CASE REPORT

Eastern Journal of Medicine
East J Med 22(2): 70-73, 2017
DOI: 10.5505/ejm.2017.76486

Epstein-Barr virus positive primary sinonasal nasopharyngeal-type undifferentiated carcinoma: A distinct entity

Farah Dayana Zahedi[1*], Nik Mohd Hazleigh Nik Hussin[2], Salina Husain[1], Ramesh Kumar[3], Balwant Singh Gendeh[1]

[1]Department of Otorhinolaryngology-head and Neck Surgery Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
[2]Department of Otorhinolaryngology-head and Neck Surgery Faculty of Medicine, Universiti Teknologi Malaysia, Selangor, Malaysia
[3]Department of Surgery Faculty of Medicine, Neurosurgery Unit, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

ABSTRACT

Primary sinonasal nasopharyngeal-type undifferentiated carcinoma (PSNPC) is a rare variant of the sinonasal undifferentiated carcinoma (SNUC). The histological classification has implications on its management.
We report a case of a 32 year old lady who presented with progressive nasal obstruction due to a sinonasal tumour. Endoscopic excision was performed and examination confirmed PSNPC with positive Epstein Barr virus in-situ hybridisation.
Identification and recognition of PSNPC as a separate clinicopathological entity from SNUC is important as it dictates the management of this rare variant. Immunohistochemical analysis is invaluable in this endeavor.

Key Words: Paranasal sinus, sinonasal, undifferentiated carcinoma, Epstein-Barr virus, nasopharynx

Introduction

Sinonasal undifferentiated carcinoma (SNUC) was first described in 1986, recognising it as a distinct clinicopathological entity more aggressive than other tumours with similar poorly-differentiated microscopic appearance, thus highlighting the importance of its identification (1). The main differential diagnoses of SNUC and small round cell tumour of sinonasal region are olfactory neuroblastoma and neuroendocrine carcinoma (both having favourable prognosis) (1) and malignant melanoma of the sinonasal region.

The description of a rare histological variant by Jeng et al. (2) has further categorized undifferentiated carcinomas into sinonasal undifferentiated carcinoma (SNUC) and primary sinonasal nasopharyngeal-type undifferentiated carcinoma (PSNPC) which differ also in their association with Epstein-Barr Virus (EBV) infection and response to radiotherapy.

Previous studies have demonstrated an association between EBV and development of SNUC, (3-5) however Cerilli et al. (6) reported the absence of this association in their series of twenty five cases.

The diagnosis of these tumours is difficult on the basis of light microscopic features, therefore, immunohistochemical analysis of undifferentiated carcinomas of the sinonasal region has proven helpful in distinguishing this heterogenous group of malignancies, guiding the multidisciplinary team of clinicians in its management (7).

Case report

A 32-year old woman with no known medical illness presented to the Otorhinolaryngology-Head and Neck Surgery (ORL-HNS) outpatient clinic with a progressive bilateral nasal obstruction of 6 duration, initially affecting the right side. The patient had 2 weeks history of intermittent epistaxis prior to presentation. There was no evidence of cranial nerve palsies, intracranial space-occupying lesions, head neck lymphadenopathy, and neither any oral cavity nor oropharyngeal masses.

***Corresponding Author:** Farah Dayana Zahedi
Department of Otorhinolaryngology-Head & Neck Surgery, Faculty of Medicine, UKM Medical Center JalanYaacob Latif, Bandar Tun Razak 56000 Cheras, Kuala Lumpur, Phone: +60124248205, Fax no: +603-91456675, E-mail: anna_firra82@yahoo.com.au
Received: 27.04.2016, **Accepted:** 27.10.2016

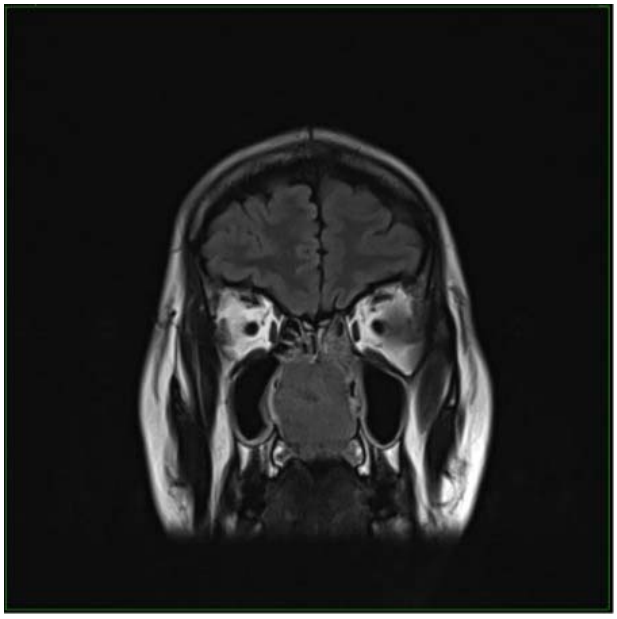


Fig. 1. MRI (coronal) showing the septal mass with multiple areas of cystic degeneration, occupying both nasal cavities.

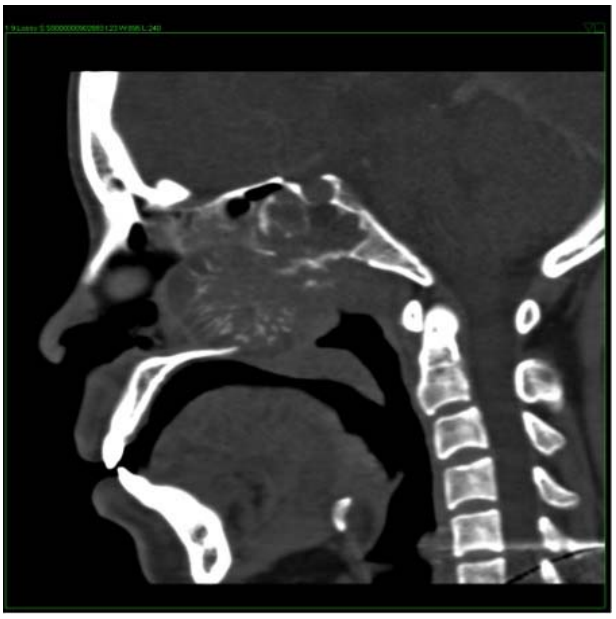


Fig. 2. CT scan (sagittal) showing the mass centred around the destructed nasal septum with amorphous linear calcification within the mass. There is evidence of erosion of the floor of the sphenoid sinus with involvement of the dorsum sella.

Her father was diagnosed and died of malignancy affecting the nasal cavity with neck lymphadenopathy.

Rigid nasendoscopy revealed a mass completely occupying the nasopharynx which appeared to be arising from the postero-inferior part of the nasal septum.

MRI of the paranasal sinuses and brain showed a large solid mass approximately 6 x 3 x 5 cm (AP x W x CC) with multiple areas of cystic degenerations arising from the nasal septum, occupying both nasal cavities with local infiltration of the roof of the nasopharynx, sphenoid sinuses and basisphenoid with dehiscence of sella turcica (Figure 1). Superolaterally, the tumour extends via the right foramen lacerum into the middle cranial fossa with discontinuity of the dura and encasement of petrous parts of both carotid arteries. There were bilateral subcentimeter level IIa and IIb lymph nodes. CT of the paranasal sinuses demonstrated calcifications within the mass, and extensive bony destruction of the basisphenoid (Figure 2).

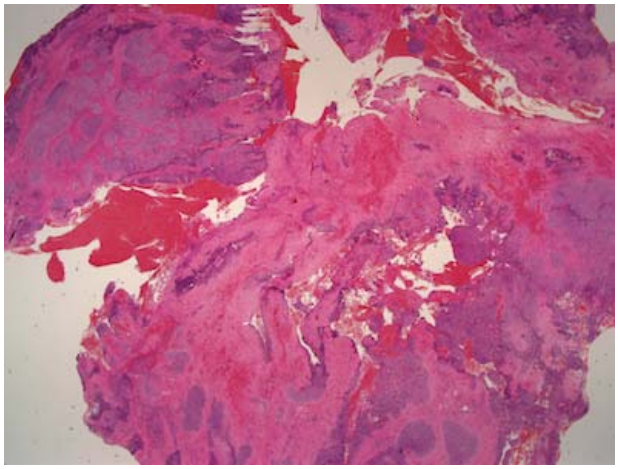
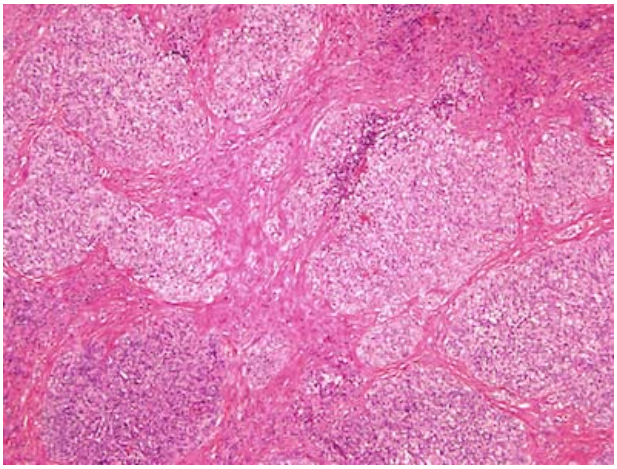
Incisional biopsy of the mass was performed and examination showed undifferentiated, non-keratinizing malignant epithelial cells infiltrating the stroma in a syncytial pattern. Immunohistochemical analysis showed strong cytokeratin positivity (CK 5/6), negative for S100 and synaptophysin, but strongly and homogenously positive for EBV RNA in-situ hybridisation (Figures 3-6).

Pitman et al. (8) reported that combined surgical therapy of similar lesions, previously considered unresectable has increased the rate. She subsequently underwent a formal nasendoscopic excision of the sinonasal tumour, with functional endoscopic sinus surgery - posterior septectomy, ethmoidectomy, middle meatal antrostomy, nasopharyngectomy, debridement of the infiltrated clivus, and repair of the dural defects in the sella and clivus with dural tissue. Intraoperatively, there was no evidence of tumour involvement of the pituitary gland. She had an uneventful and uncomplicated post-operative recovery period.

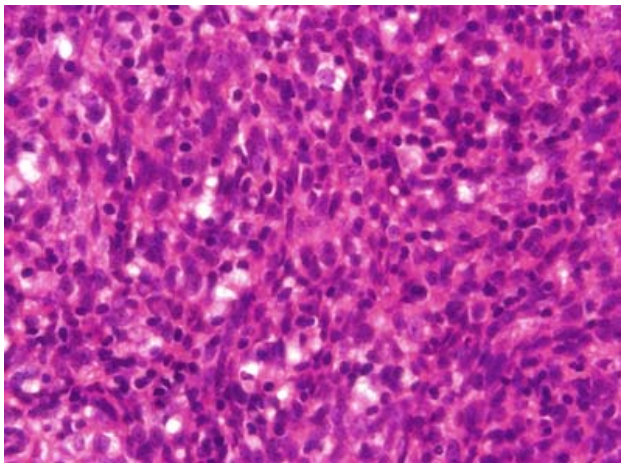
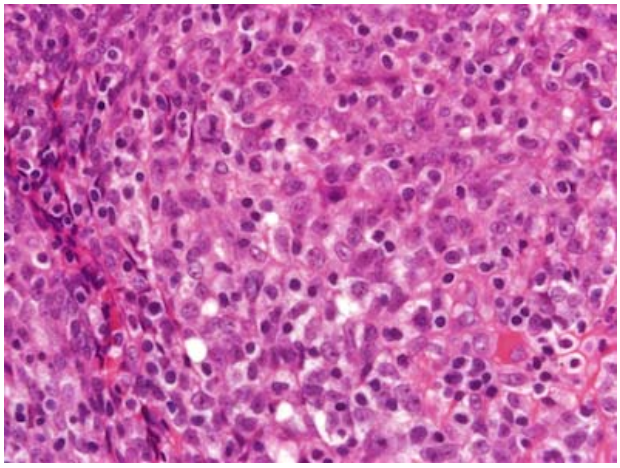
The HPE of the excisional biopsies were consistent with the findings of the preceding incisional biopsy.

As this tumour is extremely rare, there is lack of published evidence on the specific treatment plan for such malignancies. The patient underwent intensity-modulated radiotherapy (IMRT) post-operatively.

CT paranasal sinuses 5 months post-operatively confirmed residual tumour with extensive skull base destruction and left neck nodal metastases.

Figures 3 and 4. Low power view showing the tumour cells arranged in syncytial pattern with areas of haemorrhages seen.

Figures 5 and 6. The tumour cells exhibit medium sized, oval to spindle shape, vesicular to hyperchromatic nuclei with some showing prominent nucleoli. There are lymphoplasmacytic infiltrates in between the tumour cells.

Discussion

Carcinoma of the nasal cavities and paranasal sinuses rare (less than 1% of all malignancies and only 3% of head and neck malignancies). Squamous cell carcinomas (both keratinizing and non-keratinizing types) are the most commonly occuring malignant neoplasm in the sinonasal tract.

The more aggressive, high-grade undifferentiated malignant neoplasm of epithelial origin can occur, albeit less frequently than SCCs, was first described by Frierson et al (1). Differentiation of undifferentiated epithelial from non-epithelial malignant neoplasms has been made possible with immunohistochemical markers such as the cytokeratins.

Differential diagnoses for undifferentiated sinonasal tract malignancies include, SNUC, olfactory neuroblastoma, small cell undifferentiated (neuroendocrine) carcinoma, mucosal malignant melanoma, rhabdomyosarcoma, hematolymphoid malignancies (nasal-type T/NK-cell lymphoma), primitive neuroectodermal tumour/Ewing sarcoma and primary sinonasal nasopharyngeal-type undifferentiated carcinoma (PSNPC), also known as lymphoepithelial carcinoma (2,7).

The latter was described by Jeng et al. (2) in 2002 who recognised that despite SNUC and PSNPC both being undifferentiated and of epithelial origin, with similarities in microscopic appearance confirmed PSNPC is a separate clinicopathological entity from SNUC and an accepted WHO classification (6,7). This rare variant is closely related and has a histological resemblance to nasopharyngeal carcinoma, with most cases reported (13 reported cases in the literature) in the far East (2, 6, 9).

Key cytological features of PSNPC is medium-sized oval to spindle-shaped cells, enlarged nuclei, vesicular chromatin and prominent nucleoli.

Indistinct cell borders with a syncytial growth pattern, limited mitotic activity, mild to moderate (less than in NPC) lymphoplasmacytic cell infiltrate, and usually absence of necrosis and keratinization are features identifiable in PSNPC which enables its differentiation from SNUC. Presence of EBV upon EBV-RNA in-situ hybridisation also differentiates PSNPC (3-5).

Our case demonstrated histopathological, immunohistochemical and EBER-positive features consistent with those described by Jeng et al. (2) and thus far has a similar survival outcome matched to the cases in their series, with similar-staged disease.

In a conclusion, Epstein-Barr virus positive PSNPC is a highly aggressive rare variant of SNUC. Despite combined surgical techniques allowing surgical resection of these tumours that tend to be in advanced stages at presentation, the risk of recurrence is high. Patients should undergo post-operative radiotherapy for improved local control. Regular post-operative clinical and radiological surveillance is vital.

Authors' declaration: We have no conflicts of interest.

References

1. Frierson HF Jr, Mills SE, Fechner RE, Taxy JB, Levine PA. Sinonasal undifferentiated carcinoma: an aggressive neoplasm derived from Schneiderian epithelium and distinct from olfactory neuroblastoma. Am J Surg Pathol 1986; 10: 771-779.
2. Jeng YM, Sung MT, Fang CL, et al. Sinonasal undifferentiated carcinoma and nasopharyngeal-type undifferentiated carcinoma: Two clinically, biologically, and histopathologically distinct entities. Am J Surg Pathol 2002; 26: 371-376.
3. Gallo O, DiLollo S, Graziani P, Gallina E, Baroni G. Detection of Epstein-Barr virus genome in sinonasal undifferentiated carcinoma by use of in situ hybridization. Otolaryngol Head Neck Surg 1995; 112: 659-664.
4. Leung SY, Yuen ST, Chung LP, et al. Epstein-Barr virus is present in a wide histological spectrum of sinonasal carcinomas. Am J Surg Pathol 1995; 19: 994-1001.
5. Lopategui JR, Gaffey MJ, Frierson HF, et al. Detection of Epstein- Barr viral RNA in sinonasal undifferentiated carcinoma from Western and Asian patients. Am J Surg Pathol 1994; 18: 391-398.
6. Cerilli LA, Holst VA, Brandwein MS, Stoler MH, Mills SE. Sinonasal undifferentiated carcinoma: Immunohistochemical profile and lack of EBV association. Am J Surg Pathol 2001; 25: 156-163.
7. Wenig BM. Undifferentiated malignant neoplasms of the sinonasal tract. Arch Pathol Lab Med 2009; 133: 699-712.
8. Pitman KT, Constantino PD, Lassen LF. Sinonasal undifferentiated carcinoma: current trends in treatment. Skull Base Surg 1995; 5: 269-272.
9. Tsang WYW, Chan JKC. Lymphoepithelial carcinoma. In Barnes L, ed. WHO classification of tumours. Tumours of the head and neck. Lyon: IARC Press; 2005. p. 18.