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CASE REPORT

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Unusual case of skull base adenoid cystic carcinoma presenting as skull base osteomyelitis: case report

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Abstract

Background: Adenoid cystic carcinoma is a rare malignancy. Tumours of palatal region with minor salivary gland origin do not generally present at an early stage as the tumour is submucosal with symptoms prevalent only when there is evidence of perineural spread of the tumour. We report a case of adenoid cystic carcinoma of the palate with rare presentation of left ear discharge and diplopia on left lateral gaze. We discuss the case with emphasis on imaging evaluation mimicking a case of infective etiology with adjacent skull base osteomyelitis on initial presentation. However, on follow-up and further evaluation the patient was diagnosed as adenoid cystic carcinoma of hard palate on left side.

Case presentation: A 25-year-old male patient has presented to Jagadguru Sri Shivarathreeswara Hospital in August 2019 with complaints of left ear discharge and diplopia on left lateral gaze since 1 week. The clinical and imaging findings was suggestive of infective etiology and the patient was treated for the same with IV antibiotics. Repeat magnetic resonance imaging was then done which revealed definitive reduction in the severity of inflammation suggestive of response to therapy. Patient was then discharged and was followed up. Three months later, the patient came with complaints of mass in left nasal cavity. Patient was then referred for contrast enhanced computed tomography neck strongly suggestive of neoplastic etiology. The patient was then operated and histopathological examination of the biopsy revealed adenoid cystic carcinoma.

Conclusions: Tumours of palatal region with minor salivary gland origin do not generally present at an early stage as the tumour is submucosal with symptoms prevalent only when there is evidence of perineural spread of the tumour. In our case patient presented with lateral rectus palsy, involvement of meckel's cave, trigeminal nerve involvement and cavernous sinus involvement which are strong indicators of the perineural and locoregional spread of the tumour. Hence, it is important for the radiologist and clinician to strongly suspect and evaluate for a primary lesion of the head and neck when such a radiological presentation has been demonstrated.

Keywords: Carcinoma, Adenoid cystic, Cylindroma, Skull base, Osteomyelitis, Neoplasm invasiveness

Background

Adenoid cystic carcinoma (ACC) is a rare malignant neoplasm of the major and minor salivary glands with a mean crude incidence of 1.0–1.3/100000/year and they are responsible for about 20% of the malignant salivary gland tumours, 10% of all the epithelial salivary neoplasms and 1–2% of the head and neck malignancies [1].

It is important to identify features of skull base neoplasm such as perineural spread (PNS). The common neoplasms causing PNS are ACC, adenocarcinoma, squamous cell carcinoma, basal cell carcinoma, undifferentiated carcinoma, melanoma, mucoepidermoid carcinoma, carcinoma ex pleomorphic adenoma and lymphoma [1]. The most common neoplasm causing PNS

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is ACC with incidence of approximately 50% [2]. However, PNS is a late finding in ACC as it is a sign of distant metastasis [2]. Moreover, upto 50% of the patients with imaging evidence of PNS are usually asymptomatic and are usually not diagnosed based on clinical presentation itself [3]. Furthermore, clinical presentation of a patient with symptoms of PNS without a known primary is rare with the neoplasm being unrevealing despite obtaining a detailed clinical history and clinical examination [2, 3]. Even on strong clinical suspicion of PNS, surgeons are unlikely to operate or obtain a biopsy on the basis of clinical presentation alone [4]. Hence, suggesting the importance for the awareness and prompt imaging interpretation by the radiologist in such cases.

The most common modalities for detection of PNS are computed tomography (CT) and magnetic resonance imaging (MRI) [2–6]. The specificity, sensitivity and accuracy for detection of PNS on CT is 100%, 55% and 62%, respectively, and for MRI being 100%, 73% and 77%, respectively [4]. The imaging features to identify PNS includes disproportionate or unequal prominence of the affected nerve and its enhancement, loss of definition or obliteration of the fat planes adjacent to the nerve, changes of denervation of the end organs (such as affecting the muscles of mastication and facial expression in involvement of the maxillary and mandibular divisions of trigeminal nerve) and enlargement of the foramina of the corresponding nerves [2]. Table 1 shows the most important sites and its contents in assessing PNS for ACC.

The findings on CT includes assessment of the nerve and perineural fat surrounding the cranial nerves for disproportionate enlargement and loss of definition of the perineural fat [2, 3]. Whereas, CT reconstructions using bone algorithm should be used to assess for erosion, destruction and disproportionate enlargement of the foramen [2, 3].

Table 1 Important sites and contents in assessing PNS for ACC [2]

Important sites	Contents
Pterygopalatine fossa	Maxillary division (V2) of trigeminal nerve and its branches
Stylomastoid foramen	Cranial nerve VII—Facial nerve
Foramen ovale	Mandibular division (V3) of trigeminal nerve and its branches
Foramen rotundum	Maxillary division (V2) of trigeminal nerve
Cavernous sinus and Meckel cave	Trigeminal nerve and its branches

Contrast enhanced high resolution MRI should be obtained using a field of view of 18 cm, high resolution matrix of (320×192) and slice thickness of 3 mm^3. The MRI findings detailed by Stambuk et al. [3] are as described below. Normally, the intracranial cisternal portions of the cranial nerve does not normally show significant contrast enhancement due to the preserved blood nerve barrier and minimal perineural venous plexus. Whereas, the extracranial portions of the nerve shows contrast enhancement due to the perineural plexus showing a tram-track or target like enhancement. As tumor growth is seen on the nerve this can be observed as thick, nodular and mass like; however, normal portions of the nerve are normally appearing radiologically such that such uninvolved areas are skip areas. Furthermore, the involved nerves shows disproportionate enlargement and enhancement as involvement is usually unilateral. This PNS involvement is seen as loss of definition of the perineural fat which is best assessed on thin section (3 mm) coronal and axial fat suppressed T1 sequences. Whereas, end organ denvervation changes are seen on T1 and T2 sequences. Acute denervation changes includes involved muscles showing hyperintense signal on T2 sequence and showing enhancement. Whereas, subacute denervation shows T1 hyperintensity without volume loss and chronic denervations showing muscle loss, loss of enhancement and fatty atrophy. Some indirect signs have also been described such as middle ear effusion due to dysfunction of the eustacian tube secondary to denervation of the tensor veli palatine muscle. Blooming artifacts causes obscuration of the foramen ovale, rotundum and vidian canals which are observed when sphenoid sinuses are adequately aerated. This is susceptible especially on fat suppression sequence more so on 3 Tesla systems than 1.5 Tesla systems; however, this can be overcome by also using post contrast T1 sequence without fat suppression. Lack of significant interval changes in the nerves suggests stability on post-operative imaging. Furthermore, post radiotherapy can pose challenges as the soft tissue changes in the involved nerve can be seen permanently thereby posing a diagnostic dilemma.

It is also important to also note that PNS should be differentiated from perineural invasion (PNI) [2, 3]. So, PNS is detected by imaging and refers to the presence of a macroscopic tumour extension which is seen away from the primary site of the tumour [2, 3]. Whereas, PNI is diagnosed by pathological study of the specimen's histology especially in a tissue sample which incorporates the tumour involving any of the three layers of the nerve sheath [2, 3]. The incidence of PNI in head and neck neoplasms is very low and has been reported as being between 2.5 and 5.0% with incidence of PNS being even lower [2].

We report a rare case of adenoid cystic carcinoma of the palate with presentation of left ear discharge and diplopia on left lateral gaze. We discuss the case with emphasis on imaging evaluation mimicking a case of infective etiology with adjacent skull base osteomyelitis on initial presentation. However, on follow-up and further evaluation the patient was diagnosed as adenoid cystic carcinoma of hard palate on left side.

Case presentation

A 25-year-old male patient has presented to our institution in August 2019 with complaints of left ear discharge and diplopia on left lateral gaze since 1 week. The patient was apparently normal previously with no similar complaints in the past.

Clinical examination revealed discharge and congestion of the left external auditory canal, the tympanic membrane was bulging and congested. Rinne's and Weber's tests are physical examination tools to assess for conductive and sensorineural hearing loss. Both tests were performed using tuning forks utilizing their vibrating tips to appreciate the intensity of the sound. Normally, in Rinne's test air conduction is greater than bone conduction and Weber's test will not demonstrate lateralization to any ear and will be heard in the midline. However, in our case Rinne's test revealed bone conduction to be greater than air conduction at 256 Hertz (Hz), 512 Hz and 1024 Hz and Weber's test was lateralised to left, thereby suggesting conductive hearing loss in the left ear. The patient also had left lateral rectus palsy. Rest of the clinical examination including throat, oropharynx, neck and nose was normal. Laboratory investigations revealed normocytic normochromic blood picture with elevated erythrocyte sedimentation rate (ESR). Ear discharge was tested for gram staining and culture sensitivity which revealed gram positive cocci in clusters and culture of staphylococcus aureus, respectively.

High resolution computed tomography (HRCT) temporal bone (Fig. 1 and 2) done to evaluate the extent of disease, showed soft tissue density involving the left epitympanum, mesotympanum involving Prussak's space extending into mastoid air cells, opacification of petrous apex with erosive changes in adjacent bone with erosion of walls of facial canal and exposed tympanic part of facial nerve and soft tissue opacification of skull base with adjacent bony erosion suggesting a diagnosis of cholesteatoma with probable petrous apicitis and osteomyelitis of skull base. Patient was then referred to Magnetic Resonance Imaging (MRI) (Fig. 3a–c) for further evaluation. Contrast enhanced MRI temporal bone has revealed oto-mastoiditis with petrous apicitis, extension of inflammation into cavernous sinus and orbital apex with adjacent meningitis and osteomyelitis of the skull base on left side.

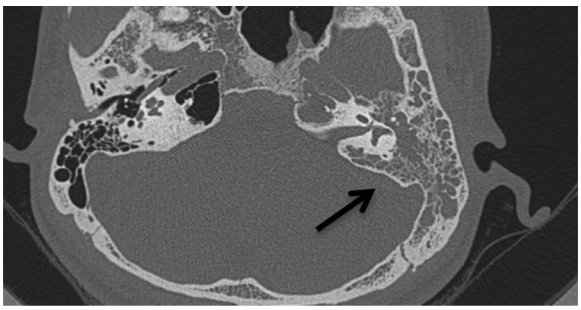

Fig. 1 A 25-year-old male patient (→ showing the following imaging features in axial section) soft tissue density in the left epitympanum, mesotympanum involving prussak's space extending into mastoid air cells, opacification of petrous apex, erosive changes in adjacent bone with erosion of walls of facial canal and exposed tympanic part of facial nerve and soft tissue opacification of skull base with adjacent bony erosion

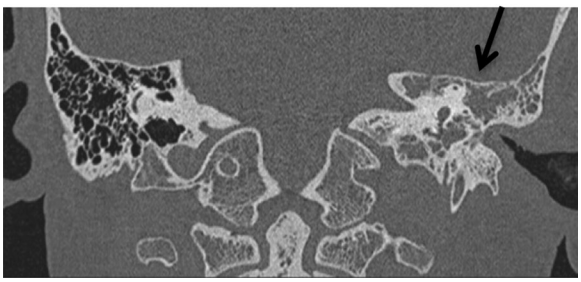

Fig. 2 A 25-year-old male patient (→ showing the following imaging features in coronal section) soft tissue density in the left epitympanum, mesotympanum involving prussak's space extending into mastoid air cells, opacification of petrous apex, erosive changes in adjacent bone with erosion of walls of facial canal and exposed tympanic part of facial nerve and soft tissue opacification of skull base with adjacent bony erosion

The above myriad of clinical and imaging findings was suggestive of infective etiology (possibly chronic suppurative otitis media with gradenigo syndrome) and the patient was treated for the same with IV antibiotics. Furthermore, 2 weeks after treatment patient has undergone oto-endoscopic examination with myringotomy which showed retracted and congested tympanic membrane on left side and IV antibiotics were continued further. Repeat MRI was then done which revealed definitive reduction in the severity of inflammation predominantly around cavernous sinus, perineural thickening and leptomeningeal enhancement on left side suggestive of response to therapy. Patient was then discharged and was followed up.

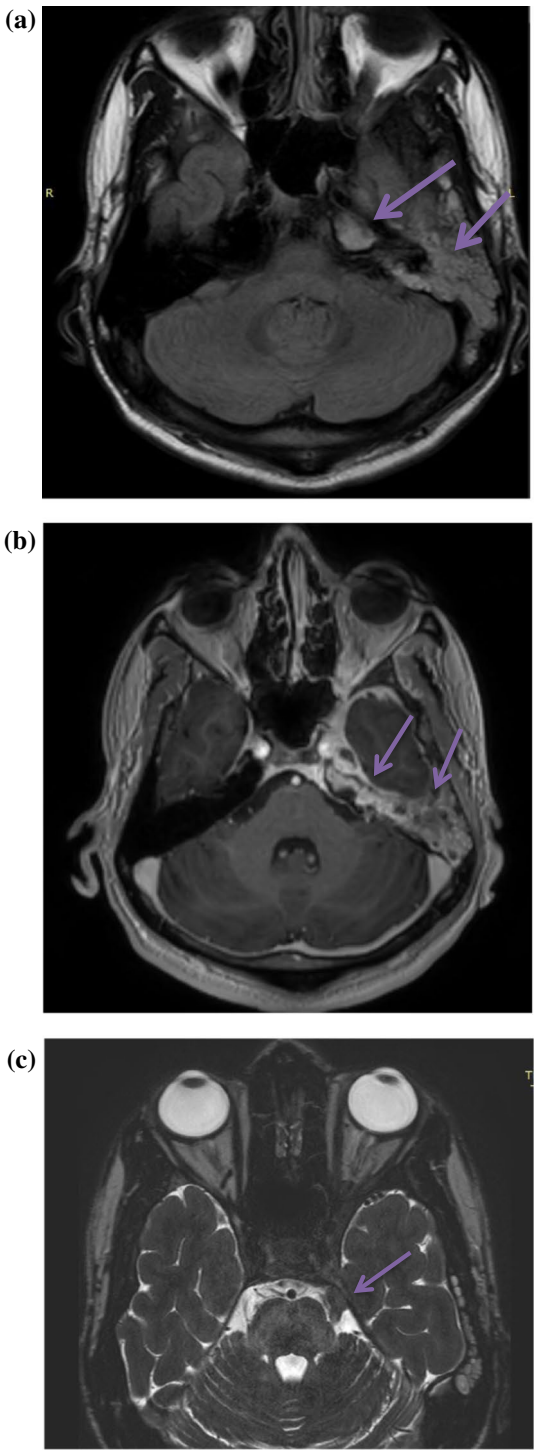

Fig. 3 **a** A 25-year-old male patient (→ showing the following imaging features) altered signal intensity seen in left middle ear cavity, petrous apex and mastoid cavity extending into the cavernous sinus and left orbital apex causing mass effect on the left ICA and altered signal intensity appearing hyperintense on FLAIR sequence in left temporal bone, clivus and sphenoid bone. **b** A 25-year-old male patient (→ showing the following imaging features) homogeneous enhancement of left middle ear cavity, petrous apex and mastoid cavity extending into the cavernous sinus and left orbital apex and heterogenous enhancement of left temporal bone, clivus and sphenoid bone. Significant pachymeningeal enhancement in the suprasellar, pre-pontine cistern, along the internal acoustic meatus and temporal regions on left side. **c** A 25-year-old male patient. CISS sequence (→ showing the following imaging features) thickened and edematous left trigeminal and abducens nerves at the entry points into the Meckel's cave and Dorello's canal

Three months later, the patient came with complaints of mass in left nasal cavity. Patient was then referred for contrast enhanced computed tomography (CECT) neck which revealed minimally enhancing soft tissue lesion inferior to the palatine process on left side with adjacent bony destruction and soft tissue extension strongly suggestive of neoplastic etiology. Biopsy with septoplasty was performed under general anaesthesia and was subjected to histopathological examination. Microscopic examination showed subepithelium with tumour cells arranged in tubular, cribriform patterns, in cords and trabeculae separated by broad hyaline septae at places. Individual cells had scanty cytoplasm with round to oval nuclei and inconspicuous nucleoli. The above features were suggestive of ACC.

Subsequently, the patient has undergone surgical resection in December 2019 under general anaesthesia for inferior partial maxillectomy on left side. The resected tissue was subjected for histopathological examination which revealed tumour cells arranged in tubular and cribriform patterns. They were also arranged in solid pattern focally. Round to oval individual tumour cells were seen with high Nuclear: Cytoplasmic (N:C) ratio, hyperchromatic nuclei and scanty cytoplasm. Perineural and bone infiltration was also identified. Hence, revealing ACC.

Follow-up

Patient was then referred to oncologist in view of postoperative chemotherapy and radiotherapy and was advised to follow-up. On receiving few cycles of chemotherapy and radiotherapy, contrast enhanced MRI of head and neck was performed in May 2020 for follow-up. MRI revealed nodular thickening in left oropharynx at the level of mandibular angle possibly suggesting radiotherapy changes or residual lesion. Furthermore, radiotherapy changes were seen in the left infratemporal fossa and left medial and lateral pterygoid muscles showing homogenous enhancement with left oto-mastoiditis, petrous apicitis and orbital apex extension.

Discussion

Adenoid cystic carcinoma is a rare malignancy with a mean crude incidence of 1.0–1.3/100000/year, represent 10% of all epithelial salivary neoplasms and 20% of all malignant salivary gland tumours [1]. The US National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) programme indicates a decline of ACC in the USA with 5-year, 10-year and 15-year survival rate among all stages of ACC in head and neck patients being 90.34%, 79.88% and 69.22%, respectively [5]. It can be observed in both young and old age however appears most frequently in the fifth to sixth decade with no gender predominance [4, 5].

The tumor predominantly involves the head and neck but it can also involve upper respiratory tract, breast, female reproductive tract, skin, thymus, prostate and esophagus [1]. The lesion can have a variable presentation. It can present as a well-defined mass or an ill-defined mass with infiltration into surrounding structures, where the latter was the presentation in our case. The lesion presented with involvement of middle ear cavity, mastoid, Prussak's space, orbital apex, cavernous sinus, perineural and adjacent skull base invasion suggesting a late presentation with T4a staging of the tumour. The invasive nature of the tumour is very peculiar. The invasion can occur by direct extension, haematogenous spread or perineural invasion wherein the last method of invasion being the most common. Intracranial invasion of the salivary gland ACC's occurs predominantly from three routes: the mandibular and maxillary nerves, the internal carotid artery and the eustacian tube [7].

In our case, T2 and FLAIR hyperintensities were seen involving left middle ear cavity, petrous apex and mastoid cavity extending into cavernous sinus and left orbital apex. There was also involvement of left trigeminal and abducens nerves at the entry points into the Meckel's cave and Dorello's canal, respectively, which are thickened and edematous with mild signal changes and homogenous post contrast enhancement. There is similar pachymeningeal enhancement in the Suprasellar, pre-pontine cistern, along the internal acoustic meatus and temporal regions on the left side. In retrospect the above findings can be attributed to the typical presentation of ACC however without prior clinical suspicion the above findings can be mistaken for other etiologies as seen in our case where only later the diagnosis of ACC has been made. Similar findings can be seen in other cases as shown in Figs. 4 and 5 which was a case of right malignant otitis externa with oto-mastoiditis, skull base osteomyelitis (involving right petrous apex and clivus) and cellulitis of right prepharyngeal and parapharyngeal space. The above case described in

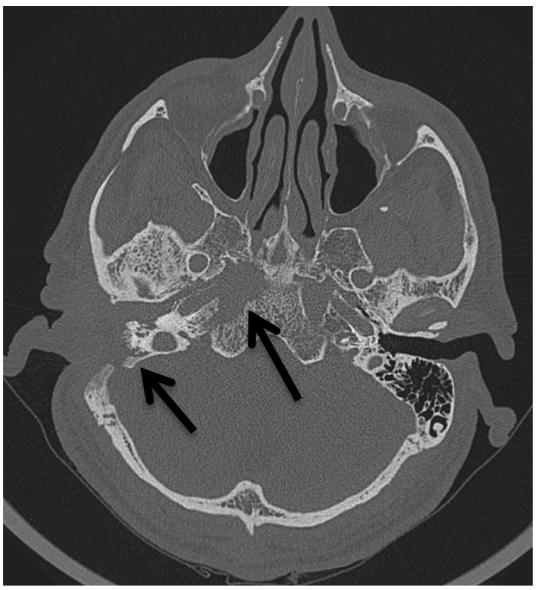

Fig. 4 A 66-year-old male (→ showing the following imaging features in axial section) right malignant otitis externa with oto-mastoiditis and skull base osteomyelitis. Shows heterodense soft tissue density lesion in the external auditory canal, mastoid air cells extending to the middle ear cavity with involvement of Prussak's space and epitympanic recess with erosion of external auditory canal, tympanic membrane, scutum, petro-mastoid and tympanic parts of right temporal bone, right inferolateral part of clivus, walls of right hypoglossal canal, anterior wall of posterior cranial fossa and tympanic part of right facial canal; Partial erosion of incus and stapes. Rarefaction of squamous and petro-mastoid parts of right temporal bone

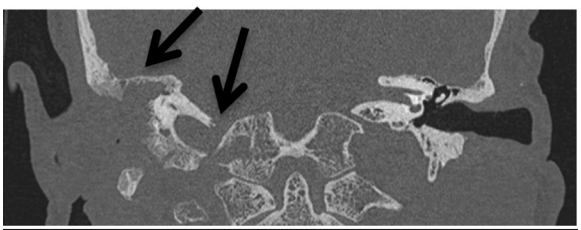

Fig. 5 A 66-year-old male (→ showing the following imaging features in coronal section) right malignant otitis externa with oto-mastoiditis and skull base osteomyelitis. Shows heterodense soft tissue density lesion in the external auditory canal, mastoid air cells extending to the middle ear cavity with involvement of Prussak's space and epitympanic recess with erosion of external auditory canal, tympanic membrane, scutum, petro-mastoid and tympanic parts of right temporal bone, right inferolateral part of clivus, walls of right hypoglossal canal, anterior wall of posterior cranial fossa and tympanic part of right facial canal; Partial erosion of incus and stapes. Rarefaction of squamous and petro-mastoid parts of right temporal bone

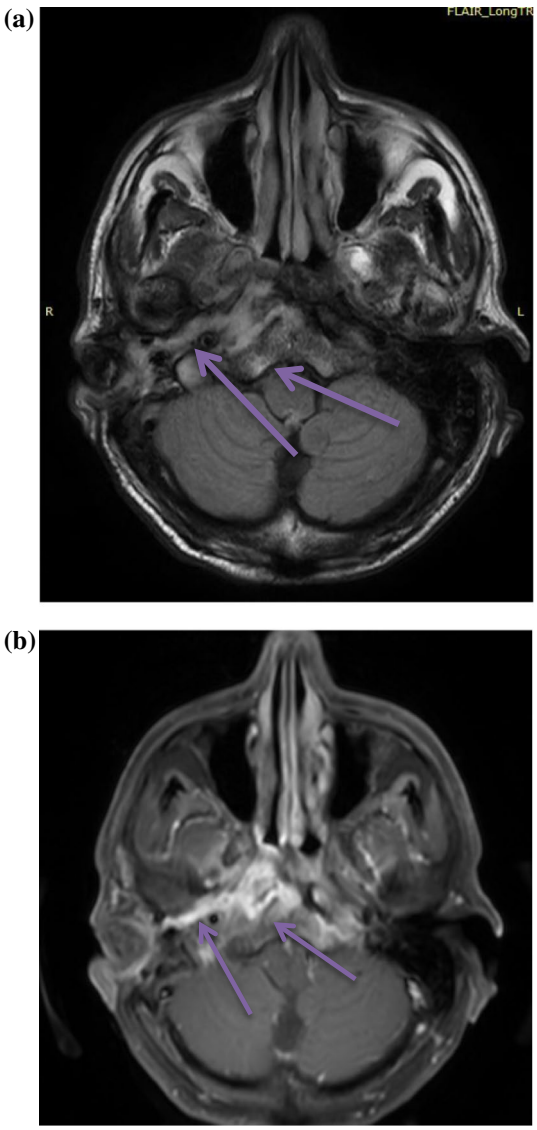

Fig. 6 **a** A 66-year-old male (→ showing the following imaging features) right malignant otitis externa with oto-mastoiditis and skull base osteomyelitis. Shows FLAIR hyperintensity in right middle ear cavity, right mastoid, right petrous apex, clivus, left occipital condyle right torus tubaris, right pterygoid space, nasopharynx, longus colli muscle and visualised right parapharyngeal and prevertebral spaces. **b** A 66-year-old male (→ showing the following imaging features) right malignant otitis externa with oto-mastoiditis and skull base osteomyelitis. Shows significant post contrast enhancement in right middle ear cavity, right mastoid, right petrous apex and clivus. Mild enhancement of right fronto-parieto-occipital pachy meninges

Figs. 4, 5 and 6 is a 66-year-old male patient with history of right ear pain and discharge since 3 months. The ear pain was pricking type and aggravated at night. The patient also had pain radiating to the post aural region, right side of head, right temporal region, retro-orbital pain, right sided facial pain and right eye diplopia. Examination revealed granulomatous discharge in the right external auditory canal right sided, non-visualisation of right tympanic membrane, fistulous discharge in the right preauricular area and right mastoid tenderness. Furthermore, Rinne's test revealed bone conduction to be greater than air conduction in the right ear and Weber's test lateralised to the right ear suggesting conductive hearing loss of the right ear. Blood examination revealed neutrophilic leucocytosis, gram stain revealed gram positive cocci and gram negative bacilli. The patient was treated with intravenous antibiotics, antifungals, anticoagulants, analgesics with supportive management after which the patient showed clinical improvement.

Diffusion weighted imaging (DWI) which demonstrates Brownian motion of water molecules within a lesion has been proposed to provide differences between benign and malignant lesions. Studies suggested that most benign lesions (excluding benign Warthin's tumours) show higher apparent diffusion coefficient (ADC) values compared to malignant lesions [8–10]. However there is a wide consensus with various studying showing contradicting findings. Some studies suggest that a significant difference exists between benign and malignant lesions whereas other studies suggest the contrary that the ADC values overlap between benign and malignant lesions. In the study by Chen et al. [6], it was suggested that overlap of ADC values occurs due to tumour heterogeneity and suggests that non-Gaussian diffusion model such as Fractional order calculus (FROC) helps to characterise heterogenous tumours more profoundly than simple Gaussian models which depends on presence of tumour homogeneity. As observed in our case, there is no evidence of diffusion restriction.

Singh et al. [11] shows that there are various sites of perineural spread of ACC depending on the primary location of the tumour. For palate, the potential sites includes the greater and lesser palatine nerves (branches of maxillary nerve, V2) and on to pterygopalatine fossa (PPF) and foramen rotundum. For nasal cavity and maxillary sinus, infraorbital nerve (branch of maxillary nerve, V2) and on to PPF and foramen rotundum. For retromolar trigone and tongue, inferior alveolar nerve and lingual nerves (branches of mandibular nerve, V3) and on to foramen ovale. For parotid gland, facial nerve (stylomastoid foramen, petrous portion internal auditory canal) and auriculotemporal branch of V3. Hence the Pterygopalatine fossa (PPF) is an important landmark for tumour spread as it links inferior orbital fissure, cavernous sinus, orbital apex with foramen rotundum, infratemporal fossa, vidian canal with the pterygomaxillary fissure, sphenopalatine foramen and greater and lesser palatine canals.

Singh et al. [11] has also described the important imaging features for perineural spread such as enlargement/erosion of foramen, nerve enlargement/enhancement, obliteration of fat plane around the nerves including PPF, enlargement and convexity of lateral cavernous sinus wall, soft tissue replacement of CSF filled Meckel's cave and muscular denervation (firstly edema and enhancement followed by atrophy). Lastly, Singh et al. [11] has also suggested how several conditions including infection, inflammation, trauma, vascular lesions and haematoma can mimic ACC. Hence, importance of clinical suspicion must be stressed upon.

Adenoid cystic carcinoma is a rare entity responsible for less than 1% of tumours arising from the head and neck, with only few cases reported in literature. In our case there was no clinical suspicion for the presence of ACC on initial presentation. The study by Badger et al. [2] suggests that the clinical symptoms of PNS such as pain, paresthesia and diplopia without the presence of a known primary head and neck tumor is a rare presentation to suggest tumor metastasis and such individuals are typically misdiagnosed to for trigeminal neuralgia. Imaging findings have been supportive of a skull base infiltration. By considering the age, clinical evaluation and imaging findings, a plausible diagnosis of an infective aetiology was considered and patient was initially diagnosed as CSOM with gradenigo syndrome.

As we have observed, ACC is difficult to distinguish based on imaging findings alone. The above myriad of findings which suggests suspicion for a diagnosis is vague unless there is a high clinical suspicion to suggest potential perineural spread of the ACC presenting as a skull base infiltrative lesion. Secondly, the presentation of ACC is typically more common in an older age group. Various studies have suggested the clinical dilemma that skull base osteomyelitis cannot be differentiated from malignancy as both entities shows skull base erosion, destruction and PNS where skull base malignancy is ruled out only on the basis of multiple negative biopsies for the latter [12–16].

Conclusions

Tumours of palatal region with minor salivary gland origin do not generally present at an early stage as the tumour is submucosal with symptoms prevalent only when there is evidence of PNS. This suggests the reason why initial clinical examination of the palate was essentially normal with no obvious lesion being detected. However, in retrospect patient presenting with lateral rectus palsy, involvement of Meckel's cave, trigeminal nerve involvement and cavernous sinus involvement are strong indicators of the perineural and locoregional spread of the tumour. Hence, it is important for the radiologist and clinician to strongly suspect and evaluate for a primary lesion of the head and neck when such a radiological presentation has been demonstrated.

Abbreviations

CSOM: Chronic suppurative otitis media; MRI: Magenetic resonance imaging; CECT: Contrast enhanced computed tomography; ESR: Erythrocyte sedimentation rate; HRCT: High resolution computed tomography; DWI: Diffusion weighted imaging; ADC: Apparent diffusion coefficient; ACC: Adenoid cystic carcinoma; N:C ratio: Nuclear: cytoplasmic ratio; PNS: Perineural spread; PNI: Perineural invasion.

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Author contributions

Dr SPS contributed to study conception and design, analysis and interpretation of data, draft manuscript preparation. Dr BSARM contributed to study conception and design, analysis and interpretation of data, draft manuscript preparation. Dr SKD contributed to supervision of the project, analysis and interpretation of data. Dr RH contributed to supervision of the project, analysis and interpretation of data. All the above authors have read and approved the manuscript.

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Availability of data and material

The datasets generated and/or analyzed during the current study are not publicly available due to privacy of the study participant.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent obtained.

Competing interests

Not applicable.

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