. This finding adds to our knowledge and understanding of the scope of the sunken eyes, sagging brain syndrome and elucidates a clinically useful radiographic sign.

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INTRODUCTION

Dynamic changes in bone are well recognized. Osteoporosis is a very familiar disease.[1,2] Age-related changes independent of osteoporosis also occur.[3,4] Neoplasm can alter bone via a number of mechanisms.[5] In the orbit, bone invasion or erosion may be indicative of malignancy. Remodeling is often the result of pressure from an expanding benign lesion. Change in the size and shape of bone is also seen in a number of unique circumstances. With disuse or zero gravity, long bones will resorb. This is thought to be a reaction to the lack of normal mechanical loading.[6] During prolonged bed rest, the skull will increase in mass.[7]

The effects of intracranial hypotension on surrounding bone are less obvious and until recently were largely unrecognized.[8,9] Although the precise mechanism was not elucidated, in 1996 Meyer and colleagues[8] described three patients with congenital hydrocephalus who developed bilateral enophthalmos following ventriculoperitoneal shunting (VPS). In a more recent report, four adult patients were described with acquired enophthalmos following VPS.[9] In two of the four patients, with adequate imaging using volumetric analysis, the mechanism was demonstrated to largely be orbital bone remodeling with expansion of orbital volume. In two of the four patients, intracranial pressure (ICP) was measured. In both it was found to be abnormally low. The term *sunken eyes, sagging brain syndrome* was coined to describe the development of enophthalmos secondary to intracranial hypotension following VPS.[9]

Bone is maintained in part by continual absorption by osteoclasts and new bone creation by osteoblasts. This balance is mediated by mechanical stress on the bone. Alteration in tension results in modification in the size and shape of the bone. With prolonged bed rest, net bone formation is thought to result from increased ICP associated with the supine position.[7] In previous work, it was proposed that the opposite process occurs in our enophthalmic patients: "With chronic intracranial hypotension, the pressure gradient across the bone of the orbital roof is altered from decreased force from the intracranial side. This effect would theoretically cause not only a net resorption of bone because of decreased stress but an effective intracranially-directed force across the roof causing orbital expansion."[9] If the orbit responds to reduced ICP, it seems logical that other if not all bones in contact with cerebrospinal fluid (CSF) would react similarly.

We hypothesize that intracranial hypotension–related skull remodeling (IHSR) is not limited to the orbits. Rather, changes are seen in additional bones that are in contact with the CSF. To test this hypothesis, structural changes of the sphenoid sinus are assessed. The sphenoid sinus is selected for analysis for two reasons. First, orbital scans, which include images of the sphenoid sinus, are available in the majority of patients with sunken eyes, sagging brain syndrome. Imaging of the remainder of the skull is not consistently available. Second, compared to other structures, such as the ethmoid sinuses, boundaries are easily defined. Assessment of the sphenoid sinus increases our understanding of the full scope of IHSR. Sphenoid expansion is also a radiographic sign of chronic intracranial hypotension, which will potentially prove useful as a diagnostic tool and for patient monitoring.

METHODS

This research adhered to the tenets of the Declaration of Helsinki, and Institutional Review Board (IRB) approval from the University of California San Francisco (UCSF) was obtained for this university-based retrospective case control study. Five patients were

From Wilmer Eye Institute, Johns Hopkins School of Medicine, Baltimore, Maryland.

identified within the neuro-ophthalmologic service at UCSF with acquired and progressive enophthalmos following VPS. We reviewed clinical findings of all patients. Four of these patients had imaging performed after the development of enophthalmos and are included in the volumetric portion of this study. One had no imaging after the development of enophthalmos and is therefore not included in the volumetric assessment.

Of the five patients included in this study, four were included in previous work assessing orbital volume expansion seen with chronic intracranial hypotension.[9] Two of those were the focus of the volumetric analysis of the orbits. In that study, no patient had volumetric assessment of any other structure, including the sphenoid sinus.

Sphenoid sinus measurements were made using imbedded digital calipers common to most imaging viewing software. For all four patients (2 males, 2 females; mean age 26.3 years, range 16-38 years) three measurements were taken. One computed tomography (CT) image from each subject was used for all measurements. The axial image that passed most centrally through the orbital apices was selected. The distance between the orbital apices was measured. Measurements were taken from the most posterior point of the orbital apex from the center of the optic nerve as it entered the optic canal. Posterior extension of the sphenoid sinus was measured from the midpoint of the line created in measuring the distance between the orbital apices. The distance between this point and the most posterior aspect of the sphenoid sinus was measured. The horizontal sphenoid width was determined by the distance between the lateral-most extent of the sinus (left and right). Figure 1 illustrates the fashion in which measurements were obtained in a control patient.

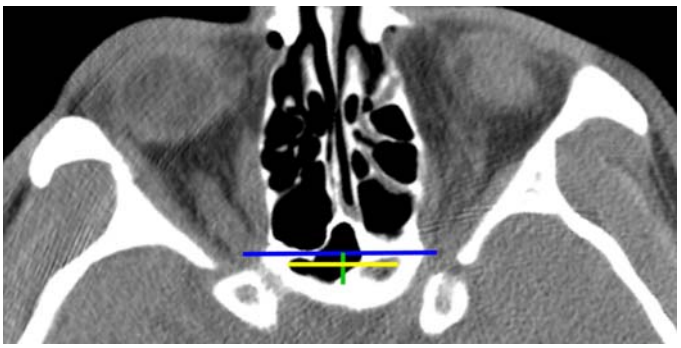

FIGURE 1

Axial computed tomography measurements of sphenoid sinus expansion with chronic intracranial hypotension. Distances between orbital apices (blue line), posterior extension of the sphenoid sinus (green line), and width of the sphenoid sinus (yellow line) are marked.

A control group (5 males, 5 females; mean age 35.6 years, range 23-45 years) without orbital pathology was used for comparison.[9] The control group was selected using a reverse chronological search through the radiology database. The mean of each measurement was determined for the enophthalmic and control groups and compared using the Student *t* test.

RESULTS

Tables 1 and 2 detail key features of the enophthalmic patients used in the volumetric analysis and the control group. Brief summaries of the histories of patients 1 through 5 are provided below.

CASE HISTORIES

Patient 1

A 38-year-old woman presented with bilateral enophthalmos 15 years following VPS after a ruptured aneurysm. On ophthalmic examination, best-corrected visual acuity (BCVA) was 20/50 OD and 20/200 OS. Pupils were symmetric and reactive with no afferent pupillary defect. Confrontation visual fields were normal. Exophthalmometry measurements were 6 mm OU. Funduscopic evaluation was normal with healthy-appearing optic nerves. Extraocular motility was decreased in all directions OU.

Enophthalmos was to the degree that the patient's eyelids were losing contact with her globes with severe corneal drying and scarring (Figure 2). A recent orbital CT image, obtained 15 years after VPS, was available for volumetric analysis. Orbital and sinus volumes were significantly increased (Figure 3, Table 1). Additional clinical details are described elsewhere.[9]

Patient 2

A 25-year-old man presented with progressive enophthalmos due to orbital volume expansion 4 years following VPS for elevated ICP related to a traumatic intracranial bleed. On ophthalmic examination, BCVA was 20/70 OD and 20/50 OS. Exophthalmometry measurements were 9 mm OU. Enophthalmos was to the degree that his eyes were losing apposition to the globes with severe corneal drying. Vertical ductions were reduced OU. Horizontal ductions were normal. On funduscopic evaluation, mild optic disk pallor was observed in both eyes.

Imaging was available from the time of injury, prior to the development of enophthalmos, and at the time of presentation with enophthalmos. The sphenoid sinus was enlarged (Figure 4, Table 1). ICP was measured at 20 mm H_2O (normal, 60-200 mm H_2O), confirming low CSF pressure. The existing shunt was replaced with a Medtronic Delta Valve Performance Level 1.5 VPS (Medtronic, Minneapolis, Minnesota). This pressure-controlled valve is calibrated to maintain the ICP between 70 and 105 mm H_2O. Mild improvement in the enophthalmos was seen within 24 hours. Additional clinical details are described elsewhere.[9]

Patient 3

A 16-year-old boy presented with severe enophthalmos 5 years following placement of a VPS for elevated ICP secondary to a ruptured aneurysm. BCVA was 20/25 OD and 20/20 OS. An incomplete left homonymous hemianopia was found on confrontational visual field testing. Exophthalmometry measurements were 10 mm and 9 mm in the right and left eyes, respectively. Extraocular motility was full, and the patient was orthophoric in all fields of gaze. His eyelids had partially lost contact with his globes with associated ocular surface disease.

Computed tomography imaging was available from the time of shunting through 5 years later. Progressive enophthalmos and sphenoid sinus expansion were easily appreciated (Figure 5, Table 1). This patient was referred from out of state and returned home for shunt replacement. Serial ICP measurements were never greater than 0 mm H_2O, while monitored with a ventricular drain over the course of 3 days. Although he was not examined after placement of a shunt with a pressure-controlled valve, his father called to report improvement in his enophthalmos and mental status following ICP correction. Additional clinical details are described elsewhere.[9]

TABLE 1. DEMOGRAPHICS AND SINUS MEASUREMENTS IN ENOPHTHALMIC PATIENTS WITH INTRACRANIAL HYPOTENSION SKULL REMODELING AND CONTROL GROUP

PATIENT NUMBER	AGE AT TIME OF IMAGING (years)	GENDER	YEARS OF VPS PRIOR TO DIAGNOSIS	EXOPH (mm)		PE (mm)	SW (mm)	DA (mm)
				OD	OS			
Enophthalmic patients								
1	38	F	16	6	6	27	44	37
2	25	M	4	9	9	21	33	36
3	16	M	4	10	9	26	49	38
4*	19	M	1	12	12	NA	NA	NA
5	26	F	1	12	13	31	31	34
Control subjects								
1	35	M	NA	NA	NA	6	30	34
2	38	F	NA	NA	NA	13	27	34
3	32	M	NA	NA	NA	9	15	32
4	36	F	NA	NA	NA	30	27	34
5	32	M	NA	NA	NA	14	17	36
6	42	F	NA	NA	NA	12	21	32
7	31	M	NA	NA	NA	13	38	37
8	23	F	NA	NA	NA	14	28	34
9	42	F	NA	NA	NA	12	28	37
10	45	M	NA	NA	NA	11	20	31

DA, distance between the orbital apices; exoph, exophthalmometry measurements; F, female; M, male; NA, not applicable; PE, posterior extension; SW, sinus width; VPS, ventriculoperitoneal shunt.
*Patient 4 was not included in the volumetric analysis.

TABLE 2. COMPARISON OF SPHENOID SINUS MEASUREMENTS IN ENOPHTHALMIC PATIENTS WITH INTRACRANIAL HYPOTENSION SKULL REMODELING AND CONTROL GROUP

MEASUREMENT	ENOPHTHALMIC GROUP	CONTROL GROUP	*P* VALUE
Posterior extension	26.3±4.1 mm	13.4±6.3 mm	.0015
Sinus width	39.2±8.7 mm	25.1±6.9 mm	.0035
Distance between apices	36.3±1.7 mm	34.1±2.1 mm	.047

Patient 4

A 19-year-old man presented following a motor vehicle accident 1 year prior to evaluation. He suffered traumatic brain injury, and several skull fractures were appreciated on CT. Multiple ethmoid air cells were opacified bilaterally, suggesting medial wall fractures; however, no bone displacement was seen. Several weeks later a VPS was placed for elevated ICP. His BCVA was difficult to assess

because of his inability to communicate, but he did foveate well on targets. His pupils were minimally reactive. Visual fields were full to confrontation. In primary gaze, he was orthotropic by corneal light reflex, and his eye movements were full except for poor supraduction bilaterally. He had nystagmus and with attempted supraduction he had some beats of convergence retraction, suggestive of a dorsal midbrain syndrome. Exophthalmometry measurements were 12 mm bilaterally. He had mild ocular surface disease related to loss of apposition between the globe and eyelids medially and to a lesser degree laterally. Fundus examination revealed a normal optic nerve in each eye.

Adequate imaging was not available following VPS, and the patient was not included in the volumetric analysis. Additional clinical details are described elsewhere.[9]

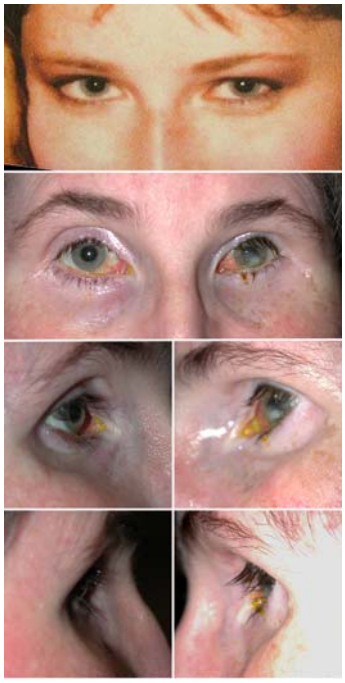

FIGURE 2

Patient 1. Enophthalmos with chronic intracranial hypotension. Top, photo taken prior shunt placement. Subsequent photos, taken 15 years after shunt placement, show enophthalmos to the degree that the eyelids are losing contact with the ocular surface.

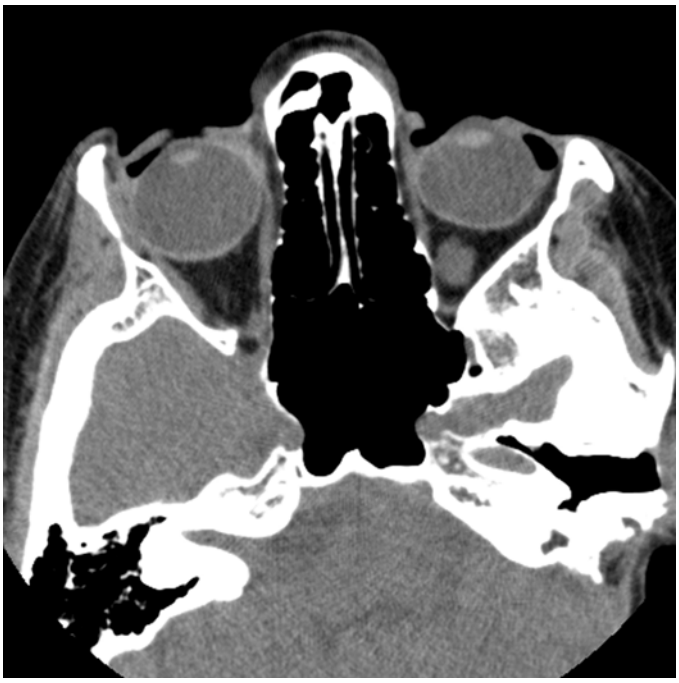

FIGURE 3

Patient 1. Axial computed tomography demonstrating sphenoid sinus expansion with chronic intracranial hypotension. Note splaying of the orbital apices.

Patient 5

Consult was requested on a 26-year-old woman for assessment of papilledema. Four years previously she had undergone transcranial resection of a pituitary tumor. Two years postoperatively she developed elevated ICP, ultimately resulting in placement of a VPS. The reason for elevated ICP was not clear, and despite a normal weight, the patient was assigned the diagnosis of idiopathic intracranial hypertension. After battling headaches due to "over-drainage" and intracranial hypotension, her shunt was removed. It had been in place for 1 year. In the records provided, all that was documented was that the ICP was abnormally low; a precise value was not included. One year thereafter she was again admitted for evaluation of recurrent headaches, which is when our service became involved. Medical history was also notable for hypertension, reflux disease, and depression. She had no visual complaint.

On evaluation, she was moderately enophthalmic, which was not present in family photos taken prior to shunting (Figure 6). BCVA measured 20/20 OU. Confrontation visual field testing was normal. Examination of the anterior segment was normal. The eyelids were in full contact with the globes, and there was no ocular surface disease. On funduscopic evaluation she was found to have trace disk edema to a greater degree on the left than the right. Pupils reacted briskly to light with no relative pupillary defect. She had a mild comitant exophoria with full extraocular motility. Exophthalmometry measurements were 12 mm and 13 mm in the right and left eyes, respectively. Neurologic evaluation was unremarkable with the exception of slight dysmetria on finger-to-nose and heal-to-shin testing to a greater degree on the left than the right. Computed tomography demonstrated bilateral enophthalmos with large sphenoid, ethmoid, and frontal sinuses (Figure 7). The mastoid air cells were also prominent.

Intracranial pressure was measured to be slightly elevated at 240 mmH_2O. Her headaches resolved after placement of a lumboperitoneal drain. She was discharged to home with continued monitoring for recurrent intracranial hypotension.

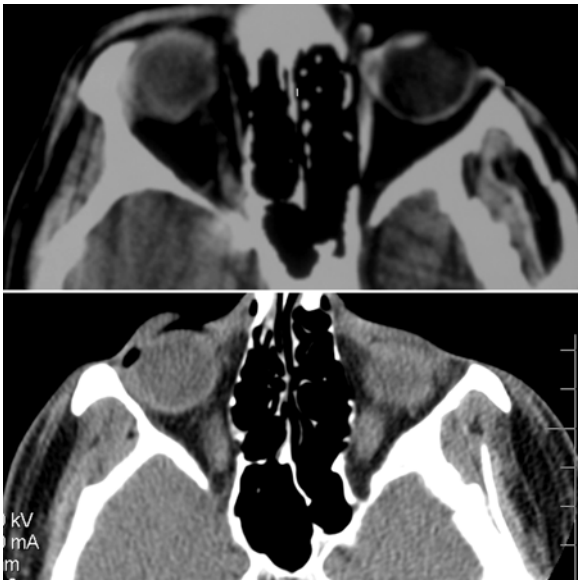

FIGURE 4

Patient 2. Sphenoid sinus expansion with chronic intracranial hypotension. Axial computed tomography at the time of ventriculoperitoneal shunt placement prior to (top) and after (bottom) the development of enophthalmos. The sphenoid sinus is seen to enlarge.

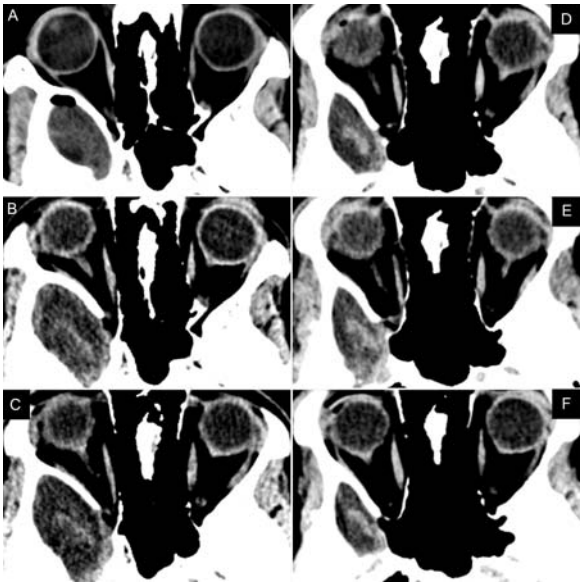

FIGURE 5

Patient 3. Sphenoid sinus expansion with chronic intracranial hypotension. Composite of axial computed tomography demonstrates the expansion of the sphenoid sinus over time: top left, shortly after shunting; middle left, 6 months after shunting; bottom left, 1.5 years after shunting; top right, 2.5 years after shunting; middle right, 3 years after shunting; bottom right, 4 years after shunting. Although lateral extension is most prominent, posterior enlargement and separation of the orbital apices can both be appreciated. Progressive enophthalmos can also be appreciated as the globes move further posterior relative the lateral orbital walls.

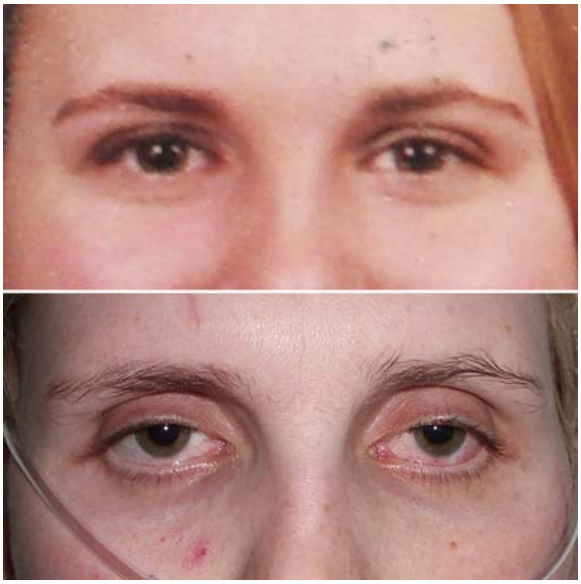

FIGURE 6

Patient 5. Enophthalmos with chronic intracranial hypotension. External photographs cropped from a family photo taken prior to shunting (top) and after the development of intracranial hypotension–related skull remodeling and enopththalmos (bottom).

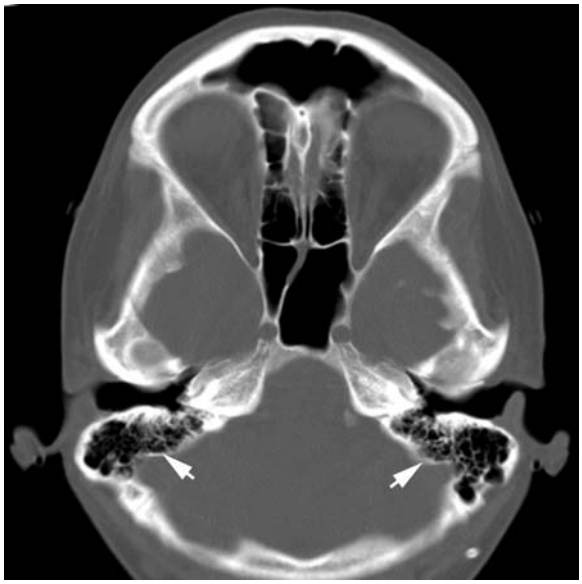

FIGURE 7

Patient 5. Sphenoid sinus expansion with chronic intracranial hypotension. Axial computed tomography demonstrates a large sphenoid sinus. Note the generous ethmoid air cells and frontal sinus. The mastoid air cells are also prominent (arrows).

VOLUMETRIC ANALYSIS

Table 2 summarizes the sphenoid sinus measurements. Posterior extension and width of the sphenoid sinus were markedly larger in the enophthalmic patients than in the control group: posterior extension (26.3±4.1 mm vs 13.4±6.3 mm, *P*=.0015, Student's *t* test), width (39.2± 8.7 mm vs 25.1±6.9 mm, *P*=.0035, Student's *t* test). Mean distance between the orbital apices was slightly greater (36.3±1.7 mm vs 34.1±2.1 mm, Student's *t* test), which was borderline significant (*P*=.047, Student's *t* test). In two patients, imaging at the time of shunting was also available, and in both, the sphenoid sinus dimensions were appreciably increased on more recent imaging (Figures 4 and 5) consistent with post-VPS sphenoid sinus enlargement.

DISCUSSION

In this study we have assessed the hypothesis that bony changes seen with prolonged intracranial hypotension are not limited to the orbits and thus expand the concept to the more global condition of IHSR. Thus far we have identified five patients with sunken eyes, sagging brain syndrome. In four of these patients with adequate imaging, we have demonstrated enlargement of the sphenoid sinus. The mean dimensions of the sphenoid sinuses of enophthalmic patients were greater than those of control patients. Possibly equal or more conclusive evidence is that the sphenoid sinus is seen to have increased in size in the two individuals with imaging after the development of enophthalmos, compared to imaging obtained at the time of shunting.

Our recognition of the full spectrum of IHSR is likely just beginning. In this study, we have confirmed that sphenoid sinus enlargement is a component of IHSR. Thus far patients have been identified on the basis of enophthalmos. This is reflective of our practices focusing primarily on ophthalmic disease. Sunken eyes, sagging brain syndrome may represent only a subset of patients with IHSR. Some IHSR patients may not have enophthalmos or could develop enophthalmos late in the disease. For this reason, we propose that the label *intracranial hypotension–related skull remodeling* be used more generically and the term *sunken eyes, sagging brain syndrome* be reserved for those that develop clinically significant enophthalmos.

Radiographic changes in the sphenoid sinus may prove to be a means of diagnosing patients with IHSR. Ideally, we would like to be able to identify patients prior to the development of enophthalmos. In advanced disease, marked enlargement of the sphenoid sinus is easily appreciated (Figures 3 and 5). However, markedly abnormal size may not be encountered before clinically relevant enophthalmos has appeared. Patient 5 had the least advanced disease in this series. In this case, the sphenoid sinus was large, but not more than that encountered in the normal population. The width of her sphenoid sinus measured 31 mm, within one standard deviation of the mean of the control group (25.1 ± 6.9 mm). Subtle findings such as this are unlikely to raise concern. A more sensitive tool than absolute size is a change in the size of the sphenoid sinus. In patients with VPS, routine documentation of sphenoid sinus dimensions would likely identify patients before the development of clinically significant enophthalmos. A larger group of patients with VPS will need to be observed to precisely determine how often and at what stage of disease changes in the sphenoid are encountered. Although the degree of bony changes presumably relates to the magnitude and duration of hypotension, with our current sample, this question cannot be answered.

We have used the terms *bubbling* or *bubble sign* to describe lateral extension of the sphenoid sinus (Figure 8). Normally the sphenoid sinus does not extend much further laterally than the orbital apices. With bubbling, the sphenoid sinus is seen to extend far lateral to the posterior orbit. Bubbling is most visible on axial CT inferior to the orbital apices (Figure 8). The bubble sign is not seen in patients 2 and 4. In patient 4, the disease was caught in its early stages, and if allowed to progress, bubbling might have formed. Patient 2 is interesting because despite having advanced enophthalmos, the sphenoid sinus did not appear overtly abnormal (Figure 4). This patient illustrates the need to look for change, as opposed to the absolute size of the sphenoid sinus. The bubble sign should be considered indicative of advanced IHSR. It may not be useful in identifying patients early in their disease course.

Another radiographic finding worth noting is aeration of the anterior clinoids (Figure 9). In two patients, coronal images through the clinoids were available. In patient 1, the enlarged sphenoid sinus is seen to extend into the anterior clinoids (Figure 9, top). Early aeration of the clinoids is seen in patient 2. Although actual air is not seen, the clinoids have started to enlarge with presumed mucosa-lined cavities emerging (Figure 9, bottom). Acquired aeration of the clinoids is also a marker of advanced disease and will likely prove useful only in identifying patients as such.

Enophthalmos is a generic term that describes relative posterior displacement of the eye. It occurs from one of two basic mechanisms: the orbital bony cavity increases or the soft tissue volume decreases.[10-12] Loss of soft tissue is not common but can be seen in a number of conditions, including human immunodeficiency virus (HIV) and age-related orbital lipoatrophy,[13-16] metastatic breast cancer,[17-26] and linear scleroderma,[27-29] among other even less common entities.[30,31] An increase in bony volume is seen most commonly with orbital fractures.[32,33]

The condition that best parallels sunken eyes, sagging brain syndrome is the silent sinus syndrome. In silent sinus syndrome, chronic maxillary sinusitis results in inferior displacement of the sinus roof, which also serves as the orbital floor. Consequent orbital volume expansion results in enophthalmos.[34,35] Previous reports on silent sinus syndrome identified an altered pressure gradient across the bone of the orbital floor from a decrease in the intramaxillary sinus pressure,[36] just as described for the orbital roof from a decrease in ICP in our patients. In addition, demineralization of the orbital floor consistent with bony remodeling has been identified in silent sinus syndrome.[37] This is consistent with our proposed mechanism for bony changes resulting from IHSR. However, despite these similarities, it should be noted that, at least in part, the pathophysiology of IHSF differs from that of silent sinus syndrome. In silent sinus syndrome, the maxillary sinus may actually have negative pressure with loss of aeration and atelectasis. Although negative pressure was measured in one of our patients, this is likely not a uniform finding in IHSR. Also, we are unaware of an intracranial parallel to atelectasis of a sinus.

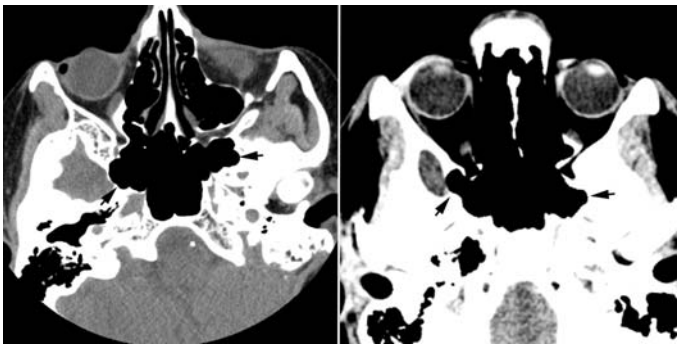

FIGURE 8

Axial computed tomography inferior to the orbital apices. Sphenoid bubble sign is seen, along with expansion of the sphenoid sinus with chronic intracranial hypotension, in patient 1 (left) and patient 3 (right). The sphenoid sinus is seen to extend far lateral to the posterior orbit (arrows). Bubbling did not occur in patients 2 and 5. This sphenoid bubbling is indicative of advanced intracranial hypotension–related skull remodeling.

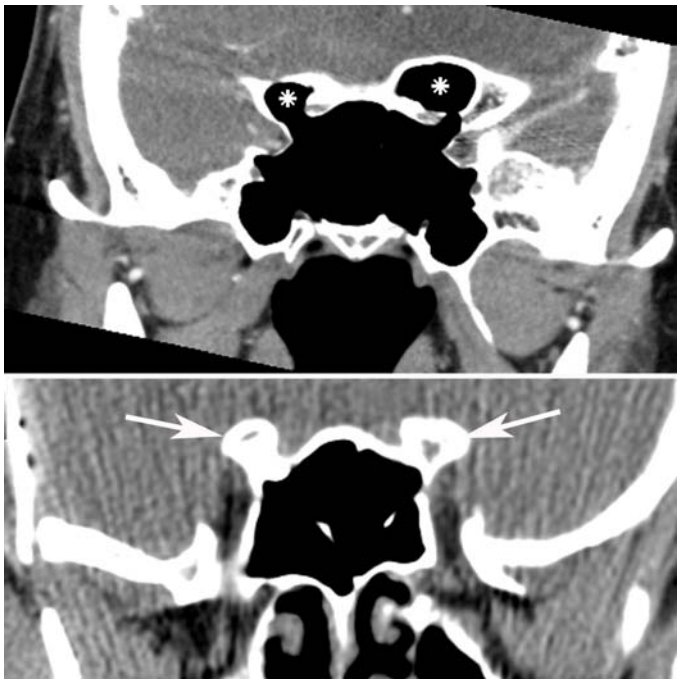

FIGURE 9

Aeration of the anterior clinoids, seen along with expansion of the sphenoid sinus with chronic intracranial hypotension, in patient 1 (top) and patient 2 (bottom). In patient 1, the enlarged sphenoid sinus has extended into the anterior clinoids (*). Early aeration of the clinoids is seen in patient 2. Actual air is not seen, but the clinoids have started to enlarge with likely mucosa-filled cavities emerging.

Pneumosinus dilatans is a somewhat uncommonly used term that describes enlargement of the paranasal air sinuses. Sinus expansion has been described to occur without an identifiable cause, or in association with other abnormalities, including fibro-osseous disease and meningiomas.[38] Presenting symptoms have included headache and ocular misalignment. Decreased visual acuity and field loss have been attributed to presumed optic nerve compression by an enlarged sphenoid sinus.[39] In contrast to IHSR, many patients have been described as presenting with proptosis, whereas in others no mention of globe position was provided.[38-40] Of particular interest, in 1992 Schayck and Niedeggen[40] described two patients with cerebral hemiatrophy who developed enlargement of the sphenoid, ethmoid, and frontal sinuses. They termed this *pneumosinus dilatans*, but noted that sinus enlargement occurred after CSF shunting. Although globe position was not documented, it seems likely that these cases represented IHSR. Perhaps other cases labeled as pneumosinus dilatans also occurred secondary to unrecognized intracranial hypotension.

The clinical consequences of IHSR with enophthalmos are potentially devastating. The cosmetic impact alone is concerning. The effect of even mild enophthalmos can be seen in patient 5 of this series (Figure 6). In advanced disease, enophthalmos develops to a degree that is truly disfiguring (Figure 2). Beyond appearance, several additional noteworthy findings were seen in our group. The most common finding for which our subjects were referred was ocular surface disease, related to loss of contact between the eyelids and the cornea. Other abnormalities seen in our cohort include abnormal ocular motility and optic atrophy.

Three of our patients had significant alterations in ocular motility. Abnormal vertical ductions can be explained by the mechanical effect of the superior bowing of the orbital roof and displacement of the superior recti muscles. This is analogous to the alteration in vertical ductions seen in patients with the inferior rectus muscle displacement through a comminuted orbital floor fracture. Malposition of the globe or muscles may adversely affect the vector with which the recti muscles relate to the globe. Abnormal horizontal ductions are more difficult to explain and may relate to shortening of the muscles with loss of optimal sarcomere filament overlap. Other possible mechanisms include neurologic from cranial nerve or brainstem disease. There is no documentation of the eye movements in any of our patients prior to the development of enophthalmos. The possibility should be considered that motility abnormalities were present prior to the onset of enophthalmos and did not developed as part of this syndrome.

Finally, in one of our patients (patient 2), bilateral optic nerve atrophy was noted. One patient in the series of Meyer and

colleagues[8] was noted to have progressive vision loss and optic atrophy, to the point of no light perception in one eye. One possible explanation is that with sphenoid sinus enlargement and splaying of the orbital apices, alterations of the bony optic canal adversely affect the optic nerves or their blood supply. Again, whether this is truly part of the sunken eyes, sagging brain syndrome or relates to associated neurologic disease remains to be determined.

When possible, initial management of sunken eyes, sagging brain syndrome should include correcting the intracranial hypotension.[9] This has been performed in two of our five patients. In both, an immediate improvement in enophthalmos was seen. This is presumably due to increased blood and CSF within the orbits. Elevation of CSF pressure would cause an increase in the pressure of the superior ophthalmic vein and, in turn, the veins of the orbits. Venous engorgement in part explains the minor improvement seen within 24 hours of ICP normalization. Increased ICP would also be transmitted to the CSF within the optic nerve sheath. Some expansion of the optic nerve sheath might also have an effect on globe position. More important, ICP normalization will likely halt disease progression. Whether resolution of the intracranial hypotension will result in correction of the bony expansion remains unknown. In a series of 23 patients with silent sinus syndrome, following re-establishing aeration of the sinus, 22 patients had partial or complete normalization of globe position.[41] Therefore, observation should be considered following normalization of ICP prior to proceeding with surgical augmentation.

When medically necessary or when improvement is not seen following normalization of ICP, surgical intervention may be considered. Volume augmentation has been reported. Both orbital floor and roof implants have been described.[6,42,43] Given that the abnormality lies primarily with the orbital roof, it is not surprising that better results have been reported with roof implants.[42,43] With floor implants, unwanted superior displacement of the globe occurred.[6] In case 1 of this series, the patient declined shunt revision as well as placement of an orbital implant. A tarsorrhaphy was performed with resolution of the patient's ocular exposure–related symptoms. Most patients would consider this procedure cosmetically inferior to shunt revision and orbital volume augmentation.

This study is limited by its small size. However, despite only four of five patients having imaging suitable for volumetric analysis, when compared to a control group the differences in the sphenoid sinus measurements were statistically significant. This attests to their consistency and magnitude. Also, the control group was selected from patients aged 18 through 45, which overlaps but is not identical to our study patients. Age-related changes in skull anatomy might contribute in part to differences seen between our study patients and the control group. However, our patients had a wide age range (16-38 years), making age-related changes unlikely to be a major contributor. In this and previous work, we demonstrated an alteration in the bones of the orbits and skull in patients with intracranial hypotension following VPS. We offer alterations in the pressure gradient across involved bones as a plausible explanation. Admittedly, other unrecognized mechanisms may factor in.

CONCLUSIONS

We have tested the hypothesis that bony remodeling is not limited to the orbits in patients with sunken eyes, sagging brain syndrome. We have demonstrated that enlargement of the sphenoid sinus is a component of IHSR and the sunken eyes, sagging brain syndrome. Following VPS, patients should be monitored for changes in the dimensions of the sphenoid sinus. Enlargement of the sphenoid sinus may be an early indicator of intracranial hypotension and allow for the identification of patients prior to the development of otherwise clinically apparent disease. Lateral extension or bubbling of the sphenoid sinus, the bubble sign, and aeration of the anterior clinoids should be considered radiographic markers of advanced disease.

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REFERENCES

1. Adams P, Davies GT, Sweetnam P. Osteoporosis and the effects of ageing on bone mass in elderly men and women. *Q J Med* 1970;39(156):601-615.
2. Lewiecki EM. In the clinic. Osteoporosis. *Ann Intern Med* 2011;155(1):1-15.
3. Eriksen EF, Mosekilde L, Melsen F. Trabecular bone resorption depth decreased with age: differences between normal males and females. *Bone* 1985;6(3):141-146.
4. MacDonald HM, Nishiyama KK, Kang J, Hanley DA, Boyd SK. Age-related patterns of trabecular and cortical bone loss differ between sexes and skeletal sites: a population-based HR-pQCT study. *J Bone Min Res* 2011;26(1):50-62.
5. Fohr B, Dunstan CR, Seibel MJ. Clinical review 165: markers of bone remodeling in metastatic bone disease. *J Clin Endocrinol Metab* 2003;88(11):5059-5075.
6. Robling AG, Castillo AB, Turner CH. Biomechanical and molecular regulation of bone remodeling. *Ann Rev Biomed Eng* 2006;8:455-498.
7. Leblanc AD, Schneider VS, Evans HJ, et al. Bone mineral loss and recovery after 17 weeks of bed rest. *J Bone Miner Res* 1990;5(8):843-850.

8. Meyer DR, Nerad JA, Newman NJ, Lin JC. Bilateral enophthalmos associated with hydrocephalus and ventriculoperitoneal shunting. *Arch Ophthalmol* 1996;114(10):1206-1209.
9. Hwang TN, Rofagha S, McDermott MW, Hoyt WF, Horton JC, McCulley TJ. Sunken eyes, sagging brain syndrome: bilateral enophthalmos from chronic intracranial hypotension. *Ophthalmology* 2011;118(11):2286-2295.
10. Athasiov PA, Prabhakarn VC, Selva D. Non-traumatic enophthalmos: a review. *Acta Ophthalmol* 2008;86(4):356-364.
11. Cline RA, Rootman J. Enophthalmos: a clinical review. *Ophthalmology* 1984;91(3): 229-237.
12. Hamedani M, Pournaras J, Goldblum D. Diagnosis and management of enophthalmos. *Surv Ophthalmol* 2007;52(5):457-473.
13. Ascher B, Coleman S, Alster T, et al. Full scope of effect of facial lipoatrophy: a framework of disease understanding. *Dermatol Surg* 2006;32(8):1058-1069.
14. Camirand A, Doucet J, Harris J. Anatomy, pathophysiology, and prevention of senile enophthalmia and associated herniated lower eyelid fat pads. *Plast Reconstr Surg* 1997;100(6):1535-1546.
15. Merchante N, García-García JA, Vergara S, et al. Bilateral enophthalmos as a manifestation of HIV infection-related lipoatrophy. *HIV Med* 2004;5(6):448-449.
16. Yip CC, Gonzalez-Candial M, Jain A, et al. Lagophthalmos in enophthalmic eyes. *Br J Ophthalmol* 2005;89(6):676-678.
17. Ashworth DR, Whear NM. Enophthalmos caused by metastatic breast carcinoma. *Br J Oral Maxillofac Surg* 2002;40(4):350-351.
18. Chang BY, Cunniffe G, Hutchinson C. Enophthalmos associated with primary breast carcinoma. *Orbit* 2002;21(4):307-310.
19. Gonçalves AC, Moura FC, Monteiro ML. Bilateral progressive enophthalmos as the presenting sign of metastatic breast carcinoma. *Ophthal Plast Reconstr Surg* 2005;21(4):311-313.
20. Kuzma BB, Goodman JM. Slowly progressive bilateral enophthalmos from metastatic breast carcinoma. *Surg Neurol* 1998;50(6):600-602.
21. Manor RS. Enophthalmos caused by orbital metastatic breast carcinoma. *Acta Ophthalmol (Copenh)* 1974;52(6):881-884.
22. Shields CL, Stopyra GA, Marr BP, et al. Enophthalmos as initial manifestation of occult, mammogram-negative carcinoma of the breast. *Ophthal Surg Lasers Imaging* 2004;35(1):56-57.
23. Smith GI, Jeffrey MJ, Zaki G. Enophthalmos caused by metastatic breast carcinoma. *Br J Oral Maxillofac Surg* 2001;39(6):487-489.
24. Stefanyszyn MA, DeVita EG, Flanagan JC. Breast carcinoma metastatic to the orbit. *Ophthal Plast Reconstr Surg* 1987;3(1):43-47.
25. Thompson PD, Wise RJ, Kendall BE. Enophthalmos and metastatic carcinoma of the breast. *J Neurol Neurosurg Psychiatry* 1985 Dec;48(12):1305-1306.
26. Wallace DK, Virata SR, Mukherji SK. Strabismus surgery complicated by "pulled in two syndrome" in a case of breast carcinoma metastatic to the medial rectus muscle. *J AAPOS* 2000;4(2):117-119.
27. Burroughs JR, Hernández Cospín JR, Soparkar CN, Patrinely JR. Misdiagnosis of silent sinus syndrome. *Ophthal Plast Reconstr Surg* 2003;19(6):449-454.
28. Fernando BS, Cannon PS, Tumuluri K, Cook AE. Linear scleroderma as a rare cause of enophthalmos: a case report. *J Med Case Rep* 2007;1:179.
29. Kirkali PA, Kansu T, Sanac AS. Unilateral enophthalmos in systemic scleroderma. *J Clin Neuroophthalmol* 1991;11(1):43-44.
30. Attia S, Zaouali S, Jeguirim H, et al. Orbital sarcoidosis manifesting with enophthalmos. *Ocul Immunol Inflamm* 2006;14(6):379-381.
31. Talar-Williams C, Sneller MC, Langford CA, et al. Orbital socket contracture: a complication of inflammatory orbital disease in patients with Wegener's granulomatosis. *Br J Ophthalmol* 2005;89(4):493-497.
32. Putterman AM. Management of orbital floor blowout fractures. *Adv Ophthalmic Plast Reconstr Surg* 1987;6:281-285.
33. Putterman AM. Management of blow out fractures of the orbital floor. III. The conservative approach. *Surv Ophthalmol* 1991;35(4):292-298.
34. Soparkar CN, Patrinely JR, Cuaycong MJ, et al. The silent sinus syndrome. A cause of spontaneous enophthalmos. *Ophthalmology* 1994;101(4):772-778.
35. Wesley RE, Johnson JJ 2nd, Cate RC. Spontaneous enophthalmos from chronic maxillary sinusitis. *Laryngoscope* 1986;96(4):353-355.
36. Davidson JK, Soparkar CN, Williams JB, Patrinely JR. Negative sinus pressure and normal predisease imaging in silent sinus syndrome. *Arch Ophthalmol* 1999;117(12):1653-1654.
37. Rose GE, Sandy C, Hallberg L, Moseley I. Clinical and radiologic characteristsics of the imploding antrum, or "silent sinus," syndrome. *Ophthalmology* 2003;110(8):811-818.
38. Lloyd GA. Orbital pneumosinus dilatans. *Clin Radiol* 1985;36:381-386.
39. Skolnick CA, Mafee MF, Goodwin JA. Pneumosinus dilatans of the sphenoid sinus presenting with visual loss. *J Neuro-Ophthalmol* 2000;20(4):259-263.
40. Schayck RV, Niedeggen A. Pneumosinus dilatans after prolonged cerebrospinal fluid shunting in young adults with cerebral hemiatrophy. A report of two cases and review of the literature. *Neurosurg Rev* 1992;15:217-223.
41. Sivasubramaniam R, Sacks R, Thornton M. Silent sinus syndrome: dynamic changes in the position of the orbital floor after restoration of normal sinus pressure. *J Laryngol Otol* 2011;125(12):1239-1243.

42. Bernardini FP, Rose GE, Cruz AAV, Priolo E. Gross enophthalmos after cerebrospinal fluid shunting for childhood hydrocephalus: the “silent brain syndrome.” *Ophthal Plast Reconstr Surg* 2009;25(6):434-436.
43. Cruz AAV, Mesquita IM, de Oliveira RS. Progressive bilateral enophthalmos associated with cerebrospinal shunting. *Ophthal Plast Reconstr Surg* 2008;24(2):152-154.