ABSTRACT
Trotter’s syndrome is a clinical triad of signs associated with tumours of the nasopharynx. The pathognomonic features could be stated as – unilateral deafness, pain in the area supplied by the mandibular nerve and asymmetry of the soft palate due to ipsilateral infiltration. This syndrome, in itself, is an ominous harbinger of an occult lesion, that could prove fatal in many instances. The article presents a review of the clinical presentation, investigative imaging and differential diagnosis of Trotter’s syndrome.

KEYWORDS: Trotter’s syndrome, imaging nasopharynx.

INTRODUCTION
Trotter’s syndrome is a unique symptom complex which classically entails a triad of specific clinical features. These include unilateral deafness, pain in the region supplied by the mandibular nerve and asymmetry of the soft palate due to ipsilateral infiltration. By Trotter’s original description (1911), these signs could only be produced by a lesion in the Sinus of Morgagni, deep to the lateral wall of nasopharynx, which did not encroach on the lumen of nasopharynx but instead crept submucously along the surface of the bone, disseminating deeply in a lateral and forwards direction and producing pressure symptoms of the structures encased there. The syndrome is also known by the moniker of Syndrome of the Sinus of Morgagni.[1,2,3]

Anatomy of Sinus of Morgagni
The sinus of Morgagni lies between the superior concave border of the superior pharyngeal constrictor muscle muscle below and the skull base above (Fig. 1). This superior constrictor gap is bridged by the buccopharyngeal fascia which is attached anteriorly to the posterior border of the medial pterygoid lamina and superiorly to the basi-occiput and apex of petrous temporal bone. The dimensions of the sinus may be stated as 1.8 cm in length (anterior to posterior) and 0.5 cm in height. It is 2.5 cm medial to the foramen ovale. From anterior to posterior, the contents of the sinus are – (i) the tensor palati muscle, (ii) the Eustachian tube and (iii) the levator palati muscle. The fossa of Rosenmüller lies posterior to the opening of Eustachian tube. Lateral to the sinus lie the foramen ovale and the mandibular nerve passing through it. Lateral to the nerve is the lateral pterygoid muscle.[1,4]

Clinical Features
The symptoms of the syndrome appear in the following sequence[1,2] and can be explained on the basis of the structures enclosed within the sinus.
1. Hearing loss results due to compression of the Eustachian tube (Fig. 2). The deafness is of the middle ear type. It is persistent but may be temporarily relieved by inflation of eustachian tube. The deafness may be accompanied by secretory catarrah in the middle ear. Though deafness is an early symptom, it may not be the leading symptom and tests may be required for its diagnosis.
2. Neuralgia or pain is caused by the compression of the mandibular nerve passing through the foramen ovale. The pain gradually transforms into anaesthesia. As the neoplastic infiltration disseminates, the maxillary nerve emerging through foramen rotundum into the pterygopalatine fossa may also be affected.
3. There may be alterations in the sensibility, i.e. anaesthesia, over the lower jaw in region of mental foramen. This may be easily overlooked and must be deliberately tested for.
4. The asymmetry of the soft palate, noticeable when the palate is relaxed, is due to infiltration of the levator palati muscle and not due to paralysis.
5. At a later stage of the disease, the infiltration may spread to the upper alveolus along the greater tuberosity. Trismus occurs when the neoplastic invasion extends to the medial pterygoid muscle.[1,4]
6. The clinical symptoms may be accompanied by involvement of cervical lymph nodes, which may even be the initial presenting symptom. Lymph node involvement forms an important part of the staging of nasopharyngeal tumours. Retropharyngeal lymph
nodes constitute the earliest site of metastasis, followed by levels II, III and occasionally levels I and IV.[3]

Incidence of Trotter’s Syndrome[1,2]
Trotter’s series (1911) reported 9 cases, with age of subjects between 18 to 35 years. Gardham (1929) recorded 9 cases and mentioned the upper limit of age as 60 years. Asherson (1951) recorded 4 cases over a duration of 25 years. The incidence is greater among males. However, the overall incidence is extremely low, especially in relation to malignant disease of maxilla or the paranasal sinuses. This is because the syndrome is neither produced by a malignancy of nasopharynx which encroaches on the lumen, nor by malignant disease of maxilla at any stage before the latter is clinically recognizable.

New (1922) reported 71 cases of malignant disease of nasopharynx, Sheldon (1919) recorded 65 cases, while Furstenberg (1935) reported 40 cases. In none of these series, Trotter’s syndrome was recognized or described. Cases of malignant disease of maxilla (including posterior paranasal sinuses), were reviewed in 1950 by six observers – three rhinologists (Wilson, Capps and Seed), two radiologists (Windeyer and Campbell), one pathologist (Hewer) and one dental surgeon (Rushton). The composite series reported hundreds of cases. In none of the subjects, Trotter’s syndrome was recognized or reported.

Differential Diagnosis[1]
Trotter’s syndrome must be distinguished from two other similar clinical syndromes – the pterygopalatine fossa syndrome and the Jacod syndrome of the carrefour petro-sphenoidale. The pterygopalatine fossa syndrome results from a lesion originating in the pterygopalatine fossa and is characterized by the early involvement of the maxillary nerve, with pain in the regions supplied by this nerve. The Jacod syndrome occurs from an intracranial lesion in the middle cranial fossa, with involvement of the nerves traversing the foramen rotundum, foramen ovale and sphenoidal fissure.[1]

For the purpose of differential diagnosis, both of these syndromes are discussed below in detail.

1. The Pterygopalatine Fossa Syndrome: this syndrome presents with the following characteristic symptoms, in the sequence mentioned below.
   a) Continuous dull or severe, but persistent neuralgia in distribution of maxillary nerve, especially referred to upper back molar teeth.
   b) Numbness in distribution of infraorbital nerve, i.e. over the cheek and infraorbital foramen area. It may be overlooked unless specially elucidated.
   c) Neuralgia referred to lower jaw, at a later stage, due to involvement of mandibular nerve.
   d) Unilateral deafness of middle-ear type.
   e) Palate affected at a later stage by paralysis and anaesthesia.
   f) Fullness in temporal fossa, externally visible at a later stage.
   g) Paralysis of pterygoid muscles, producing deviation of lower jaw on mouth opening.
   h) Unilateral blindness may appear at later stage, due to extension of tumour through inferior orbital fissure to optic nerve.
   i) Fullness in lateral wall of nasopharynx, examined by posterior rhinoscopy.
   j) Enlargement of deep cervical and retropharyngeal lymph nodes, unilateral or bilateral.

The pterygopalatine fossa syndrome arises when the pathologic lesion is situated in pterygopalatine fossa, and not the sinus of Morgagni. Hence, involvement of maxillary nerve precedes involvement of mandibular nerve.

2. Jacod Syndrome
In Jacod’s syndrome, the origin of lesion is intracranial, along the floor of middle cranial fossa, where the antero-medial end of petrous temporal bone abuts the greater wing of sphenoid. Jacod named this latter area as “Carrefour petro-sphenoidale”. Jacod diagnosed the pathologic lesion as a “peritubular sarcoma”[2], which would spread through osseous portion of Eustachian tube to reach the floor of middle cranial fossa, in the region of Carrefour petro-sphenoidale, so that the IIth to VIth cranial nerves are involved by the lesion. The nerves emerging through jugular fossa escape involvement. However, in Trotter’s syndrome, cranial nerves IIth, IIIth and IVth are not involved by pathology.

Pathology of Lesions Implicated
The neoplastic afflictions of the nasopharynx may be classified into benign and malignant. The benign lesions mainly comprise of juvenile angiofibroma (most common), vascular tumours, congenital tumours (hamartoma, choristoma, teratoma), dermoids, chondroma, craniopharyngioma, rhabdomyoma, salivary gland anlage tumours in neonates, inverted papilloma, solitary fibrous tumour, paraganglioma (chemodectoma) and meningioma. The malignant lesions comprise of nasopharyngeal carcinoma, malignant lymphoma, melanoma, rhabdomyosarcoma, olfactory neuroblastoma (esthesioneuroblastoma), Ewing sarcoma, primitive neuroectodermal tumours, chordoma, adenocarcinomas and cystic adenoid carcinomas. Nasopharyngeal carcinoma (NPC) is the most common malignant neoplasm originating in the nasopharynx.[8,9,10] The WHO classification[11] (2005) classifies NPC into – (i) Keratinizing squamous cell carcinoma; (ii) Non-keratinizing carcinoma, which is further divided into (a) Differentiated type and (b) Undifferentiated type; (iii) Basaloid squamous cell carcinoma. It must be emphasized that the signs exclusive of Trotter’s Syndrome will be produced when any of the lesions listed above, infiltrates towards the skull base rather than encroaching on the lumen of the nasopharynx. However, as stated by Trotter, Gardham and Asherson.[1,2] the
symptom complex of Trotter’s syndrome is most commonly produced by an “endothelioma”, which is now classified as non-keratinizing undifferentiated (Type II) nasopharyngeal carcinoma. That is because this lesion has a typical tendency towards an endophytic submucosal spread, rather than invade the lumen of nasopharynx in exophytic manner.

Clinical Investigations
The clinical diagnosis of tumours of the nasopharynx is based on diagnostic endoscopy, biopsy and various imaging techniques including CT, MRI and PET-CT. The neoplastic infiltration of the sinus of Morgagni and its three dimensional dissemination to adjacent areas can be readily visualized with CT and MRI. Fat planes obliteration and loss of definition of muscular margins comprise highly useful diagnostic findings. Contrast enhanced MRI (gadolinium) with fat suppression has shown to be superior to CT in soft tissues evaluation, both in superficial and deep nasopharyngeal regions. It also helps to clearly differentiate lymphoid tissue from musculature.

This is a very important diagnostic advantage of MRI since the most important prognostic factor in NPC is the depth and degree of infiltration into neighbouring structures and not the tumour size. Apart from this, MRI helps to identify cranial nerve involvement.\textsuperscript{5,6}

However, CT is superior to MRI in evaluating the involvement of the bone structures in the skull base. PET-CT is important for the assessment of recurrent tumours and small lymph nodes.\textsuperscript{5,7}

Fig. 1: A schematic diagram illustrating the lateral view of sinus of morgagni

Fig 2: A schematic diagram illustrating the structures related to sinus of morgagni as analysed from the basi-occiput view.
METHODS
Using Pubmed and Google™ Scholar, a literature search was performed up until March 2016, for articles published in English, using the search terms ‘Trotter’s syndrome’, ‘imaging nasopharynx’. The abstracts of all the studies found in the search were analysed to judge their relevance and inclusion. Articles with insufficient data were excluded. References of the selected articles were searched to identify further related studies. The lack of prospective studies and randomization precluded a formal meta-analysis.

RESULTS
Trotter’s syndrome is a well recognised clinical presentation of nasopharyngeal pathology. Though very few case series are available for study of this unique clinical symptom complex, the differential diagnosis is now well understood and investigative imaging allows proper evaluation of pathology implicated in this syndrome.

CONCLUSIONS
Advances in imaging diagnosis and an understanding of the pathogenesis and differential diagnosis of this syndrome, have brought a paradigm shift in the war against tumours of skull base implicated in this syndrome.

CONFLICT OF INTERESTS
The author declares that there is no conflict of interests that could influence this work.

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