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Sinonasal Schwannoma: Retrospective Review of Cases from 1997-2016 at A Tertiary Referral Centre

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Abstract **Original Research Article**

Sinonasal schwannomas (SNS) are benign neoplasms of peripheral nerve sheaths within sinonasal cavities and little is known about them. We aim to expand current literature by analysing all cases of SNS at the National University of Malaysia Medical Centre (UKMMC). There were five females and one male in this study. Mean age was 52.3±2.1 years (range 42-75). The mean tumour size was 3.6cm±0.1 (range 1.50-5.90cm). Tumours originated from outside the sinonasal cavities (n=4) and inside (n=2). Extension was present in five patients. The sinonasal cavity most frequently involved is the maxillary sinus (n=3). Clinical presentation corresponded to site of involvement with facial numbness being the most common presentation. All histopathologically diagnosed cases showed regions of Antoni A, Antoni B, Verocay Bodies and immunoreactivity with S100 protein. Four patients underwent Functional Endoscopic Sinus Surgery (FESS). The presentation of SNS corresponds to their site. Site of involvement is more informative than the site of origin. Endoscopy, CT scans and MRIs are helpful in facilitating an accurate diagnosis. SNS show specific histopathological findings and its main treatment is FESS.

Keywords: Sinonasal, Schwannoma, retrospective review, imaging, treatment.

INTRODUCTION

Schwannomas are benign, slow growing neoplasms arising purely from peripheral nerve sheaths [1, 2]. About 25-40% of schwannomas are located in the head and neck region [3, 4]. The most frequent site of origin is the vestibulochoclear nerve [3, 4]. Sinonasal schwannomas (SNS) are rare, accounting for <4% of head and neck schwannomas [2, 3, 5, 6]. The clinical presentation of SNS is varied and non-specific. Nasal obstruction, epistaxis, anosmia, rhinorrhoea and facial pain, are common presenting complains reported in literature [2, 6, 7]. The clinical symptomatology depends largely on the site and extent of the tumour rather than the type of tumour itself.[2] A diagnosis of SNS is often facilitated by endoscopy, Computed Tomography (CT) scans and Magnetic Resonance Imaging (MRI). However, the confirmation of schwannomas relies heavily on histopathology [1, 4]. Schwannomas will almost always show specific tissue findings and strong immunoreactivity with S100 protein [2, 8].

SNS are normally treated by radical surgical excision with preservation of essential anatomical structures and neural functions [1, 2, 3, 7, 8]. Lately, functional endoscopic sinus surgery (FESS) has become the mainstay treatment due to its advantages [2, 7, 8]. In this study, we aim to identify and analyse all the cases of SNS handled by the Otorhinolaryngology Department at the National University of Malaysia Medical Centre (UKMMC) for the past 19 years. By comparing and contrasting different aspects of these cases with other publications, we aspire to share our experience and to expand on the limited knowledge about this rare disease in terms of patient demographics, clinical presentation, imaging findings, management, follow up and histopathology.

MATERIALS AND METHODS

(Supplemented by algorithm in Figure 1)

In this retrospective study, we reviewed all recorded surgeries performed from January 1997 to March 2016 (19years, 3months) by the

Otorhinolaryngology Department of UKMMC, a national tertiary referral teaching hospital. By looking at the pre- and immediate post-operative diagnoses recorded on the surgical log books we initially included 32 of the 15268 cases. These cases were SNS or those suggestive of SNS (n=32)**.** Of these patients, 26 were eliminated after careful review of their case files, imaging and histopathological reports as their eventual definitive diagnoses did not fulfil the criteria of SNS. Six cases diagnosed as schwannomas of the sinonasal cavity remained as sample size at the end of the elimination processes and the files and records were reviewed thoroughly. The information obtained from each patient includes demographics, clinical presentations, radiological imaging and histopathological findings, initial and definitive diagnosis, and management and follow up. The ethical approval for this study was authorised by the Research Ethics Committee of the National University of Malaysia and the Institutional Review Board of Perdana University. We also compared and contrasted our findings to seven recent publications which were obtained from PubMed by using key words 'Sinonasal' and 'Schwannoma' and by limiting the search results to 10 years.

RESULTS

Demographics

Five females and one male were included in the study. The mean age was 52.3±5.2 years (range 42-75). Four of the five females presented were in their 40s. The three Chinese, two Malays and one Indian were all were married and non-smokers. None of them had any significant past medical history or family history related to tumours or schwannomas except one who had a father with intestinal carcinoma.

Presentation

Data concerning the clinical presentation of the six patients are summarised in Table 1.The chief symptoms reported were facial numbness (n=3), nasal obstruction (n=2) and headache (n=1). Mean symptom duration was 9.3±3.2 months (range 2-24). Symptoms most commonly experienced were; nasal symptoms like nasal obstruction (n=3) and rhinorrhoea (n=3), paranasal symptoms like facial numbness (n=4) and facial pain (n=3) and intracranial symptoms like headache (n=3), visual problems (n=2), nausea and vomiting (n=1), vertigo (n=1) and orbital pain (n=1).

Diagnostic Findings

Nasal endoscopy was only performed on four patients and all showed a mass in the nasal cavity (n=3) and or a deviated nasal septum (n=2). Of the six patients, three had both CT and MRI scans done while two others had only a CT scan and an MRI scan done respectively. Sites of origin on radiological imaging were the infratemporal fossa (n=2), pterygopalatine area (n=2) and nasal cavity (n=2). The right side was more commonly involved (n=4) than the left (n=2) and the mean tumour size was 3.6cm±0.4 (range 1.50-5.90cm). Tumours in five patients showed extension commonly involving neighbouring structures namely the maxillary sinuses (n=3) and the intracranial region (n=3) followed by the ethmoid sinuses (n=2), sphenoid sinuses (n=2), nasal cavity (n=1) and the pterygopalatine area (n=1). Infiltration was reported in three patients. Additional findings on Endoscopy, CT and MRI scans include nasal septal deviation (n=2), fluid retention (n=2), bony (n=1) and mucosal erosion (n=3).

Management

Surgical approach was chosen as a form of management for five patients; endoscopic sinus surgery (ESS) (n=4) and craniotomy (n=1) while one patient was treated with radiotherapy through the CyberKnife technique. Four of the five surgical patients underwent total tumour resection and one had a subtotal (>95%) resection. No intraoperative complications were reported in any of these five patients. The mean duration from presentation to management was 93.1±76.3 weeks (range 3–473).

Follow Up

Patients were followed up on for a mean duration of 31.3±29.3 months (range 1-86). Post-operative complications such as swelling (n=2) and facial numbness (n=2) were reported in three patients. No recurrence was noted in all surgical patients.

Histopathology

Samples for histopathological findings were obtained intraoperatively via surgical biopsy in all five surgical patients while the patient who was managed by Cyber Knife therapy underwent a Caldwell-Luc trans-antral biopsy prior to management. Of the six cases sent for histopathology, four cases were confirmed by characteristic histopathological findings of SNS. Antoni A regions, Verocay Bodies and Antoni B regions were represented in all four cases while regions of haemorrhagic necrosis were only noted in one. S-100 protein was positive for all these cases.

Literature Review

A review of seven recent articles on 18 patients was performed by our team. Results obtained were compared to our results and demonstrated in Tables 2a and 2b. Demographics and tumour characteristics of SNS in this study and seven recent studies compared in Table 2. Clinical presentation and symptoms of SNS in this study and seven recent studies compared in Table 3.

DISCUSSION

SNS arise from Schwann cells of intranasal nerves, the ophthalmic and maxillary divisions of the trigeminal nerve and the autonomic nerves (sympathetic fibres of the carotid plexus and parasympathetic fibres of the sphenopalatine ganglion) [9, 10]. In current literature, SNS frequently involve the ethmoid sinuses,

followed by (with decreasing order of frequency), the maxillary sinuses, the nasal fossa, the sphenoid sinuses and the frontal sinuses [4]. Several explanations justify this trend. For instance, schwannomas occur most commonly in the ethmoid sinuses because they house more massive complex nerve innervations while schwannomas rarely occur in the frontal sinuses because they house olfactory nerves which are devoid of Schwann cells [11]. Another explanation is that schwannomas in certain sinuses ie. Ethmoid sinuses cause earlier and more frequent symptoms than when they are in other sinuses, thus increasing the probability of tumours in these areas being detected and documented [5].

In our study, four patients had SNS originating from outside the sinonasal cavities while only two had schwannomas arising from sinonasal cavities [8]. There are several reasons as to why our study did not demonstrate the trend reported in literature [4]. The infratemporal and pterygopalatine fossas are located close to and are in some locations connected to the sinonasal cavities [4, 5, 12]. This makes the task of identifying the site of origin and or differentiating between sites of origin and extension difficult and inaccurate especially in cases where multiple sinuses are involved.

Our study places more emphasis on the sites of involvement (origin and extension) rather than just the site of origin. This approach is more informative in terms of correlation to symptomology and management. The sinonasal cavity most commonly involved is the maxillary sinus. Besides the inherent number of schwannomas originating from this sinus [4], its anatomical location, being anterolateral to the infratemporal fossa and anteromedial to the pterygopalatine area offers schwannomas originating from the said areas a higher accessibility into this space [4, 12]. This may have contributed significantly to the numbers seen in this study. The lack of extension of the schwannoma in patient six could be explained by the relatively small and slow growing nature of that particular tumour. Note that this patient had the longest presentation to surgery time (473 weeks).

Like other sinonasal tract diseases, the clinical symptomology of SNS is varied and non-specific [6, 7, 13]. Signs and symptoms depend more on the site and extent of the tumour rather than the type of tumour itself [2]. Therefore, a schwannoma in the nasoethmoid complex commonly presents with nasal obstruction and epistaxis (nasal symptoms) whereas patients with paranasal sites of involvement like the maxillary sinus are more likely to present with facial pain (paranasal symptom) [2, 6]. In cases of intra-orbital and intracranial extension, a patient can present with strabismus, proptosis, epiphora, cranial nerve palsies and a decreased level of consciousness (intracranial symptoms) [2,6,7].

To better demonstrate and make sense of this plethora of signs and symptoms, we classified them into three categories according to the anatomical regions involved. Firstly, 'Nasal' signs and symptoms include nasal obstruction, rhinorrhoea and epistaxis. Secondly, 'Paranasal', signs and symptoms manifest in the form of facial pain and facial numbness. Lastly, 'Intracranial' signs and symptoms include problems with vision, cranial nerves, consciousness and other mental functions for example, epiphora and decreased level of consciousness.The concept was consistent with the results we obtained. In all our patients, schwannoma involving a particular anatomical location produced symptom(s) specific to that anatomical group. There were also no reports of symptoms manifesting independently of a tumour involving a particular location. However, Patient 6 who had a lesion confined to the nasal cavity presented with both nasal and intracranial symptoms (headache and vertigo). The intracranial symptoms can be explained by her continuous use of Loratadine. Loratadine, commonly used to treat symptoms of allergies is also known to cause side effects like headaches and drowsiness [14]. Besides this, the patient's age of 75 might have caused the episodes of headaches and vertigos independently of the tumour in the nasal cavity. Nevertheless, it is also possible that unlike nasal and paranasal symptoms, SNS can cause intracranial symptoms irrespective of whether they have extended into the intracranial space. The ambiguity of intracranial symptoms should be studied in subsequent researches.

An understanding of this concept will allow clinicians to better gauge the extent of involvement of the sinonasal tract and surrounding structures in a suspected SNS. This can be done by asking for symptoms and stratifying them accordingly or screening for common symptoms in each symptom group. This will improve focus on radiological imaging and subsequently patient management. However, not all the articles in our literature review showed this relationship because majority only reported the chief complaints or major symptoms. Moreover, because there was no negation of symptoms in these publications, we cannot infer that the symptoms that should have been present (but were not reported) were indeed absent, overlooked or not reported. Although endoscopy, Computed Tomographic (CT) scans and Magnetic Resonance Imaging (MRI) are not definitive in diagnosing SNS, they are very useful in aiding a patient's pre-operative diagnosis, pre-biopsy and surgical planning [6, 15]. On endoscopy, a unilateral polypoid nasal mass is typically visualised in cases of nasal schwannomas [2, 7, 8]. However, there is a need to determine whether the mass is a schwannoma or other more common benign epithelial lesions like polyps, papillomas and angiomas or malignant counterparts like squamous cell carcinomas [11]. CT scans and MRIs generally reveal nonspecific features but are still helpful in giving pre-

operative diagnostic clues [6]. CT scans and MRIs of Patient 4 are discussed in Figure 2.

CT scans are excellent at mapping the site and extent of a tumour, especially the intracranial extent and involvement of soft tissues as well as vital structures like the orbits [1, 13]. (See Panel A and B in Figure 2). By using CT, the image of soft tissue tumours can be delineated and the skeletal margins can also be outlined well enough to exclude invasion [1]. Schwannomas usually exhibit mild enhancement, show a mottled central lucency and peripheral intensification on contrast-enhanced CT scan [1, 10]. (See Panel A in Figure 2).

The heterogeneous enhancement represents areas of increased vascularity or neovascularity with adjacent necrotic regions [1, 2, 14]. One should be apt in avoiding the common pitfalls when interpreting CT scans of schwannomas. Fluid in blocked sinuses may be misinterpreted as part of the tumour due to their increased density [7]. Benign schwannomas rarely cause bone erosions, but when present, bone remodelling can be appreciated on a CT scan [2, 6, 7]. This is due to pressure necrosis from the gradually expanding mass and should not be mistaken as malignancy [11].

MRI is superior in distinguishing soft tissue neoplasms from inflammatory changes and sinus obliterations [7]. (See Panel C, D, E and F in Figure 2). Most MRI characteristics of schwannomas demonstrate specific signs like split fat, target and fascicular signs.[15] Schwannomas also show specific signal patterns such as intermediate T1-weighted and variable T2-weighted signal intensity masses, depending on the cystic characteristics and also cellularity of the lesion [2, 4, 5, 8, 10, 11]. Furthermore, MRIs demonstrate features such as obvious tissue vascularity or dense vasculature which require more care and pre-biopsy planning [6, 15]. Unconventionally, Patient 6 had only an endoscopy with no radiological imaging scans performed on pre-management workup because the small tumour was confined to the nasal septum and its edges were clearly visible on endoscopy with no evidence of extra-nasal extension.

Histologically, schwannomas exhibit two different characteristic findings: Antoni A and B [2, 11, 13]. In Antoni A, the tissue is hypercellular, fasciculated, organised and contains densely packed, palisading and spindle shaped cells with indistinct cytoplasmic margins and stacking nuclei arranged in digitating fascicles. Verocay bodies, a region where bands of fusiform nuclei alternate with clear zones devoid of nuclei may also be present [2, 16]. The tissue in Antoni B however, is hypocellular, reticulated and oedematous. They show degeneration, no spindle cells and are sometimes haemorrhagic necrosis. The volume of Antoni B is often scant and the cells within it are thin, contain lymphocytes, lipid laden histiocytes and hyalinised blood vessels [16]. Antoni B areas often intermingle with Antoni A, but they still appear well demarcated [2, 16]. S100 protein is a specific marker demonstrating a tumour's neuroectodermal origin [2, 8]. Schwannomas will almost always show strong nuclear and cytoplasmic immunoreactivity with S100 protein which is essential in differentiating it from other tumours [1, 7].

Treatment approaches are chosen based on the lesion's size, location and extent [3, 10]. The aim is to have excellent exposure and visualization of the sinonasal region while considering the cosmetic burden [1, 10]. Techniques advocated previously, include lateral rhinotomy, frontal craniotomy, midface degloving and Caldwell-Luc approach [2, 10]. Some cases require a combination of techniques [1]. Now, Functional Endoscopic Sinus Surgery (FESS) is preferred to other traditional invasive methods since it does not require external incision and is associated with improved cosmesis, diminished blood loss, lower morbidity and shorter hospital stay [2, 7, 8].

Schwannomas normally show good progress by just surgical resection and recurrence is rare after complete excision [2, 8]. However, follow up is needed as relapses or persistence occurs in 10% of cases [8]. Post-operative radiation therapy is reserved for malignancies [12]. At UKMMC, four of six patients were treated by FESS, the center's preferred technique. Patient 2 was deemed unsuitable for FESS because of the possibility of inducing unwanted morbidity like ocular opthalmoplegia. Therefore, patient opted for Cyber Knife, a less invasive form of intervention [17]. Patient 4 had an intracranial surgery because imaging demonstrated that her tumour had extensive intracranial involvement.

CONCLUSION

In conclusion, our research adds to existing work previously published. SNS are rare and their presentations often correspond to their site. In addition, we suggest that the site of involvement (origin and extension) of SNS is more informative than the site of origin. We also suggest that following studies give equal attention to SNS that arise from outside the sinonasal cavity. Endoscopy, CT scans and MRIs are helpful in facilitating an accurate diagnosis [6, 15] SNS show specific histopathological findings which are important in differentiating them from other types of tumour [2, 7, 16]. The main treatment for SNS is Functional Endoscopic Sinus Surgery (FESS) because of its fewer surgical complications, better prognosis and lower recurrence rate as shown in our study [2, 7, 8].

Table-1: Relationship between location of tumour and presenting symptoms

Pt	Site (Side)	Extension	Infiltration	Chief Complaint (months)	Other Symptoms
1	Nasal cavity (R)	M,E	None	Nasal Obstruction (6)	Nasal,Paranasal
2	Pterygopalatine area (R)	I	Plt Musc	Facial Numbness (12)	Paranasal,Intracranial
3	Infratemporal fossa (R)	P,M,I	Pty Musc	Headache (6)	Paranasal,Intracranial
4	Infratemporal fossa (R)	NC,S,E,I	Inf Turb	Facial Numbness (2)	Nasal,Paranasal,Intracranial
5	Pterygopalatine area (L)	IF+M,S	None	Facial Numbness (6)	Paranasal
6	Nasal cavity (L)	None	None	Nasal Obstruction (24)	Nasal,Intracranial

Table-2: Demographics and tumour characteristics (present study and seven recent studies)

Study (Year)	Sex(No.Pts)	Age	Site	Size (cm)	Extension	Infiltration
PRESENT STUDY	F(5), M(1)	52.3 ± 5.2	2 Nasal cavity, 2 Paranasal sinus, 2 Infratemporal fossa	3.6 ± 0.4	N/a	N/a
Kim (2013)[6]	F(5), M(7)	37.1 ± 1.4	N/a	3.5 ± 0.5	N/a	N/a
Yu (2006)[5]	F(1)	27	Nasal cavity	Not stated	I	Absent
Mangubat (2011)[18]	M(1)	35	Frontal sinus	Not stated	Ns	Absent
Ulu (2009)[7]	F(1)	71	Nasal cavity	3.8 ± 0.6	E, F, Io	Present
Kodama (2010)[19]	F(1)	81	Nasal cavity	Not stated	M	Absent
Somasekhar (2008)[13]	F(1)	28	Nasal cavity	Not stated	M	Absent
Ohashi (2013)[20]	F(1)	31	Nasal cavity	Not stated	E, S	Absent

Table-3: Comparisons of clincal presentations (present study and seven recent studies)

Study	Chief Complaint (months)	Symptoms
THIS STUDY	3 Facial numbness (6.7± 2.9), 2 Nasal obstruction (15± 9), 1 Headache (6) [Mean(9.3± 3.2)]	N/a
KIM'13 [6]	6 Nasal obstruction (5.0± 1.0), 2 Rhinorrhoea (13± 11), 1 Headache (1),1 Epistaxis (2), 1 Exophthalmos (1), 1 Anterior cheek pain (3) [Mean(5.3±1.8)]	N/a
YU'06[5]	Nasal Obstruction (8)	Nasal
MANGUBAT'11[18]	Incidental findings after accident	None
ULU'09[7]	Medial deviation and diplopia of left eye (1.5)	Nasal, Intracranial
KODAMA'10[19]	Nasal obstruction (Not stated)	Nasal
SOMASEKHAR'08[13]	Nasal obstruction (48)	Nasal, Intracranial
OHASHI'13[20]	Anosmia (3)	Nasal, Intracranial

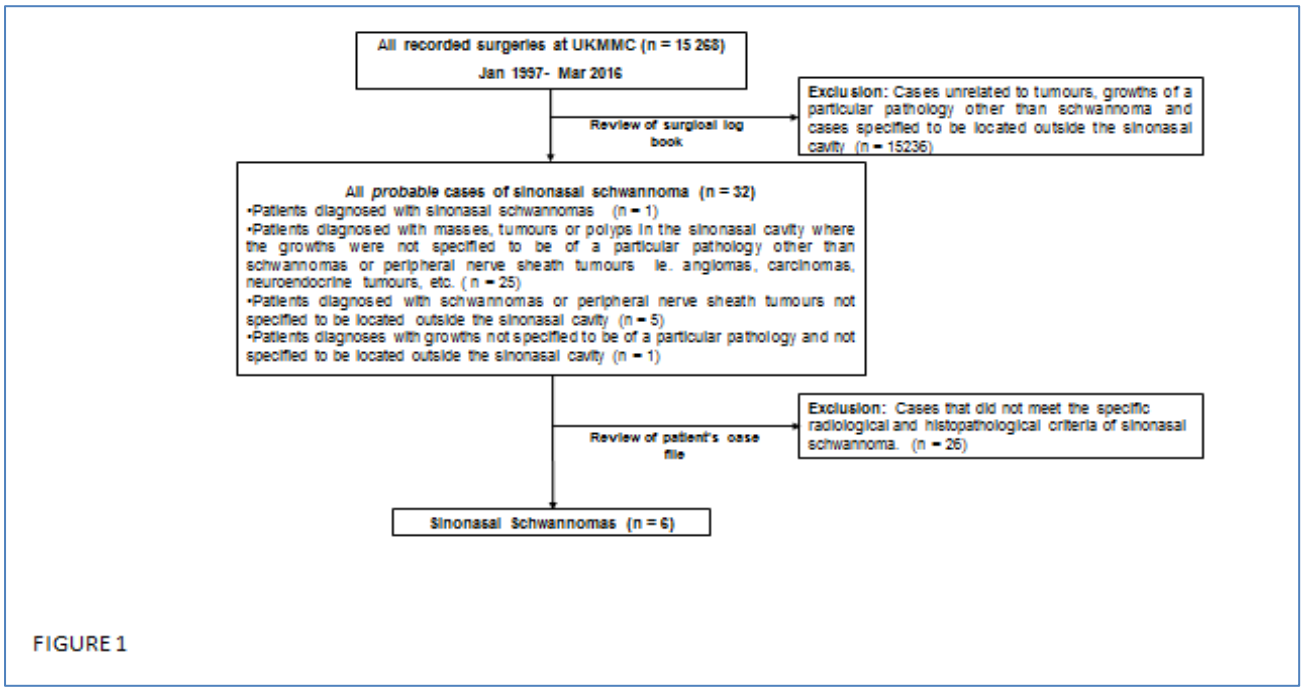

Fig-1: Algorithm demonstrating the process of inclusion and exclusion of sinonasal schwannoma cases seen at the National University of Malaysia Medical Centre

A, Postcontrast CT scan shows a large mass with ill-defined border exhibiting central lucency extending superiorly into the intracranial cavity and inferiorly without intraorbital involvement.

B, Axial CT scan shows a mildly enhancing mass in the right infratemporal fossa. It compresses anteriorly onto the right maxillary sinus with scalloping and thinning of the posterior wall of the maxillary sinus, however there is no bony erosion. Thinning of pterygoid plate can be seen.

C, Coronal T1-weighted MRI shows marked and heterogenous enhancement of the mass at the lateral wall of the right cavernous sinus.

D, Coronal T2-weighted MRI shows heterogenous signal intensity of the mass extending from the middle cranial fossa through the base of skull into the right infratemporal fossa.

E, Coronal T1-weighted MRI shows the extension of the mass into the right middle meatus with early encroachment onto the right middle turbinate. The mass has also eroded the floor of the right maxillary sinus.

F, Axial T2-weighted MRI shows fluid retention in both maxillary sinuses and also right sphenoid sinus.

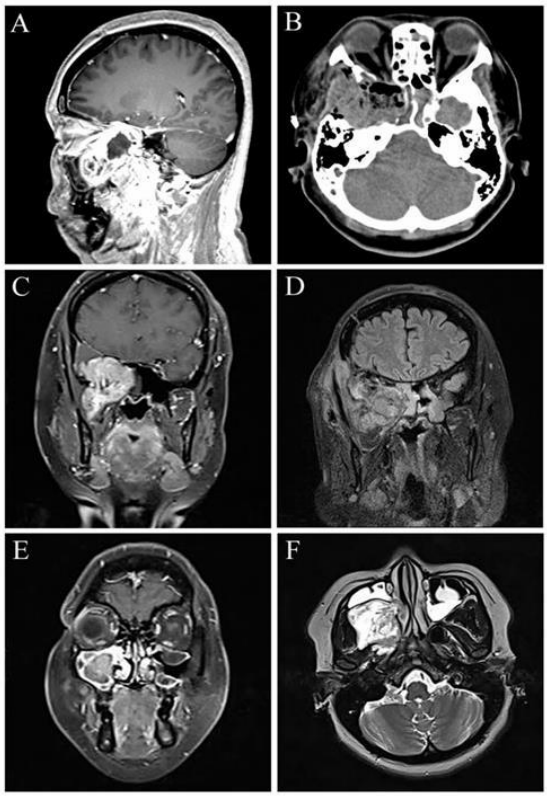

Fig-2: Representative radiological image from Patient 4. Schwannoma of the infratemporal fossa infiltrating the inferior turbinate in a 42-year-old female

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