CASE REPORT

Large retropharyngeal abscess: a case of mistaken identity

N Makaram, R Gohil, Q Gardiner, J Manickavasagam

Department of
Otorhinolaryngology, Ninewells
Hospital, Dundee, UK

Correspondence to
R Gohil,
rohit.gohil@nhs.net

Accepted 30 August 2016

SUMMARY

We report an unusual case of nasopharyngeal carcinoma (NPC), presenting initially as a retropharyngeal collection. We discuss the investigation, diagnosis and management of NPC and furthermore review the literature of NPC, emphasising the varied presentation. A 44-year-old Caucasian male ex-smoker presented with a 10-day history of a painless left-sided neck lump; progressive dysphagia and unintentional weight loss. Examination demonstrated a large left posterior pharyngeal swelling with soft palatal effacement, confirmed on nasoendoscopy. A CT scan revealed a fluid collection in the retropharyngeal space, which partially occluded the nasopharynx, and numerous satellite lesions were identified along with cervical lymphadenopathy. The suspected abscess was drained in theatre and nasopharyngeal biopsies were taken. These revealed Epstein-Barr virus-positive NPC. Staging investigations revealed a T4N2M0 carcinoma. Treatment consisted of radical chemoradiation therapy with curative intent. NPC is known for its varied and late presentation, and is an important condition to be aware of when considering a differential diagnosis of pharyngeal masses.

BACKGROUND

Nasopharyngeal carcinoma (NPC) is an uncommon cancer, which is particularly rare in the Western world. The age-adjusted incidence for both genders is <1 per 100 000 population. In 2008, there was an approximate incidence of 84 400 cases of NPC and 21 600 NPC-related deaths internationally.^{1 2} It is extremely common in Southeast Asia, especially in Guangdong—being 25 times as common here, than the global rate.³

NPC has a striking geographical variation, being much more common in Africa, Southern and Eastern Asia than the Western world. It is also strongly associated with several environmental factors, including Epstein-Barr virus (EBV) infection, dietary factors (including salted fish), smoking, alcohol consumption and occupational exposures.^{4–7}

NPC is noted for its often deceptive and varied presentations, resulting in late presentation and subsequent diagnosis in most patients—when the cancer is advanced and potentially metastatic. The ability to provide a means of curative therapy proves extremely challenging, and thus mortality remains high despite significant advances in oncological therapy. Mortality is quoted as 50% overall at 5 years, although older populations have poorer survival rates, with populations between 65 and 74 having an overall 5-year survival rate of 35%.⁸

CASE PRESENTATION

A 44-year-old Caucasian male ex-smoker was referred with a presumed peritonsillar abscess, suffering a 10-day history of a worsening painless left neck lump associated with progressive dysphagia for solids. He had unintentional weight loss of 5 kg over the preceding 3 months, new febrile episodes and general malaise. There were no other ‘red-flag’ symptoms such as bloody nasal discharge, nasal obstruction or unexplained weight loss; his airway was not compromised. There was no symptom of unilateral hearing loss or focal neurological deficits. The patient had no significant medical history.

Clinical examination demonstrated a large pharyngeal swelling arising from the left posterior wall effacing against the soft palate, there was no trismus but a hyponasal voice was exhibited. Diffuse left-sided lymphadenopathy was also demonstrated. Flexible nasoendoscopy confirmed the pharyngeal origin of this swelling, with a patent hypopharyngeal airway distal to it.

The initial differential diagnosis of peritonsillar abscess was disputed as the swelling was of posterior pharyngeal and not peritonsillar origin, nor did the patient have uvular deviation or trismus on examination.

INVESTIGATIONS

Full blood count, white cell count, liver function, all electrolytes and coagulation studies were within normal limits. Of note was a raised C reactive protein titre of 36 mg/L.

A contrast CT of the neck demonstrated an extensive enhancing fluid collection in the retropharynx, with partial nasopharyngeal/oropharyngeal occlusion; there were scattered smaller collections superiorly. Abnormal infiltrative soft tissue was identified at the nasopharynx extending up to the skull base, along with cervical lymphadenopathy (figure 1). A further CT scan of the neck, chest and abdomen to assess for distant metastases was performed.

An incision and drainage of the collection was undertaken, and the collection wall and nasopharynx were examined and biopsied (figure 2).

Histology confirmed poorly differentiated squamous cell carcinoma infiltrating native sinonasal mucosa. In situ hybridisation demonstrated strong expression of EBV. A diagnosis of NPC was made.

Following multidisciplinary team discussion, a postintervention MRI was undertaken (figure 3). The final staging was T4N2M0 type 2b non-keratinising undifferentiated lymphoepithelial NPC. This was due to the extent of the primary tumour,

CrossMark

To cite: Makaram N, Gohil R, Gardiner Q, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-216718

Figure 1 Axial (A) and sagittal (B) CT images showing extent of nasopharyngeal tumour and associated collection.

especially through the left foramen ovale of the skull base and minimal extension intracranially.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses of nasopharyngeal masses include:

- ▶ Tumours of the skull;
- ▶ Other primary nasopharyngeal malignancies:
- ▶ Lymphoma,
- ▶ Adenocarcinoma,
- ▶ Carcinosarcoma,
- ▶ Extramedullary plasmacytoma,
- ▶ Fibrosarcoma,
- ▶ Melanoma,
- ▶ Rhabdomyosarcoma,
- ▶ Sinonasal mucosal melanoma,
- ▶ Nasopharyngeal tuberculosis,
- ▶ Nasopharyngeal angiofibroma,
- ▶ Chondrosarcoma,
- ▶ Chordoma,
- ▶ Persistent benign adenoidal tissue.

TREATMENT

The malaise and fevers settled with intravenous antibiotic management; however, the pharyngeal swelling persisted.

After extensive discussion with oncology colleagues, combined radical chemoradiotherapy with curative intent was

deemed to be optimal therapy. This consisted of two cycles of induction chemotherapy with cisplatin/5-fluorouracil followed by 6 weeks of radical concurrent chemoradiation. Surgery was not considered as is not indicated in the primary management of NPC.

OUTCOME AND FOLLOW-UP

The last follow-up at 6 months posttreatment has shown no local or regional recurrence of the tumour, and the patient remains clinically well. This was illustrated with a 6-month post-treatment MRI (figure 4). He is due to undergo long-term follow-up at increasing intervals with the head and neck oncology team.

Figure 2 Intraoperative image showing the nasoendoscopic view of the nasopharynx following drainage of collection and prior to nasopharyngeal biopsy. Note the haemorrhagic swelling and association with the contralateral Eustachian tube orifice.

Figure 3 Coronal T2-weighted MRI of the tumour following surgical drainage of retropharyngeal collection. The tumour is noted to be invading into the left lateral aspect of the prevertebral space, posterior and left lateral oropharynx, left masticator space and superiorly at the left foramen ovale.

Figure 4 T1-weighted axial MRI at the level of the nasopharynx which shows complete response of the tumour to treatment.

DISCUSSION

NPC is classed as a non-lymphomatous, squamous-cell carcinoma, presenting in the epithelial lining of the nasopharynx. The carcinoma is classically seen at the fossa of Rosenmüller, posterior to the medial crura of the Eustachian tube opening in the nasopharynx.⁹

The presentation of NPC mimicking a retropharyngeal abscess is extremely rare. Only one previous study was identified, reported in 1999, where a 45-year-old oriental man presented with fever, sore throat and a painful neck swelling.¹⁰

Furthermore, since 1999, there have been significant advances both in the diagnosis and treatment of this rare carcinoma. We provide below an outline of current knowledge of NPC, including an illustration of these diagnostic and therapeutic advances.

Classification of NPC

The classification of NPC has undergone several iterations over the past four decades. It is broadly divided into keratinising, non-keratinising or undifferentiated (and basaloid—most common subtype).¹¹

This is due to the influence of this distinction on prognosis of these tumours, with non-keratinising being more radiosensitive.¹² The presence of keratin is associated with reduced local control and survival.¹³

The latest classification was devised by the WHO and their document in 1978, which has been updated on several occasions.¹⁴

The diagnosis of keratinising and basaloid NPC is facilitated by the identification of malignant epithelium that shows overt keratinisation. Non-keratinising carcinomas have subtle morphological features that are often obscured by dense lymphoid stroma, which gives the alternative title for this subtype, lymphoepithelial carcinoma. Non-keratinising NPC is almost always associated with EBV infection markers.^{15 16}

EBV and NPC

There is strong evidence to show that infection or colonisation of EBV is correlated with patients diagnosed with NPC. The EBV-encoded RNA signal is shown in almost all tumour cells when subjected to in situ hybridisation.¹⁶ In contrast, normal tissue almost always fails to express EBV-encoded RNA, except perhaps for a few lymphoid cells.¹⁷ As is consistent with the literature, the tumour we encountered in this patient was strongly positive for EBV-harboring malignant cells. Specifically, as previously stated, non-keratinising NPC is particularly closely associated with EBV, with serological markers of EBV infection detected in almost all cases of non-keratinising NPC.¹⁸

EBV infects >90% of the world's population.¹⁶ Among other malignancies, EBV has a strong association with the development of NPC.

Certain specific EBV genes have been shown to be consistently expressed in NPCs and in early premalignant lesions, and the proteins encoded have been shown to have significant aberrant effects on cellular growth, and native cellular gene expression, which has been implicated as a significant predisposing factor in the development of the highly invasive, malignant growth of the carcinoma.¹⁸ EBV may additionally have influence in the most common molecular alteration seen in NPC tumourigenesis, the inactivation of the p16 tumour suppressor gene on 9p21 by homozygous deletion and methylation.^{19 20} However, further research on EBV's role in NPC tumourigenesis is required to characterise its influence.

Indeed, it is now known that all non-keratinising carcinomas harbour EBV. This has enabled enhanced diagnostic methods, such as the use of in situ hybridisation for EBV-encoded early RNA (EBER), latent membrane protein-1 (LMP-1) and quantitative PCR to detect EBV nucleic acid (DNA and RNA) in NPC cells, serum and plasma.^{15 20}

Presentation

NPC is often associated with varied, atypical and late presentations; however, there are more typical and common presenting features which are crucial to be aware of.

Patients with NPC tend to present with symptoms from one or more of the following four categories:

1. Presence of tumour mass in the nasopharynx leading to epistaxis, nasal obstruction and discharge;
2. Tinnitus and deafness due to extension of the tumour to the paranasopharyngeal space and disruption of the Eustachian tube;
3. Perineural infiltration leading to V and VI cranial nerve palsy, producing symptoms such as diplopia, headache and facial pain or paraesthesia;
4. Neck masses, particularly in the upper levels of the neck and often bilateral due to the midline location of tumour, in combination with systemic features of anorexia, weight loss and malaise, which should arouse suspicion of distant spread.¹⁸

Other reported presentations include conductive hearing loss with unilateral persistent middle ear effusion (due to Eustachian tube obstruction) and cranial nerve dysfunction (particularly of III, IV, V and VI, due to tumour infiltration into skull base exit foramina. Our patient was observed to have tumour invasion into the left foramen ovale, but had no manifest symptoms from this.^{15 21}

Lee *et al*¹⁹ performed a recent large retrospective analysis investigating the relative incidence of presenting symptoms of NPC. They found that the most common presenting symptom

was neck mass (76%), followed by nasal dysfunction (73%), aural dysfunction (62%), headache (35%), diplopia (11%), facial numbness (8%), weight loss (7%) and trismus (3%).

The same study identified the physical signs most commonly coexisting at first presentation to be enlarged neck nodes (75%) and cranial nerve palsy (20%), with the most commonly affected nerves being III, V, XII.¹⁹

Several theories postulating an aetiology similar to our patient's presentation of NPC have been put forward. One proposed theory for abscess formation in a tumour is that the centre of the malignant lesion is susceptible to infection due to tumour necrosis, which results from an insufficient vascular supply.²² This appears to be an apt mechanism for the presentation described in our patient.

It is, however, not uncommon for the infection to coexist with malignancy, which can also confound the clinical picture and lead to delayed diagnosis, and may well have contributed to the unusual presentation of the tumour in our patient.

Advances in diagnosis and treatment

Laboratory studies

As previously mentioned, the identification of the role of EBV in NPC has greatly facilitated diagnosis of NPC. Since all non-keratinising NPCs harbour EBV, methods to detect EBV have been invaluable in early identification of NPC cells. In situ hybridisation for EBER and, to a lesser extent, identification of the expression of LMP-1 are useful tools in EBV-associated NPC diagnosis.^{9 23} Indeed, EBER is the most sensitive and specific analysis available at present.²¹

Additionally, ~90% of patients have EBV-positive serologies, and thus IgA against viral capsid antigen (VCA) and early antigens (EAs) are useful screening tools to identify susceptible individuals, who may as yet be asymptomatic.^{9 20 23}

In a similar vein, serological markers of EBV are present in almost all cases of non-keratinising carcinoma, and have thus been used in the monitoring of disease progression and response to treatment.^{5 21} VCA and EAs are the most commonly used tests.

Histopathology

Until the late 1980s, the conventional method of diagnosing NPC was by clinical examination of the nasopharynx with a mirror and examining an ethmoid biopsy specimen removed with a pair of forceps.¹³ Wei and colleagues described the increased use of fibre optic flexible endoscopy in examining and obtaining biopsies, of the nasopharynx, as well as in assessing the extent of NPC at diagnosis and monitoring the effect of radiation therapy in treatment.^{9 13} Additionally, studies in this period found that the vast majority of NPC originated from the fossa of Rosenmuller, suggesting that in the examination procedure of the nasopharynx for the purposes of suspected NPC, the pharyngeal recesses should be specifically examined meticulously and multiple biopsy specimens taken from this region.¹³

Histological biopsy in the aforementioned manner is the gold standard method of NPC diagnosis.⁹ Additional supportive methods of cytological diagnosis include fine needle aspiration (FNA) of an enlarged lymph node, nasopharyngeal aspirates or brush samples, which can help with initial diagnosis or staging. Usually, there are irregular clusters of large cells with overlapping vesicular nuclei and large nucleoli.⁹ However, FNA is significantly poorer in sensitivity when compared with biopsy.

Imaging studies

Clinical examination can provide valuable information regarding mucosal involvement and tumour extension in suspected head and neck malignancies, particularly endoscopic examination. Until the advent of cross-sectional radiology, only plain radiographs could be used to image soft tissue masses in the head and neck region, which predominantly assessed bone involvement and gave a rough estimation of the soft tissue lesion size.^{23 24}

Information regarding the presence of deep extension, intracranial spread, distant metastases and precise invasive margins could not be ascertained prior to cross-sectional imaging, and although flexible fibre optic nasoendoscopy is invaluable in tumour diagnosis and investigating extension into the nasal fossae and oropharynx, it cannot ascertain deep extension, skull base erosion or intracranial spread.¹³

The heralding of cross-sectional imaging has enabled a wealth of diagnostic and prognostic information to be provided in NPC. CT has revealed paranasopharyngeal extension as one of the most common modes of extension of NPC; it has shown perineural spread through the foramen ovale to be an important route of intracranial extension, and with it the pathogenesis of cranial nerve deficits characteristically associated with NPC.^{25 26}

MRI has a higher degree of soft tissue characterisation when compared with CT. MRI is also more sensitive for differentiating tumour from soft tissue, as well as in the identification of retropharyngeal and deep cervical nodal metastases.^{27 28} CT should be undertaken when the clinician is required to assess the base of the skull and tumour invasion into the basal skull foramina.²⁹

In our patient, MRI was sufficient to demarcate both tumour extent and invasion clearly, enabling choices regarding radiochemotherapy to be undertaken.

The value of positron emission tomography (PET) scanning in NPC diagnosis has been debated in the literature. Recent guidelines advise PET-CT imaging in the investigation of an occult primary, when evaluating the patient presenting with metastatic lymph nodes and unknown primary origin. It is especially useful in assessing recurrence of NPC (17) and has also been reported to be more sensitive than both CT and MRI in this regard.^{15 30}

Treatment

Treatment for NPC can be divided as per the modalities most commonly involved, namely radiotherapy, chemotherapy and rarely surgery.

Radiotherapy

Radiotherapy has become the standard treatment for NPC. NPC is highly radiosensitive and thus is the backbone of treatment for all stages of NPC without distant metastases. The anatomical location of the tumour, with its characteristic tendency for invasion of surrounding tissues, renders surgical excision too morbid an option to be used as first-line curative therapy in these tumours. Although efficient, radiotherapy has been noted to produce undesirable and significant complications from treatment, predominantly due to the location of the tumour at the base of the skull, with critical organs limiting the strength of therapy such as the brainstem, spinal cord, pituitary-hypothalamic axis, temporal lobes, eyes, ears and parotid glands.¹³

Conventional two-dimensional (2D) radiotherapy depends heavily on large lateral opposing fields. One of the most

common approaches in this vein is to start phase 1 treatment with large lateral opposing fasciocervical fields, thus covering the primary tumour and the upper neck lymphatics in one volume, with matching lower anterior cervical field for lower neck lymphatics. Shieldings protect the brainstem, spinal cord, eyes and oral cavity.^{31 32}

Radical dose of 65–75 Gy is normally given to the primary tumour and 65–70 Gy to the involved neck nodes, while the dose for prophylactic treatment for a node-negative neck is 50–60 Gy.³²

The literature has reported 2D conventional radiotherapy successfully controlling T1 and T2 tumours with rates of 75–90%, and T3 and T4 tumours in 50–75% of cases.^{33 34}

Significant research into therapeutic modalities in NPC has led to striking advances in the efficacy of non-surgical treatment. Ali and Vokes proposed chemotherapy as an adjunct in NPC treatment in the late 1990s.^{35 36} Following on from this, a recent Cochrane review by Bajaut *et al*³⁷ assessed chemotherapy as an adjunct to radiotherapy in NPC, and found a small but significant treatment effect of adjunctive chemotherapy in locally advanced NPC in terms of overall survival and event-free survival. Indeed, a recent study by Blanchard *et al*³⁸ showed a similar beneficial effect of concomitant chemoradiotherapy.

Chemotherapy

As described above, significant literature now exists describing the benefits to patient outcome and survival when chemotherapy is used as an adjunct to radiotherapy in NPC treatment; this has led to patients being treated concurrently with chemoradiotherapy for NPC. Cisplatin-based chemotherapy is commonly used in this regard, and although much less robust literature exists regarding neoadjuvant chemotherapy applications, a combination of cisplatin and fluorouracil is commonly used in this setting. Indeed, the current national guidance in the UK recommends concurrent chemoradiotherapy due to its significantly improved outcomes in overall survival in stage III and IV disease, with chemotherapy alone having a role purely in the palliative setting.¹⁵

Surgery

Surgery only has a role in the investigative stages of primary NPC in obtaining tissue for diagnosis, obtaining tissue for identifying clinically involved neck nodes, or in management to tackle the complication of otitis media with effusion.^{39 40} There is a limited role for surgery in residual and recurrent disease, for example, where the tumour is resistant to radiotherapy or concurrent chemoradiotherapy.^{41 42}

Prognosis

Prognosis in NPC depends primarily on the stage of the tumour and additionally on the age of the patient. Table 1 illustrates the

5-year relative survival rates of patients with NPC based on stage at diagnosis.

Following radiotherapy, overall 5-year survival in NPC stage I and IIA is quoted at 90% and 84%, respectively.⁴³ Following concurrent chemoradiotherapy, the risk of death in stages 3 and 4 NPC is reduced by 18% and there is an increase in 5-year overall survival of between 4% and 6%.^{44 45}

Large studies report a 5-year disease-free survival of 40–60% with radiotherapy alone (85–95% in stage 1, 70–80% in stage 2, 24–80% in stages 3–4). Better results occur in patients from Southeast Asia. The *Intergroup Study 0099* showed that North American patients with advanced NPC (stages III–IV) benefit from concurrent chemotherapy (CCRT), improving the 5-year overall survival from 37% to 67%. Five-year overall survival in stages I–II is >90% with CCRT.^{46 47}

By age, overall 5-year survival rates for NPC are around 70% (overall for all stages) for patients diagnosed under the age of 45, and 35% for patients diagnosed between the ages of 65 and 74. As discussed, undifferentiated (type 3) nasopharyngeal cancer has higher survival rates than keratinising type (type 1), as undifferentiated NPC responds more significantly to both radiotherapy and chemotherapy.⁸

Learning points

- Nasopharyngeal carcinoma (NPC) is known for its varied and late presentation, and its prompt recognition and subsequent management is crucial. It is important to consider a differential diagnosis of malignancy when faced with significant masses and swellings with non-classical histories or clinical features.
- There is a strong association with Epstein-Barr virus (EBV).
- Previously documented cases of NPC presenting as retropharyngeal abscess are extremely rare. Nevertheless, if the diagnosis is missed, the tumour spreads quickly and can become difficult if not impossible to eradicate.
- Flexible nasoendoscopy and biopsy is the gold standard for diagnosis, and CT and MRI are the investigations of choice to determine extension and invasion, and enable treatment choices to be undertaken.
- Chemoradiotherapy has been shown to be highly successful in treatment of this tumour if it is identified at an early stage.

Contributors NM is responsible for the creation of this manuscript and undertook relevant research so as to complete the literature review. RG was involved in the patient's care and assisted in the creation of this manuscript. QG was responsible for the patient's acute care and management. JM was responsible for the patient's longer term care under ENT.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Parkin DM, Whelan SL, Ferlay J, eds. *Cancer Incidence in Five Continents*, Vol. VII. IARC Scientific Publications, 1997, No. 143, Lyon, IARC.
- 2 Jemal A, Bray F, Center MM, *et al*. Global cancer statistics. *CA Cancer J Clin* 2011;61:69–90.
- 3 Chang ET, Adami HO. The enigmatic epidemiology of nasopharyngeal carcinoma. *Cancer Epidemiol Biomarkers Prev* 2006;15:1765–77.
- 4 Young LS, Rickinson AB. Epstein-Barr virus: 40 years on. *Nat Rev Cancer* 2004;4:757–68.

Table 1 Five-year overall survival rates of NPC by stage⁸

Stage	Relative 5-year survival rates
I	72%
II	64%
III	62%
IV	38%
NPC, nasopharyngeal carcinoma.	

- 5 Ho HC, Ng MH, Kwan HC, *et al.* Epstein-Barr-virus-specific IgA and IgG serum antibodies in nasopharyngeal carcinoma. *Br J Cancer* 1976;34:655–60.
- 6 Hildesheim A, West S, DeVeyra E, *et al.* Herbal medicine use, Epstein-Barr virus, and risk of nasopharyngeal carcinoma. *Cancer Res* 1992;52:3048–51.
- 7 Jia W, Qin H. Non-viral environmental risk factors for nasopharyngeal carcinoma: a systematic review. *Semin Cancer Biol* 2012;22:117–26.
- 8 Cancer Research UK (2015) *Nasopharyngeal cancer*. <http://www.cancerresearchuk.org/about-cancer/type/nasopharyngeal-cancer/> (accessed 6 Aug 2016).
- 9 Sham JS, Wei WI, Zong YS, *et al.* Detection of subclinical nasopharyngeal carcinoma by fibre optic endoscopy and multiple biopsy. *Lancet* 1990;335:371–4.
- 10 Pak MW, Chan KL, van Hasselt CA. Retropharyngeal abscess. A rare presentation of nasopharyngeal carcinoma. *J Laryngol Otol* 1999;113:70–2.
- 11 NIH National Cancer Institute. Head and Neck Cancer. <http://www.cancer.gov/types/head-and-neck/patient/nasopharyngeal-treatment-pdq> (Last accessed 24/2/2016)
- 12 Peterson BR, Nelson BL. Nonkeratinizing undifferentiated nasopharyngeal carcinoma. *Head Neck Pathol* 2013;7:73–5.
- 13 Wei W, Sham JST. Nasopharyngeal carcinoma. *Lancet Seminar* 2005;365:2041–54.
- 14 Shanmugaratnam K, Sobin LH. Histological typing of tumors of upper respiratory tract and ear. In: Shanmugaratnam K, Sobin LH, eds. *International histological classification of tumours*. 2nd edn. Geneva: WHO, 1991:32–3.
- 15 Roland NJ, Paleri V, eds. *Head and Neck Cancer: Multidisciplinary Management Guidelines*. 4th edition. London: ENT UK; 2011.
- 16 Raab-Traub N. Epstein-Barr virus in the pathogenesis of NPC. *Semin Cancer Biol* 2002;12:431–41.
- 17 Young LS, Murray PG. Epstein-Barr virus and oncogenesis: from latent genes to tumours. *Oncogene* 2003;22:5108–21.
- 18 Reddy SP, Raslan WF, Gooneratne S, *et al.* Prognostic significance of keratinization in nasopharyngeal carcinoma. *Am J Otolaryngol* 1995;16:103–8.
- 19 Lee AWM, Foo W, Law SCK, *et al.* Nasopharyngeal carcinoma—presenting symptoms and duration before diagnosis. *HK Med J* 1997;3:355–61.
- 20 Thompson LDR. Update on nasopharyngeal carcinoma. *Head Neck Pathol* 2007;1:81–6.
- 21 Ho HC, Kwan HC, Ng MH, *et al.* Serum IgA antibodies to Epstein-Barr virus capsid antigen preceding symptoms of nasopharyngeal carcinoma. *Lancet* 1978;1:436.
- 22 Sham JS, Cheung YK, Choy D, *et al.* Nasopharyngeal carcinoma: CT evaluation of patterns of tumor spread. *AJNR Am J Neuroradiol* 1991;12:265–70.
- 23 Hoeffner EG, Mukherji SK, Srinivasan A, *et al.* Neuroradiology back to the future: head and neck imaging. *Am J Neuroradiology* 2012;33:2026–32.
- 24 Som PM, Curtin HD. eds. *Head and neck imaging*. St Louis, MO: Mosby-Year Book, 2003.
- 25 Sham JS, Cheung YK, Choy D, *et al.* Nasopharyngeal carcinoma: CT evaluation of patterns of tumour spread. *Am J Neuroradiol* 1991;12:265–70.
- 26 Dillon WP, Mills CM, Kjos B, *et al.* Magnetic resonance imaging of the nasopharynx. *Radiology* 1984;152:731–8.
- 27 King AD, Vlantis AC, Tsang RK, *et al.* Magnetic resonance imaging for the detection of nasopharyngeal carcinoma. *AJNR Am J Neuroradiol* 2006;27:1288–91.
- 28 Olmi P, Fallai C, Colagrande S, *et al.* Staging and follow-up of nasopharyngeal carcinoma: magnetic resonance imaging versus computerized tomography. *Int J Radiat Oncol Biol Phys* 1995;32:795–800.
- 29 Cellai E, Olmi P, Chiavacci A, *et al.* Computed tomography in nasopharyngeal carcinoma: part II: impact on survival. *Int J Radiat Oncol Biol Phys* 1990;19:1177–82.
- 30 Yen RF, Hung RL, Pan MH, *et al.* 18-fluoro-2-deoxyglucose positron emission tomography in detecting residual/recurrent nasopharyngeal carcinomas and comparison with magnetic resonance imaging. *Cancer* 2003;98:283–7.
- 31 Ozyar E, Atahan IL, Akyol FH, *et al.* Cranial nerve involvement in nasopharyngeal carcinoma: its prognostic role and response to radiotherapy. *Radiat Med* 1994;12:65–8.
- 32 Wei WI, Kwong DL. Current management strategy of nasopharyngeal carcinoma. *Clin Exp Otorhinolaryngol* 2010;3:1–12.
- 33 Lee AW, Poon YF, Foo W, *et al.* Retrospective analysis of 5037 patients with nasopharyngeal carcinoma treated during 1976–1985: overall survival and patterns of failure. *Int J Radiat Oncol Biol Phys* 1992;23:261–70.
- 34 Wang CC. Improved local control of nasopharyngeal carcinoma after intracavitary brachytherapy boost. *Am J Clin Oncol* 1991;14:5–8.
- 35 Vokes EE, Liebowitz DN, Weichselbaum RR. Nasopharyngeal carcinoma. *Lancet* 1997;350:1087–91.
- 36 Ali H, Al-Sarraf M. Chemotherapy in advanced nasopharyngeal cancer. *Oncology (Huntingt)* 2000;14:1223–30.
- 37 Bajaj B, Audry H, Bourhis J, *et al.* Chemotherapy as an adjunct to radiotherapy in locally advanced nasopharyngeal carcinoma. *Cochrane Database Syst Rev* 2006;18: CD004329.
- 38 Blanchard P, Lee A, Marguet S, *et al.* Chemotherapy and radiotherapy in nasopharyngeal carcinoma: an update of the MAC-NPC meta-analysis. *Lancet Oncol* 2015;16:645–55.
- 39 Ho WK, Wei WI, Yuen APW, *et al.* Otorrhoea after grommet insertion for middle ear effusion in patients with nasopharyngeal carcinoma. *Am J Otolaryngol* 1999;20:5–12.
- 40 Xu YD, Ou YK, Zheng YQ, *et al.* The treatment for post irradiation otitis media with effusion: a study of three methods. *Laryngoscope* 2008;118:2040–3.
- 41 Hao SP, Tsang NM, Chang KP, *et al.* Nasopharyngectomy for recurrent nasopharyngeal carcinoma: a review of 53 patients and prognostic factors. *Acta Otolaryngol* 2008;128:473–81.
- 42 Chang KP, Hao SP, Tsang NM, *et al.* Salvage surgery for locally recurrent nasopharyngeal carcinoma-A 10-year experience. *Otolaryngol Head Neck Surg* 2004;131:497–502.
- 43 Chan ATC. Nasopharyngeal carcinoma—symposium article. *Ann Oncol* 2010;21: vii308–12.
- 44 Langendijk JA, Leemans CR, Buter J, *et al.* The additional value of chemotherapy to radiotherapy in locally advanced nasopharyngeal carcinoma: a meta-analysis of the published literature. *J Clin Oncol* 2004;22:4604–12.
- 45 Baujat B, Audry H, Bourhis J, *et al.* Chemotherapy in locally advanced nasopharyngeal carcinoma: an individual patient data meta-analysis of eight randomized trials and 1753 patients. *Int J Radiat Oncol Biol Phys* 2006;64:47–56.
- 46 Al-Sarraf M, LeBlanc M, Giri PG, *et al.* Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. *J Clin Oncol* 1998;16:1310–17.
- 47 Zhang L, Chen QY, Liu H, *et al.* Emerging treatment options for nasopharyngeal carcinoma. *Drug Des Devel Ther* 2013;7:37–52. <http://dx.doi.org/10.2147/DDDT.S30753>

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow