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Case report

Infiltrative mass of the skull base and nasopharynx: A diagnostic conundrum

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HIGHLIGHTS

- Timely thorough investigation is critical to reduce the risk of irreversible damage.
- Prompt biopsy is essential to exclude both neoplasia and inflammatory conditions.
- Early corticosteroid administration is necessary to limit local infiltration.

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ABSTRACT

Inflammatory skull base masses are enigmatic and often behaviourally unpredictable. We present a case of idiopathic hypertrophic pachymeningitis (IHP) forming a central skull base mass to illustrate the process required when one investigates such skull base lesions. This is the first description of mass forming or tumefactive IHP extending into the nasopharynx. A 32-year old woman presented with frontal headaches and nasal discharge. She then deteriorated and was admitted with worsening headaches, serosanguinous nasal discharge and bilateral ophthalmoplegia. Multimodality imaging confirmed a destructive central skull base soft tissue mass involving the posterior clivus, floor of sphenoid sinus, nasopharynx and extending into both cavernous sinuses. Unfortunately, the patient continued to deteriorate despite treatment with broad-spectrum antibiotics. Cerebrospinal fluid, blood tests and transnasal biopsies for histology and microbiology did not reveal a diagnosis. Further neuroimaging revealed extension of the mass. Early corticosteroid treatment demonstrated radical improvement although an initial reducing regime resulted in significant rebound deterioration. She was stable on discharge with slowly reducing low dose oral prednisolone and azathioprine. We discuss the complexity of this case paying special attention to the process followed in order to arrive at a diagnosis of idiopathic hypertrophic pachymeningitis based on both the clinical progression and the detailed analysis of serial skull base imaging. Knowledge of the potential underlying aetiologies, characteristic radiological features, common pathogens and the impact on blood serology can narrow the potential differentials and may avoid the morbidity associated with extensive resective procedures.

1. Introduction

The investigation and management of skull base lesions often presents a challenge to the clinician. Inflammatory skull base masses are rare and unpredictable but can be associated with significant morbidity [1]. The differential diagnosis is extensive. Performing a diagnostic biopsy is often associated with risk of significant morbidity and hence the decision to opt for definitive or adjuvant surgical management further amplifies these risks. Knowledge of the potential underlying aetiologies, characteristic radiological features, common pathogens and the impact on blood serology can narrow the potential differentials and may avoid the morbidity associated with extensive resective procedures.

We present a case of idiopathic hypertrophic pachymeningitis (IHP) forming a central skull base mass to illustrate the process required when one investigates such lesions. This is the first description of mass forming IHP extending into the nasopharynx.

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2. Case presentation

A 32-year-old Nigerian woman presented to her primary care physician with a 1-month history of frontal headaches and serous nasal discharge. She was commenced on enteral antibiotics for presumed bacterial sinusitis. However, her symptoms progressed over the following 2 months. She was admitted to a tertiary care centre with worsening frontal headaches, ophthalmoplegia and serosanguinous nasal discharge. She had no other relevant past medical history. Examination demonstrated a right abducens palsy with associated mild right proptosis and ptosis.

Preliminary blood tests revealed a raised C-reactive protein (CRP) of 88 mg/L, erythrocyte sedimentation rate (ESR) of 128 mm/h, white cell count of 14.9×10^9/l, and neutrophils 12.8×10^9/l. Magnetic resonance imaging (MRI) confirmed an extensive destructive central skull base soft tissue mass involving the posterior clivus, floor of sphenoid sinus and nasopharynx. The mass extended into both cavernous sinuses, more marked on the right, with compression of both internal carotid arteries, for which she was started on prophylactic aspirin. The paranasal sinuses, orbits and brain parenchyma remained uninvolved. (See Fig. 1)

Causes of pachymeningitis were explored. Serum angiotensin converting enzyme (ACE), anti-nuclear antibodies (ANA), rheumatoid factor (RF) and anti-neutrophilic cytoplasmic antibodies (ANCA) levels were within normal limits and both her initial and repeat human immunodeficiency virus (HIV) test were negative. Cerebrospinal fluid (CSF) virology was negative, no organisms were grown on culture and protein was mildly raised at 0.48 mg/dL. She underwent two endoscopic transnasal biopsies of the lesion, both of which suggested reactive lymphoid hyperplasia alongside acute-on-chronic inflammation. This was thought to represent a possible acute response to infection. There were no features suggestive of lymphoma, granuloma or other malignancy. On advice from Infectious Disease a thorax/abdominal/pelvis CT was arranged, which did not reveal any other sites of inflammation.

She was commenced on intravenous meropenem 2 g three times daily, but continued to deteriorate with worsening right-sided ophthalmoplegia and ptosis. Microbiology and Neurology teams advised both anti-fungal and antituberculous treatment regimens along with prednisolone 50 mg once daily to minimise neurological morbidity. There was gradual improvement over the following two to three weeks with marked reduction in both ophthalmoplegia and ptosis. Her daily corticosteroids were slowly reduced, however this resulted in a dramatic deterioration in her visual acuity to perception of light in the left and finger counting in the right. Bilateral ophthalmoplegia recurred. Urgent MRI brain revealed progression of the mass to involve the pituitary fossa, further into both cavernous sinuses and increased compression of the internal carotid arteries. (See Fig. 2) She was commenced on high dose intravenous methylprednisolone. Within the first 24 h of therapy the patient noted a remarkable improvement in her visual acuity and her antibiotics were ceased.

An endoscopic transsphenoidal biopsy of sphenoid sinus mucosa and pituitary lesion was then undertaken. During the procedure thickened fibrotic dura was noted. Gram, Ziehl–Neelsen and periodic acid-Schiff staining were all negative. The histopathology excluded tuberculosis, sarcoidosis, granulomatosis with polyangitis and lymphoma. Immunoglobulin G4 (IgG4) serum levels were noted to be within normal limits excluding IgG4-related sclerosing disease. With these exhaustive investigations being negative, a diagnosis of idiopathic tumefactive hypertrophic pachymeningitis was proposed.

The patient continued to improve on the methylprednisolone and was converted to prednisolone 60 mg. Under supervision by the Neurology team she was commenced on azathioprine 100 mg, gradually increased to 200 mg once daily with a weaning course of corticosteroids.

At discharge she was stable on 200 mg azathioprine, 15 mg prednisolone and long-term low dose corticosteroids. The investigative MRI at this stage demonstrated significant reduction in uptake and size of the skull base lesion. Near vision had improved to N6 on the left and N8 on the right. (See Fig. 3) She is currently under close outpatient supervision and should she remain asymptomatic, a final MRI is planned for three years.

3. Discussion

Central skull base lesions extending into the nasopharynx are a rare occurrence. IHP is an uncommon condition characterised by diffuse or localised thickening of the dura mater (pachymeninges), causing progressive neurological deficits [2]. It is a diagnosis of exclusion. It is very uncommon for pachymeningeal hypertrophy to manifest as a large enhancing mass more accurately known as idiopathic tumefactive hypertrophic pachymeningitis (ITHP) [3]. We present an extremely rare case of ITHP extending into the nasopharynx, which has not previously been described in the literature. Our case highlights the importance of thorough diagnostic evaluation of any skull base or nasopharyngeal lesion to exclude infective, inflammatory, neoplastic and connective tissue aetiologies (see Table 1).

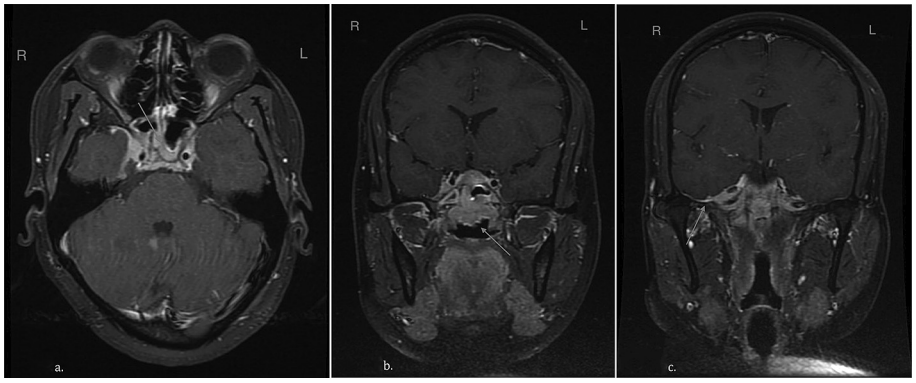

Fig. 1. a) MRI head T1 weighted post contrast axial slice. Demonstrating high uptake central skull base lesion at sphenoid sinus (arrow), cavernous sinus with compression of carotid arteries. b) MRI head T1 weighted post contrast coronal slice. A more anterior coronal slice demonstrating mass lesion at cavernous sinus, sphenoid sinus and extension into nasopharynx (arrow).c) MRI head T1 weighted post contrast coronal slice. A more posterior coronal slice demonstrating extension of mass into the right middle cranial fossa (arrow).

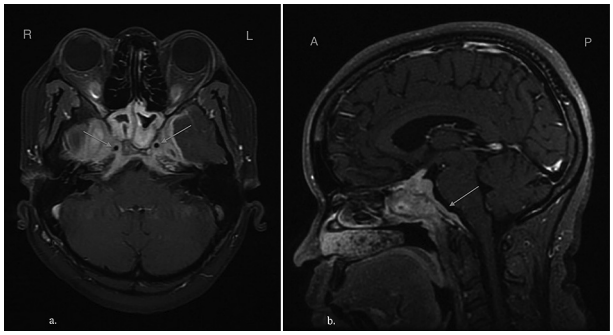

Fig. 2. a) MRI head T1 weighted post contrast axial slice. After termination of corticosteroids, MRI demonstrates significant hypertrophy of skull base lesion with further compression of internal carotid arteries in cavernous sinuses (arrows). b) MRI head T1 weighted post contrast saggital slice in midline. After termination of corticosteroids, MRI demonstrates mass extending from skull base into pituitary fossa, through sphenoid sinus and into nasopharynx. Involvement of posterior clivus is clear (arrow).

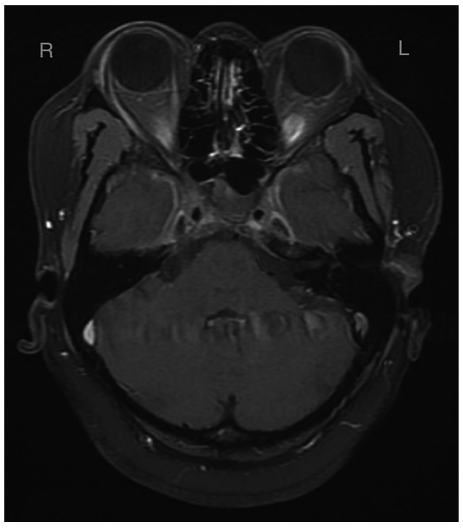

Fig. 3. MRI head T1 weighted post contrast axial slice. After long-term treatment, MRI demonstrates significant resolution of the central skull base lesion, in both size and uptake. The internal carotid diameters are normalised.

A clinical entity similar to IHP was first described by Charcot and Joffroy in 1869 but the term was first mentioned in 1949 by Naffziger and Stern as a chronic inflammatory process of the dura [4]. Since then it has been reported numerous times in the literature, but never as a central base of skull mass extending into the nasopharynx. IHP commonly presents with headache and cranial neuropathy, which typically present with two distinct spectra depending on the site of pachymeningeal involvement: cavernous sinus to superior orbital fissure or falcotentorial to posterior fossa [5]. Due to the intricacy of structures involved, ITHP can present with complex focal neurology and psychiatric symptoms [2]. Our patient presented with headache and diplopia, but also serosanguinous nasal discharge, which has not been associated with ITHP or IHP in the historical literature.

Neuroimaging is essential in diagnosing the extent of skull base lesions. Gadolinium-enhanced MRI is superior when imaging the pachymeninges, and commonly demonstrates IHP with smooth or nodular dural thickening that is isointense or hypointense with both T1-and T2-weighted sequences, with clear enhancement after administration of contrast [3]. Interestingly, in a study of nine patients with intracranial pachymeningeal thickening, Gadolinium-enhanced MRI was able to characterise different patterns of meningeal thickening which also correlated to the clinical pattern of presentation [6]. Correlation with clinical course and symptomatic improvement is disputed however [7,8]. A delay in contrast MRI has been suggested as the most common cause of delayed diagnosis [9]. Thorax/abdomen/pelvis CT may also be useful in excluding systemic vasculitic phenomena such as granulomatosis with polyangitis [5].

Numerous pathologies that can cause pachymeningeal thickening need to be excluded through a combination of neuroimaging, serology and histological analysis. In our patient, due to the presence of normal serum ACE and the absence of non-caseating granuloma or extracranial manifestations, neurosarcoidosis was excluded [5,10]. A negative Ziehl–Neelsen staining of the tissue sample and negative culture for mycobacteria excluded tuberculous pachymeningitis [5]. Rheumatoid pachymeningitis was excluded through the absence of articular features and negative ANA and RF. Fungal infection and other infective causes were rejected as diagnoses through CSF analysis and microbial tissue culture [5]. Dural carcinomatosis, lymphoma and meningioma were excluded histopathologically and through negative CSF

Table 1
Causes of hypertrophic pachymeningitis.

Causes of hypertrophic pachymeningitis	
Infective	Tuberculous meningitis
	Mycosis (Cryptococcus, Histoplasma, Coccidioides)
	Lyme disease
	Syphilis
	Human T-cell lymphotrophic virus 1
	Cysticercosis
Inflammatory	Sarcoidosis
Neoplastic	Carcinomatous meningitis
	Lymphomatous meningitis
	Meningioma
Connective tissue disorders & vasculitides	Rheumatoid arthritis
	Wegener's granulomatosis
	Orbital pseudotumour
	Tolosa–Hunt syndrome
	Multifocal fibrosclerosis
	IgG4-related disease
Miscellaneous	Spontaneous intracranial hypotension
	Chronic haemodialysis
	Mucopolysaccharidosis
	Chronic intrathecal drug administration
Idiopathic	No cause identified after extensive investigation and follow up.

cytology. IgG4-related disease was also excluded through normal serum IgG4 levels [11].

The goal of therapy is to avoid permanent cranial neuropathy [5]. Corticosteroids appear to consistently alleviate symptoms and reverse progression of IHP, though there are reports of progression during corticosteroid therapy [5]. Bosman et al. report the successful use of oral methotrexate in a patient with IHP who was non-responsive to corticosteroid therapy [12]. They present this as an alternative in those who develop resistance or serious side effects from chronic corticosteroid use. Empirical trials of antituberculous medication has been advocated in the past, however this was not successful in our patient [13]. Surgical excision is an option when medical therapy fails in order to relieve the compressive effects of the lesion and has been shown to provide lasting relief when decompressing the optic canal [3,5,14]. Radiotherapy has been attempted in cases of IHP and in an orbital pseudotumour with pachymenigitic features but was ineffective [15,16]. The clinical course of ITHP is variable. Our patient deteriorated upon steroid reduction but underwent remission upon re-institution of intravenous high dose methylprednisolone.

4. Conclusion

We illustrate the comprehensive process necessary when investigating skull base masses and associated nasopharyngeal lesions. Our case highlights the importance of early CT and MRI in diagnosing base of skull lesions as well as a full panel of microbiological and serological investigations to narrow the differential diagnosis. Prompt biopsy of lesions involving the skull base or nasopharyngeal is essential to exclude neoplasia or other life-threatening conditions and this should be followed by timely corticosteroid administration to limit local infiltration. We advise this should be undertaken prior to consideration of more definitive treatment, whether surgical resection or alternative adjuvant therapy.

Ethical approval

Written consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of Annals of Medicine and Surgery.

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Author contribution

MMG led the case write up and literature review overall. JG participated in the management of this patient, gained consent for use of images for publication of this case. JG also made large contributions to drafting this manuscript several times. KAS lead initial drafts of the entire manuscript. RB led the care of this patient, advised on themes to cover for drafting and edited the manuscript on multiple occasions. All authors have read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflicts of interests.

Guarantor

Manish M George.

Unique Identifying Number (UIN)

Not applicable.

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