Pneumosinus Dilatans: An exploration into the association between Arachnoid Cyst, Meningioma and the pathogenesis of Pneumosinus Dilatans

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ABSTRACT

Objectives: To investigate the association between certain intracranial masses (meningioma and arachnoid cyst) and the incidence of Pneumosinus Dilatans (PSD) – including whether the size of the mass correlates with severity of the condition.

Patients and methods: A review of the available case reports on PSD was performed. Clinical data was extracted from 111 case reports for analysis. A further case-control study was performed using CT Head datasets to investigate the aetiological relationship between intracranial masses and PSD. Cases included patients with confirmed arachnoid cyst or meningioma. Controls included patients with no intracranial masses.

Results: PSD is most common in the frontal (48%) and sphenoid sinuses (43%). Men are twice as likely to be affected as women. 58% of cases occur in patients aged 35 or under. The most common symptoms reported are facial deformities (39%), headache (24%) and visual loss (15%). Unexplained visual changes (e.g. diplopia, reduced visual acuity) are strongly correlated with sphenoid sinus involvement. PSD is more common in patients with skull-base meningioma (OR 5.67) and middle cranial fossa arachnoid cysts (OR 10.00). Mean sinus volume in patients with PSD can increase by up to 4 times.

Conclusion: We present the first direct investigation into the relationship between meningioma, arachnoid cyst and Pneumosinus Dilatans. There is a statistical correlation between skull-base meningioma and middle cranial fossa arachnoid cysts and the incidence of PSD. This specific anatomical relation suggests that local factors contribute to the pathogenesis of the condition. Alterations in intracranial pressure due to mass effect or vascular occlusion, in addition to the localised release of bone growth factors (IGF-1, IGF-2, PDGF), are possible mechanisms for this. The first peak in incidence of PSD coincides with the completion of normal sinus pneumatisation, which raises the further possibility that predisposing genetic factors also contribute.

1. Introduction

Pneumosinus Dilatans (PSD) is a condition in which one or more of the paranasal sinuses become hyperaerated beyond their normal anatomical boundaries. It is rare with 134 reported cases to-date. It can present with symptoms or remain asymptomatic (being discovered incidentally). It most commonly affects the frontal sinuses, but the most severe complications are associated with sphenoid and ethmoid sinus involvement. It can also affect all of the paranasal sinuses and mastoid air cells in a condition known as Pneumosinus Dilatans Multiplex. It is usually associated with young men in their 20s to 40s, but it can affect both sexes at any age.

PSD was formally defined by Benjamins in 1918 [1], but despite being known for over a century, clinical awareness of the condition is limited and the aetiology remains hypothetical and contested. Recently, there has been an increasing focus on the association between PSD, meningioma and arachnoid cysts [2–10]. In 2014, Ricci et. al [2] demonstrated the association between these conditions and PSD, but to-date there has been no substantive exploration of their aetiological relationships.

In this study, we explore the aetiological relationship between meningioma, arachnoid cyst and PSD. Via a systematic review and primary analysis of computerised tomography (CT) data, we assess the association between these conditions and PSD – and present what we believe to be the first evidence-based discussion for the possible contribution of these intracranial lesions to the pathogenesis of PSD.

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2. Materials and methods

A systematic review of the available literature on PSD was conducted using Medline, EMBASE and PubMed – focusing on case reports and meta-analyses. Articles not available in English or full-text were excluded, resulting in a total of 66 articles containing 111 individual case reports. Each article was reviewed in full and the clinical features of each case were collated into a database containing patient demographics, clinical presentation, duration of symptoms, location of affected sinuses, findings on imaging and relevant co-morbidities.

To explore the relationship between meningioma, arachnoid cyst and PSD, we undertook primary analysis of CT datasets on a sample of 100 patients focusing on sinus volumes. Our sample was generated at University Hospitals Coventry and Warwickshire using anonymised patient records. An ICD-10 code search of the patient records from the period October 2013 to October 2018 identified a total of 151 cases of meningioma and arachnoid cyst diagnosed within our facility. From this, we selected a case sample of 50 patients. A further control sample of 50 patients was identified using records of all patients who had undergone a CT Head in the same period. Patients whose CT scan did not demonstrate the full extent of the paranasal sinuses were excluded. We used a number randomisation method to select our sample from the identified records, ensuring that our control sample matched the demographics of our case sample to avoid confounding bias.

The DICOM data for each CT scan was analysed using the Insignia software package. Measurement of the paranasal sinuses was conducted in three planes in accordance with similar studies [11–14]. These included height (cranio-caudal), width (transverse) and depth (anterior-posterior) measured in centimetres using standardised views (Fig. 1a, b, c). In accordance with other studies [14], we took the maximum distance between two bony prominences in a straight line as the recorded measurement for that plane. Wherever possible, we measured the left and right frontal sinuses separately (as this condition has a predilection for this site) but where the dividing septum was undetectable, we recorded each side as the total distance of the sinus divided by half. To calculate the estimated volume of each sinus, we used Bargouth et. al's Sinus Volume Index equation [13]. This uses a simplified ellipsoid formula and is calculated as $SVI = \frac{1}{2} \cdot a \cdot b \cdot c$ where a, b and c represent our three planes of measurement.

We also collected information on demographics, primary diagnosis, evidence of pathological changes and the site, number and size of any intracranial masses.

In total, we identified 16 cases of PSD in our CT datasets. These diagnoses were based on Urken et al's classification of Pneumosinus Dilatans as a dilated sinus that extends beyond the normal anatomical boundaries [15] and were verified by an independent reviewer. The clinical features of these cases were then collected from anonymised patient records and added to our case report data (Fig. 2). Data analysis was performed using the IBM SPSS Statistics 24 software package.

3. Results

Our analysis identified 127 cases of PSD. In accordance with previous studies [16], our analysis shows that male patients are affected nearly 2 times more often than females (Table 1). More than half of cases (58%) occurred in patients aged 35 or under, with 42% presenting before age 26 (Fig. 3). There appears to be a bimodal distribution in incidence with most cases presenting between age 16–20 and 31–35 (Fig. 4). The mean duration of symptoms was 37.6 months (Table 1).

The most common sinus involved is the frontal (48%) followed by the sphenoid sinus (43%). Involvement of the other sinuses is less common. Over 70% of cases involved a single sinus – with only 10% involving more than two sinuses. Our analysis investigated the relationships between different sinuses in cases where multiple sinuses were affected in an attempt to identify common patterns of involvement. Only the ethmoid sinus had a significant association with other sinuses – notably the frontal (59%) and sphenoid (52%) sinuses (Table 2). The relationships between anatomically distant sinuses appear to be weak.

Facial deformities involving the brow and maxillae was the most common presenting symptom, followed by headache and visual loss (Table 3). Patients were more likely to report pain (38.6%) than not (9.4%), and in a small number of cases [15] patients reported symptoms of higher cognitive dysfunction – including inattention, memory impairment and cognitive impairment. We clustered symptoms together to evaluate the relationship specific sinus involvement and the presenting symptom. We found that there is a significant relationship between facial deformities and PSD involving the frontal and maxillary sinuses. Most importantly, there is a significant relationship between visual changes and PSD involving the sphenoid and ethmoid sinuses (Table 3).

Using logistical regression models, we identified which cluster of symptoms were specifically related to PSD involving individual sinuses (Table 4). These models demonstrate that a patient who has visual changes has a 14-fold increased likelihood of sphenoid sinus involvement, whereas a patient with bony deformities of the face has a 10-fold increased likelihood of frontal sinus or a 6-fold increased likelihood of maxillary sinus involvement. These models also confirmed that frontal sinus involvement can often be asymptomatic.

Our analysis also considered the relationship between meningioma, arachnoid cyst and PSD (Table 5). Of the 111 case reports with PSD, 22 (19.8%) had meningioma and 11 (9.9%) had arachnoid cyst. Of the 16 identified cases of PSD in our CT dataset, 10 (25.0%) had meningioma and 1 (10.0%) had an arachnoid cyst. Having a meningioma or
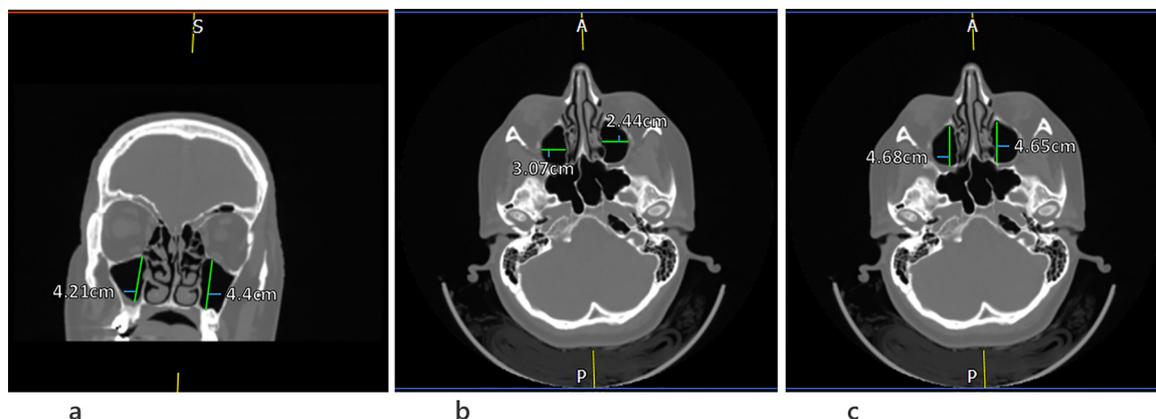

Fig. 1. Methods of paranasal sinus measurement on CT scan datasets. a Cranio-caudal distance was used to measure height. b Transverse distance was used to measure width. c Anterior-posterior distance was used to measure depth.
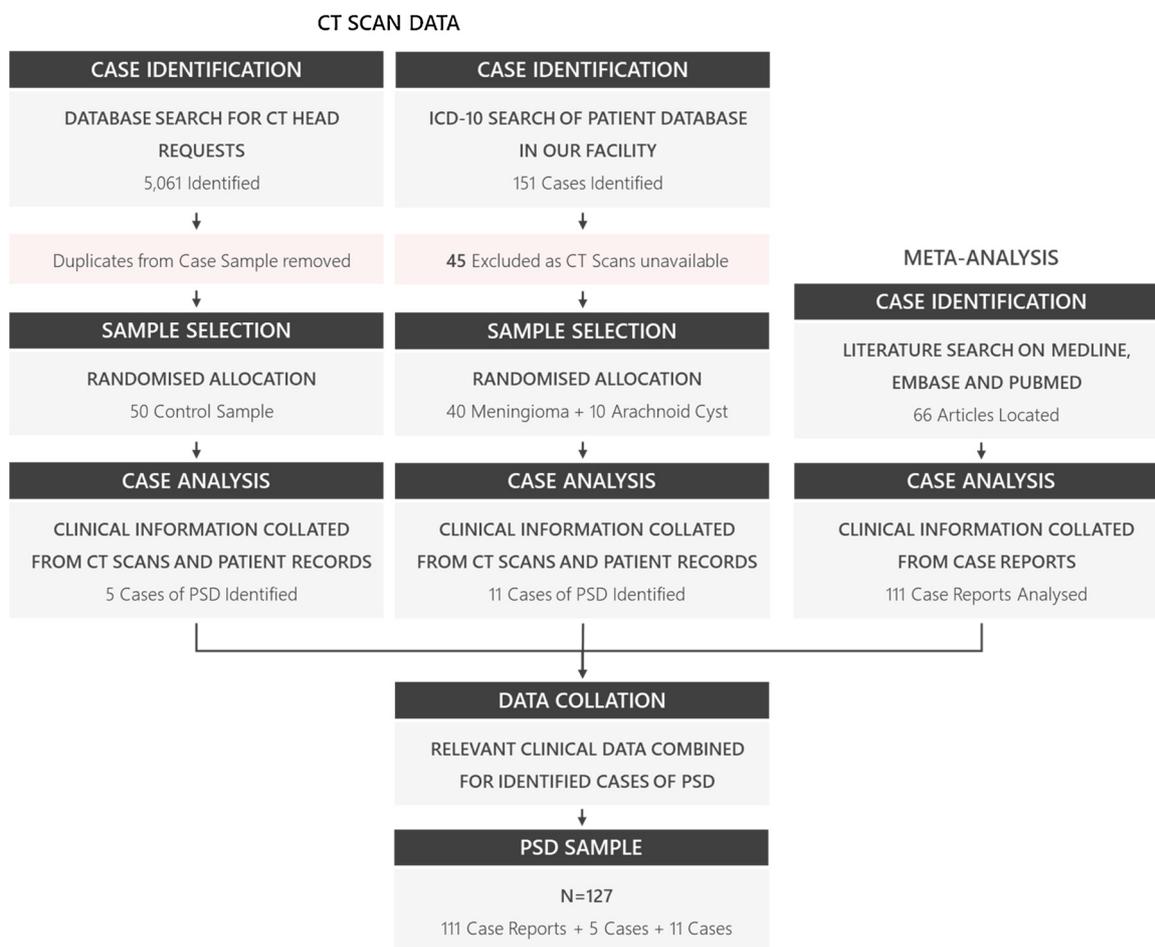
CT SCAN DATA

CASE IDENTIFICATION	CASE IDENTIFICATION	
DATABASE SEARCH FOR CT HEAD REQUESTS 5,061 Identified	ICD-10 SEARCH OF PATIENT DATABASE IN OUR FACILITY 151 Cases Identified	

↓ ↓

Duplicates from Case Sample removed	45 Excluded as CT Scans unavailable	META-ANALYSIS
		CASE IDENTIFICATION

↓ ↓

SAMPLE SELECTION	SAMPLE SELECTION	LITERATURE SEARCH ON MEDLINE, EMBASE AND PUBMED 66 Articles Located
RANDOMISED ALLOCATION 50 Control Sample	RANDOMISED ALLOCATION 40 Meningioma + 10 Arachnoid Cyst	

↓ ↓ ↓

CASE ANALYSIS	CASE ANALYSIS	CASE ANALYSIS
CLINICAL INFORMATION COLLATED FROM CT SCANS AND PATIENT RECORDS 5 Cases of PSD Identified	CLINICAL INFORMATION COLLATED FROM CT SCANS AND PATIENT RECORDS 11 Cases of PSD Identified	CLINICAL INFORMATION COLLATED FROM CASE REPORTS 111 Case Reports Analysed

↓

DATA COLLATION
RELEVANT CLINICAL DATA COMBINED FOR IDENTIFIED CASES OF PSD

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PSD SAMPLE
N=127 111 Case Reports + 5 Cases + 11 Cases

Fig. 2. Flow chart demonstrating the sampling process to create our database of confirmed PSD cases for analysis.

Table 1
Epidemiological data on Pneumosinus Dilatans from identified case reports and primary CT data.

TOTAL NUMBER OF CASES		
n	127	
Gender		
Male	81	(63.8%)
Female	44	(34.6%)
Unknown	2	(1.6%)
Sinus Afffected		
Frontal	61	(48.0%)
Sphenoid	54	(42.5%)
Maxillary	29	(22.8%)
Ethmoid	27	(21.3%)
Pneumosinus Multiplex	3	(2.4%)
Number Of Sinuses Affected		
One	91	(71.7%)
Two	21	(16.5%)
Three	6	(4.7%)
Four	4	(3.1%)
All (PSM)	3	(2.4%)
Unknown	2	(1.6%)
Duration of symptoms (months)[a]		
Mean (S.D.)	37.6	(38.9)
Minimum Duration	1	
Maximum Duration	120	

[a] Where cases reported the duration of symptoms as "a couple of years" or "several years" we classified this as 24 months. We classified "several months" as 4 months.

arachnoid cyst itself does not significantly increase the likelihood of having PSD (Table 5). However, the data does show that for patients with meningioma or arachnoid cyst there is an increased risk of developing PSD depending on the location of their pathology. Patients who had skull base meningioma were more likely to have PSD (OR 5.67 (95% confidence interval 1.26–25.50)) compared to those with non-skull base tumours. Similarly, patients who had a middle cranial fossa arachnoid cyst were more likely to have PSD (OR 10.00 (95% confidence interval 1.28–78.12)) compared to arachnoid cysts located elsewhere.

There are no discernible variations in the number of sinuses affected in patients with either meningioma or arachnoid cyst (Table 6). However, there is an association between the site of a meningioma and the sinus affected in PSD with skull base meningiomas being significantly linked to sphenoid sinus PSD (Fig. 5).

The mean sinus volumes of the affected paranasal sinuses were significantly larger in patients with PSD than in those without (Table 7). However, a Pearson correlation analysis (Table 8) demonstrated that there was no obvious relationship between the volume of a space occupying lesion and the mean sinus volume in our CT dataset.

4. Discussion

Pneumosinus Dilatans is traditionally considered to be a rare disorder, although its true incidence is likely to be unknown due to the lack of awareness of the condition among clinicians. Indeed, none of the 16 cases identified in our study had been recognised, despite some demonstrating dramatic infiltration of the sinuses into the surrounding anatomical structures (Fig. 6a-d).
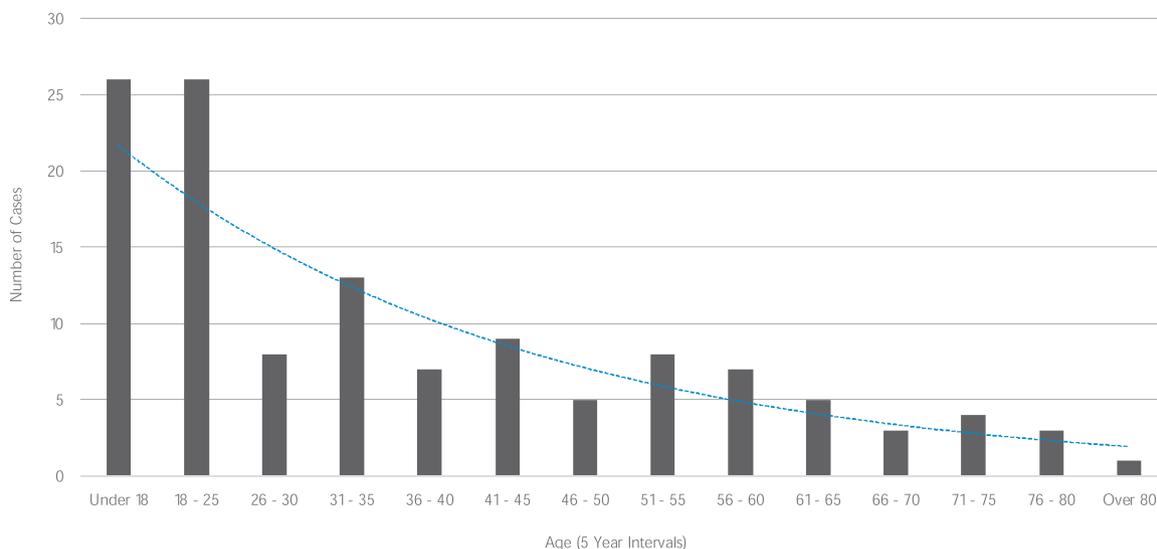
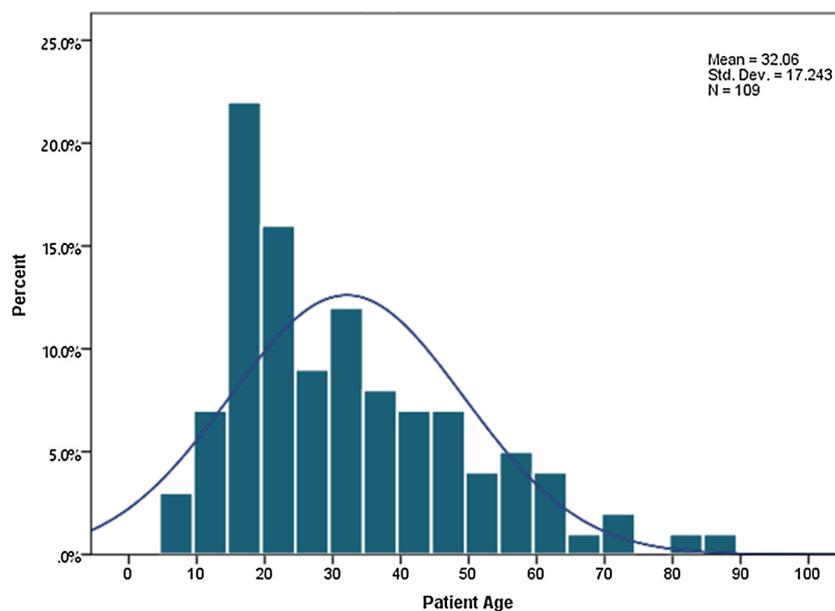**Fig. 3.** The incidence of Pneumosinus Dilatans by age of the patient in 5 year intervals (N = 127).

Fig. 4. Incidence of Pneumosinus Dilatans by age of the patient as reported in case reports (N = 111).

Table 2
Frequency of sinus involvement with the other paranasal sinuses in patients with PSD (Row Percentages).

	Frontal sinus	Ethmoid sinus	Sphenoid sinus	Maxillary sinus	Anterior clinoid
Frontal sinus (N = 61)	–	26.2% [a]	24.6%	16.4%	9.8%
Ethmoid sinus (N = 27)	59.3% [a]	–	51.9% [a]	33.3% [a]	14.8%
Sphenoid sinus (N = 54)	27.8%	25.9% [a]	–	18.5%	7.4%
Maxillary sinus (N = 29)	34.5%	31% [a]	34.5%	–	17.2%
Anterior clinoid (N = 11)	54.5%	36.4%	36.4%	45.5%	–

Patients with PSD of the Ethmoid Sinus were significantly more likely to also have involvement of the other paranasal sinuses.
  [a] Indicates statistical significance (p < 0.05) based on 95% Confidence Interval. Test adjusted using Bonferroni correction.

Our results add to the growing body of evidence around PSD. Our data confirm that the incidence of PSD is higher in men and those 35 or under, and that the most commonly affected sinus is the frontal sinus. Furthermore, we have demonstrated that when multiple sinuses are affected these tend to be close anatomical relations – indicating that the pathogenesis of this condition may be due to local (rather than systemic) factors. Our data has also demonstrated that patients with PSD

are statistically more likely to have an associated skull-base meningioma or MCF arachnoid cyst. However, the incidence of PSD itself is not increased among patients with intracranial lesions. This unidirectional association suggests that such lesions may exert some form of localised influence in predisposed populations that can result in the development of PSD.

While clinical imaging studies have been recommended for patients

Table 3
Analysis on presenting symptoms in cases of Pneumosinus Dilatans.

Most Common Symptoms (Individual)		
Facial Deformity	50	(39.4%)
- Orbital Swelling	27	(21.3%)
- Frontal Bossing	23	(18.1%)
Headache	31	(24.4%)
Visual Loss	19	(15.0%)
Facial Pain	17	(13.4%)
Cognitive Dysfunction	15	(11.8%)
Most Common Symptom Clusters		
Pain	49	(38.6%)
Facial Deformity	44	(34.6%)
Visual Changes	35	(27.6%)
Neurological Deficit	30	(23.6%)
Nasal Symptoms	18	(14.2%)
No Pain	12	(9.4%)
Orbital Deformity	11	(8.7%)
Asymptomatic	10	(7.9%)
Dizziness & Nausea	4	(3.1%)
Inflammation	3	(2.4%)
Other	3	(2.4%)

Relationship between symptoms and sinus involved

	Frontal sinus (N = 61)	Ethmoid sinus (N = 27)	Sphenoid sinus (N = 54)	Maxillary sinus (N = 29)	Anterior clinoid (N = 11)
Asymptomatic	80% [a]	50% [a]	60.0%	20.0%	0.0%
Dizziness & Nausea	25.0%	25.0%	50.0%	0.0%	0.0%
Facial Deformity	68.2% [a]	11.4%	11.4%	36.4% [a]	2.3%
Inflammation	66.7%	33.3%	0.0%	0.0%	0.0%
Nasal Symptoms	38.9%	16.7%	22.2%	22.2%	5.6%
Neurological Deficit	43.3%	13.3%	46.7%	26.7%	20.0%
No Pain	33.3%	33.3% [a]	41.7%	41.7% [a]	0.0%
Orbital Deformity	45.5%	45.5%	27.3%	27.3%	0.0%
Pain	46.9%	8.2%	40.8%	16.3%	6.1%
Visual Changes	34.3%	31.4% [a]	68.6% [a]	11.4%	0.0%
Other	66.7%	33.3%	66.7%	33.3%	33.3%

Patients are significantly more likely to present with certain symptoms based on which sinus is involved in PSD.
[a] Indicates statistical significance ($p < 0.05$) based on 95% Confidence Interval. Test adjusted using Bonferroni correction.

Table 4
Binary logistical regression models demonstrating which symptoms are predictive of PSD in that sinus.

Sinus	Symptom	Odds Ratio [a]	p
Frontal sinus	Asymptomatic	15.91	(0.007)
($R^2 = 0.34$)	Facial Deformity	9.97	(0.000)
Sphenoid sinus	Visual Changes	14.33	(0.005)
($R^2 = 0.55$)	Facial Deformity	0.09	(0.001)
	Orbital Deformity	0.03	(0.002)
Ethmoid sinus	Pain	0.23	(0.039)
($R^2 = 0.24$)			
Maxillary sinus	Facial Deformity	6.19	(0.020)
($R^2 = 0.23$)			

Increased likelihood that a patient will have involvement of this sinus if presenting with this symptom.
[a] Exponentiation of B co-efficient.

Table 5
Odds ratios demonstrating the relationship between PSD and co-morbidities.

Likelihood of having PSD		
Total Population (N = 211)		
(Case Reports + Case Sample + Control Sample)		
	OR	95% CI
Arachnoid Cyst	0.87	(0.35 - 2.16)
Meningioma	0.61	(0.33 - 1.10)

Likelihood of having PSD		
Co-Morbid Population		
	OR	(95% CI)
Arachnoid Cyst (N = 13)		
ACF	0.70	(0.08 - 6.22)
MCF	10.00	(1.28 - 78.12)
PCF	0.00	(N/A)
Meningioma (N = 62)		
Skull Base	5.67	(1.26 - 25.50)
Non-Skull Base	0.18	(0.06 - 0.55)

Note: Despite the low sample size in Arachnoid Cyst the OR for MCF cysts remains significant.

with suspected PSD, until now there has been no evidence-based examination of the specific symptoms associated with PSD to guide clinicians in their differential diagnosis. To the best of our knowledge, this is the first study to demonstrate statistical correlation between PSD in specific sinuses with clinical symptoms – and the information in Tables 3 and 4 can be used to facilitate clinical decision-making when assessing patients with these symptoms. PSD should be a differential diagnosis for any patient who presents with frontal bossing, supraorbital or infraorbital bony deformities or unexplained visual changes and appropriate radiological imaging (X-Ray Series; CT) should be ordered. Clinical suspicion should be higher in patients aged 35 or under and in

those with unexplained visual changes (such as blurred vision, diplopia, reduced visual acuity and visual loss) due to the association between these symptoms and PSD of the sphenoid sinus. Furthermore, there

Table 6
Incidence of PSD in patients with Meningioma and Arachnoid Cyst.

INCIDENCE OF PSD BY CO-MORBIDITY		
Patients with Arachnoid Cyst	12	(9.9%)
Case Reports	11	(9.9%)
CT Scan Data	1	(10.0%)
Patients with Meningioma	32	(21.2%)
Case Reports	22	(19.8%)
CT Scan Data	10	(25.0%)
INCIDENCE OF PSD BY LOCATION OF PATHOLOGY		
Arachnoid Cyst		
ACF	2	(16.7%)
MCF	10 *	(83.3%)
PCF	0	(0.0%)
Meningioma		
Skull Base	26 *	(81.3%)
Non-Skull Base	6 Ɨ	(18.8%)

NUMBER OF SINUSES AFFECTED			
	ALL	ARACHNOID CYST	MENINGIOMA
One	71.7%	66.7%	74.2%
Two	16.5%	33.3%	22.6%
Three	4.7%	0.0%	3.2%
Four	3.1%	0.0%	0.0%
All (PSM)	2.4%	0.0%	0.0%
Unknown	1.6%	0.0%	0.0%

* Indicates statistically significant positive relationship (p < 0.05) at 95% Confidence Interval.
Patients with an arachnoid cyst located in the MCF or skull-base meningioma have an increased likelihood of having PSD.
Ɨ Indicates statistically significant inverse relationship (p < 0.05) at 95% Confidence Interval.
Patients with non-skull-base meningioma have a decreased likelihood of having PSD.

should be an awareness that patients with skull-base meningioma also have an increased risk of developing PSD of the sphenoid sinus – and so patients with progressive visual symptoms of unknown cause should be considered for investigation for possible meningioma.

Reaching an adequate understanding of the pathogenesis of PSD remains frustrating and difficult. Numerous theories have been proposed, but so far none have convincing evidence to support them. The most widely accepted hypothesis is that of a ball-valve mechanism, in which an obstruction within the sinus results in a one-way valve that

Table 7
Comparison in mean sinus volume between patients with PSD and those without.

SINUS VOLUME	PSD		NO PSD		% CHANGE
cm^3 (+S.D.)					
Left Frontal Sinus	14.46 * (N = 8)	(± 2.69)	3.26 (N = 92)	(± 0.35)	4.44
Right Frontal Sinus	10.30 * (N = 6)	(± 4.60)	2.93 (N = 94)	(± 0.30)	3.52
Left Sphenoid Sinus	8.13 * (N = 5)	(± 2.18)	4.72 (N = 95)	(± 0.32)	1.72
Right Sphenoid Sinus	8.78 * (N = 5)	(± 1.54)	3.96 (N = 95)	(± 0.29)	2.22
Ethmoid Sinus	Base size too low for analysis (N = 1)		(N = 99)		–
Left Maxillary Sinus	31.19 * (N = 3)	(± 5.78)	17.42 (N = 97)	(± 0.71)	1.79
Right Maxillary Sinus	25.75 * (N = 3)	(± 7.29)	16.58 (N = 97)	(± 0.66)	1.55

* Indicates statistical significance (p < 0.05) based on 95% Confidence Interval. Test adjusted using Bonferroni correction.

Table 8
Pearson Correlation values demonstrating relationship between sinus volume and volume of space occupying lesion.

SINUS	PSD PRESENT CO-EFFICIENT	NO PSD PRESENT CO-EFFICIENT
Left Frontal Sinus	0.21	0.00
Right Frontal Sinus	0.11	− 0.20
Left Sphenoid Sinus	− 3.45	0.04
Right Sphenoid Sinus	− 1.73	− 0.51
Ethmoid Sinus	0.37	− 0.12
Left Maxilllary Sinus	0.15	− 0.03
Right Maxillary Sinus	0.03	0.09

No significant co-efficients were found. No statistical significance was found at 95% confidence interval.

allows air into (but not out of) the sinus. The resultant increase in intrasinus pressure up-regulates osteoclast and osteoblast activity leading to bone remodelling and expansion. There are several problems with this hypothesis. The first is that the presence of obstructive lesions (such as an ostial polyp) within the sinus is uncommon in patients with PSD. Our review only identified two cases in which polyps were present and three in which chronic sinusitis was reported. In cases where the
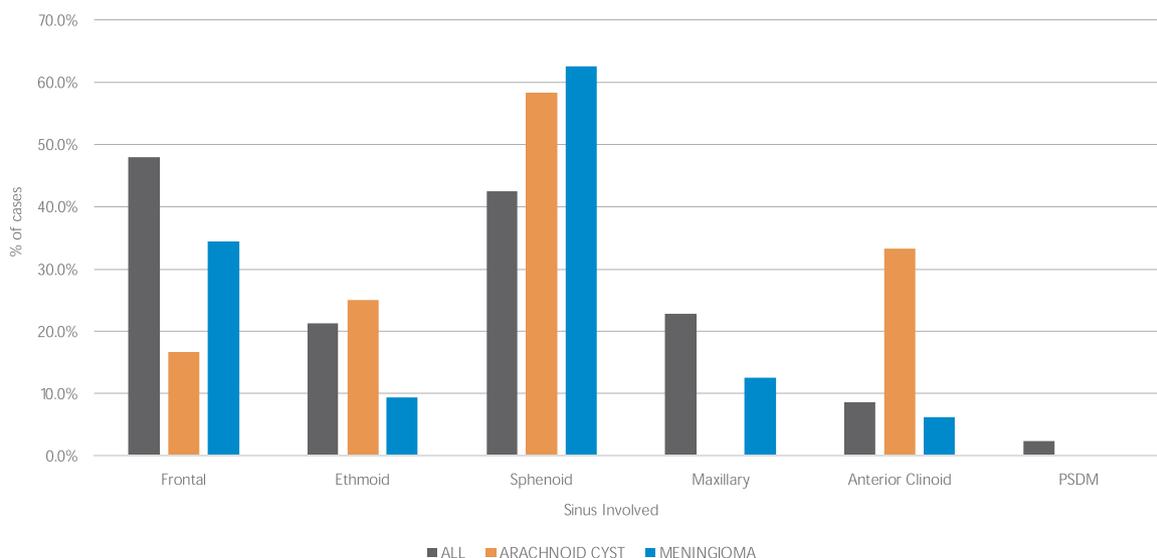

Fig. 5. Paranasal sinus involved in confirmed cases of PSD (n = 127).
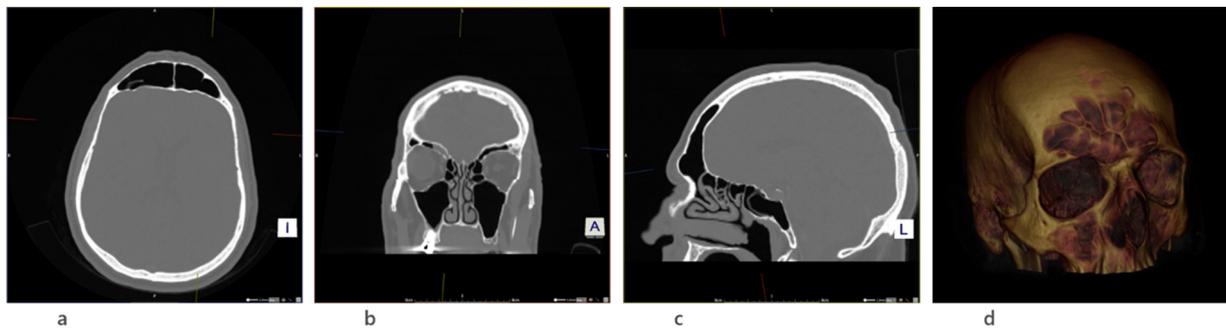
Fig. 6. CT scans demonstrating extensive Pneumosinus Dilatans of the frontal sinus. 6a The frontal sinuses are hyper-aerated resulting in frontal bossing. 6b There is evidence of supraorbital displacement with aeration of the supraorbital space. 6c The frontal sinuses have infiltrated the superior aspect of the frontal bone. 6d There is extension pneumatisation of the frontal sinuses.

mucosa was examined it was found to be histologically normal [18–20]. Secondly, in cases where patients underwent surgical correction, there was no evidence of ostial obstruction [3,7,18,21]. Thirdly, Breidahl et. al [18] correctly contend that an obstruction of the ostia should also affect mucus drainage from the sinus, but no such findings have been reported. Finally, a ball-valve mechanism might be expected to result in an acute expansion of the sinus with associated pain and discomfort, as in tension pneumothorax. However, our data show that the development of PSD is chronic in most cases, occurring over a mean duration of 37.6 months.

The ball-valve mechanism also fails to explain the association of PSD with skull-base meningioma and MCF arachnoid cysts. This association has been raised in several case reports, but to-date no coherent pathophysiological mechanism for their association has been proposed. We propose that these intracranial lesions contribute to the pathogenesis via two possible mechanisms: alterations in intracranial pressure (ICP) due to disrupted CSF dynamics (mechanical factors) and up-regulation of bone remodelling via paracrine hormone release (biochemical factors).

Disruptions in CSF dynamics may result in dilatation of the paranasal sinuses via alterations in ICP. A possible link between PSD and disrupted CSF dynamics has been known since van Schayck and Niedeggen's report of two patients with long-term CSF shunting who subsequently developed PSD in multiple sinuses [22]. CSF dynamics are reliant on three main factors: rate of production, rate of absorption and cerebral blood flow [23]. Both arachnoid cyst and meningioma are able to disrupt CSF dynamics via compression of cerebral blood flow. The exact mechanism behind this is disputed, but our suggestion is that compression of the cerebral arteries results in impaired CSF flow within the ventricular system due to the loss of pulsatile pressure within the cranial cavity. Conversely, compression of the cerebral veins would result in increased venous pressure resulting in inhibited CSF absorption if the hydrostatic pressure within the venous system increases above the ICP. A third mechanism involves simple obstruction of the CSF outflow as in obstructive hydrocephalus. Such mechanisms may explain the specific association between PSD and arachnoid cysts within the middle cranial fossa. These masses exert pressure on the Sylvian fissure and can result in compression of the middle cerebral vessels that sit within. Indeed, Seur and Kooman showed using cerebral angiography that not only can these cysts displace the middle cerebral artery, but that the middle cerebral veins can be absent entirely [9].

Disruptions in CSF dynamics may result in dilatation of the paranasal sinuses via alterations in ICP. Normal bone maintenance is dependent in part on the mechanical stress exerted on it and in the case of the calvarium, this originates from the ICP. Alterations in ICP are known to cause bone remodelling in the skull [24]. Intracranial hypotension related skull modelling (IHSR) is seen in patients with ventriculoperitoneal shunts and results in expansion of the orbits and in some cases sinus enlargement. Bone remodelling is also seen in cerebral

hemiatrophy where reduced brain mass results in intracranial hypotension [7,22,25]. In all cases, bone remodelling occurs due to the imbalance in the pressure gradient across the external and internal tables. Such a hypothesis is attractive because it would resolve the problem of how an expansile mass, such as an arachnoid cyst, could cause an expansion in the sinuses, while also accommodating the hypothesis that sinus expansion occurs as an ex vacuo response to spontaneous regression of a cyst. It is also attractive because theoretically the bone remodelling could result in either anterior expansion of the sinus (if the ICP is high) or posterior expansion into the intracranial compartment (if the ICP is low). This could explain why some cases of frontal sinus PSD present with clear frontal bossing, but others do not. However, our data demonstrate no significant relationship between the size of intracranial pathology and the increased volume of the paranasal sinuses. Future studies should focus on the identification of changes in ICP and CSF dynamics to elucidate or refuse this hypothesis.

Local chemical factors may also play a role in the development of PSD. In over 70% of cases, PSD affects a single sinus, suggesting that the disease process occurs within an isolated area. When multiple sinuses are affected, these tend to be close anatomical relations and may represent an extension of this localised disease process along a continuous anatomical plane. Thirdly, the specific association with skull-base meningioma suggests that the interplay between tumour and bone is a critical factor.

Hirst et. al [26] suggested that meningioma of the optic nerve sheath could stimulate the skull-base bones to bulge via mechanical or chemical mechanisms. It is well-established that meningiomas can result in bone changes, such as hyperostosis or erosion. Up to 90% of sphenoid wing meningioma demonstrate hyperostosis [27]. The mechanisms underpinning these changes are suggested to include hyperperfusion of the bone or cellular interactions. The latter is of particular interest, as immunohistological analysis of meningioma cells has demonstrated significant expression of growth factors – notably IGF-1, IGF-2 and PDGF which are also stimulators of bone growth [28]. While these growth factors exert an autocrine influence that drives tumour growth, it is also possible that they have some unintended influence within the internal structures of the bone – such as up-regulation of osteoblasts and osteoclasts. Indeed, it has been demonstrated using PET-CT that in patients with PSD, F-NaF uptake – an isotope used in the diagnosis of bone disease – is increased in the affected sinus's bone [20], with histological analysis of these bone sections revealing diffuse and bone remodelling, in addition to large numbers of active osteoblasts and osteoclasts. Interestingly, these chemical mechanisms may explain why recurrence of the condition does not occur following osteotomy of the affected bone.

Why then does PSD not occur in all patients with these intracranial lesions? Ricci [16] suggested that the bi-modal distribution of PSD could be due to a genetic predisposition in the younger population which made them more susceptible to its development. The increased

incidence in males, young age of onset and association with other congenital conditions suggest a genetic component. Indeed, specific congenital bone diseases such as osteogenesis imperfecta have been associated with increased pneumatisation of the sinuses [29]. It is also interesting that the first peak in incidence occurs at 16 years old, the same time that pneumatisation of the paranasal sinus enters its final phase [30]. Is it possible that in some people this process is disrupted, resulting in continued pneumatisation that eventually manifests as PSD? In one case of PSD [31], serial x-rays taken over the course of a decade demonstrated evidence of new septum formation in the affected sinus which seemed to mimic the process of normal sinus pneumatisation – adding weight to this hypothesis.

Unfortunately, the current data is too limited to allow us to evaluate this hypothesis further. We must increase awareness of this condition to aid diagnosis and increase the number of cases available for study.

Future research is needed to investigate whether disruptions in CSF dynamics and ICP contribute to PSD, ideally using MRI or SPECT scans. Further study focusing on the associations between skull-base meningioma and PSD may also shed further light on possible pathophysiological mechanisms for this rare disease.

Declaration of Competing Interest

The author declares no special interests or conflicts of interest.

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Appendix A. Detailed breakdown of the symptom clusters used in Table 3

SYMPTOM CLUSTER	INCLUDED INDIVIDUAL SYMPTOMS
Pain	Facial Pain | Facial Pressure | Headache | Tooth Pain
Facial Deformity	Facial Asymmetry | Frontal Bossing | Supraorbital or Infraorbital Swelling
Visual Changes	Blurred Vision | Diplopia | RAPD | Reduced Visual Acuity | Visual Loss (Unilateral or Bilateral)
Neurological Deficit	Anosmia | Ataxia | Higher Cognitive Dysfunction | Hemiparesis | Paraesthesia | Seizure
Nasal Symptoms	Nasal Obstruction | Rhinitis | Rhinorrhoea | Sinusitis
No Pain	–
Orbital Deformity	Enophthalmos | Exophthalmos | Proptosis
Asymptomatic	–
Dizziness & Nausea	Dizziness | Nausea | Syncope
Inflammation	Erythema | Fever | Periorbital Oedema
Other	Facial Crepitations | Galactorrhoea | Periodontal Abnormality

NOTE: Symptoms were collated from the case report text and from clinical correspondence.

References

[1] L.E. Benjamins, Pneumosinus frontalis dilatans, Acta Otolaryngol. 1 (1918) 412–422.

[2] N.S. Desai, S.S. Saboo, A. Khandelwal, J.A. Ricci, Pneumosinus Dilatans: Is It More Than an Aesthetic Concern? J. Craniofac. Surg. 25 (2014) 418–421.

[3] B.A. Gibbons, W.R. Miele, J.E. Florman, C.B. Heilman, M.A. Horgan, Pneumosinus dilitans and meningioma: a case series and review of the literature, Neurosurg. Focus 30 (2011) E13.

[4] A. Scuotto, D. Saracino, M. Rotondo, A. Izzo, F. Urraro, S. Cappabianca, S. Sampaolo, Sphenoidal pneumosinus dilatans due to anterior skull base meningiomas - CT and MRI aspects: report of two new cases and literature review, Neuroradiology Review 29 (2016) 295–297.

[5] A. Nair, S. Behari, M. Jain, A.K. Jaiswal, Bilateral primary optic nerve sheath meningiomas with pneumosinus dilatans, Acta Neurochir. (Wien) 153 (2011) 2495–2497.

[6] M.R. Khalatbari, H. Borghei-Razavi, Y. Moharamzad, Intradiploic orbital roof meningioma with pneumosinus dilatans in a child: a case report and review of the literature, Paediatric Neurosurgery 47 (2011) 66–71.

[7] A.J. Martin, J.M. Jarosz, N.W. Thomas, The strange association of pneumosinus dilatans and arachnoid cyst: case report and review of the literature, Acta Neurochir. (Wien) 143 (2001) 197–201.

[8] P.E. Dross, J.F. Lally, B. Bonier, Pneumosinus dilatans and arachnoid cyst: a unique association, Am. J. Neuroradiol. 13 (1992) 209–211.

[9] N.H. Seur, A. Kooman, Arachnoid cyst of the middle fossa with paradoxical changes of the bony structures, Neuroradiology 12 (1976) 177–183.

[10] K. Ziahosseini, I. Din, J. Bhargava, Intracranial arachnoid cyst; an unusual cause of epiphora, Orbit 32 (2013) 211–213.

[11] P. Sahlstrand-Johnson, M. Jannert, A. Strömbeck, K. Abul-Kasim, Computed tomography measurements of different dimensions of maxillary and frontal sinuses, BMC Med. Imaging 11 (2011) 1471–2342.

[12] O. Cohen, M. Warman, M. Fried, H. Shoffel-Havakuk, M. Adi, D. Halperin, Y. Lahav, Volumetric analysis of the maxillary, sphenoid and frontal sinuses: a comparative computerized tomography based study, Auris Nasus Larynx 45 (2018) 96–102.

[13] G. Barghouth, J.O. Prior, D. Lepori, B. Duvoisin, P. Schnyder, F. Gudinchet, Paranasal sinuses in children: size evaluation of maxillary, sphenoid, and frontal sinuses by magnetic resonance imaging and proposal of volume index percentile curves, Eur. Radiol. 12 (2002) 1451–1458.

[14] S. Pirner, K. Tingelhoff, I. Wagner, R. Westphal, M. Rilk, F.M. Wahl, F. Bootz, W.G. Eichhorn, CT-based manual segmentation and evaluation of paranasal sinuses, Eur. Arch. Oto-Rhino-Laryngology 266 (2009) 507–518.

[15] M.L. Urken, P.M. Som, W. Lawson, D. Edelstein, A.L. Weber, H.F. Biller, Abnormally large frontal sinus. II. Nomenclature, pathology, and symptoms, Laryngoscope 97 (1987) 606–611.

[16] J.A. Ricci, Pneumosinus dilatans: over 100 years without an etiology, J. Oral Maxillofac. Surg. 75 (2017) 1519–1526.

[18] A.F. Breidahl, P. Szwajkun, Y.-R. Chen, Pneumosinus dilatans of the maxillary sinus: a report of two cases, Br. J. Plast. Surg. 50 (1997) 33–39.

[19] J. Bouguila, M.B. Rejeb, M. Omezzine, R. Mani, H. Khochtali, Pneumosinus dilatans: rare cause of slowly changing frontal contours, Aesthet. Surg. J. 35 (2015) 47–53.

[20] R. Jankowsi, S. Kuntzler, N. Boulanger, O. Morel, J. Tisserant, N. Benterkia, J.-M. Vignaud, Is pneumosinus dilatans an osteogenic disease that mimics the formation of a paranasal sinus? Surg. Radiol. Anat. 36 (2014) 429–437.

[21] O.A. Pospisil, M.C. Balmer, Pneumosinus dilatans, Br. J. Oral Maxillofac. Surg. 26 (1988) 375–380.

[22] R. van Schayck, A. Niedeggen, 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. 15 (1992) 217–223.

[23] M. Czosnyka, Z.H. Czosnyka, P.C. Whitfield, J.D. Pickard, Cerebrospinal fluid dynamics, in: G. Cinalli, C. Sainte-Rose, W.J. Maixner (Eds.), Pediatric Hydrocephalus, Springer, Milano, 2005, pp. 47–63.

[24] T.J. McCulley, W.J. Piluek, J. Chang, Intracranial pressure and skull remodelling, Saudi J. Ophthalmol. 29 (2015) 57–62.

[25] C.G. Dyke, L.M. Davido, C.B. Masson, Cerebral hemiatrophy with homolateral hypertrophy of the skull and sinuses, Surgery, Gynecology & Obsterics 57 (1933) 588–600.

[26] L.W. Hirst, N.R. Miller, F.J. Hodges, J.J. Corbett, S. Thompson, Sphenoid pneumosinus dilatans: a sign of meningioma originating in the optic canal, Neuroradiology 22 (1982) 207–210.

[27] K. Terstegge, W. Schomer, H. Henkes, N. Heye, N. Hosten, W.R. Lanksch, Hyperostosis in meningiomas: MR findings in patients with recurrent meningioma of the sphenoid wings, Am. J. Neuroradiol. 15 (1994) 555–560.

[28] D.A. Hilton, A. Shivane, L. Kirk, K. Bassiri, D.G. Enki, C.O. Hanemann, Activation of multiple growth factor signalling pathways is frequent in meningiomas, Neuropathology 36 (2016) 250–261.

[29] R. Shapiro, S. Schorr, A consideration of the systemic factors that influence frontal sinus pneumatization, Invest. Radiol. 15 (1980) 191–202.

[30] A.C. Patel, J.A. Hammoudeh, M.M. Urata, Pneumosinus dilatans: a rare cause of frontal sinus expansion: case report and review of literature, J. Oral Maxillofac. Surg. 66 (2008) 2380–2386.

[31] R. Suryanarayanan, G. Abbott, Pneumosinus dilatans: demonstrated by sinus expansion on serial sinus X-rays with discussion of possible aetiology, J. Laryngol. Otol. 121 (2007) 96–99.