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## CASE REPORT

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# Nasopharyngeal Carcinoma Recurrence with Orbital Metastasis through the Nasolacrimal Duct: Uncommon Presentation of a Common Phenomenon

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## INTRODUCTION

Nasopharyngeal carcinoma (NPC) is one of the most common malignancies with the tenth highest mortality of all malignancies in Hong Kong in 2016.<sup>1</sup> Despite the emergence of more advanced treatments such as intensity-modulated radiotherapy, tumour recurrence is still encountered. The presentation of NPC recurrence is known to be highly variable. We report an uncommon presentation with metastasis through the nasolacrimal duct detected on positron emission tomography-computed tomography (PET-CT).

## HISTORY

A 44-year-old man was diagnosed with undifferentiated NPC in July 2015 (Figure 1). He first presented with nasal obstruction, postnasal dripping with blood stained saliva, and self-palpated neck mass for 2 months. Nasoendoscopy revealed a left nasopharyngeal mass and biopsy confirmed an undifferentiated NPC. Ultrasound of the neck revealed multiple cervical lymph nodes. PET-CT and magnetic resonance imaging scans showed a corresponding hypermetabolic tumour at the left

nasopharynx with involvement of the left parapharyngeal space, pterygoid base, and prevertebral muscles. Multiple hypermetabolic left cervical and supraclavicular lymph nodes were also detected. Initial tumour staging was cT3N2.

The patient was commenced on chemoradiotherapy. A total of six cycles of cisplatin and radiation therapy at a dose of 61.48 Gy in 29 fractions were given. Subsequent nasopharyngoscopy showed no residual tumour and biopsy was negative for malignancy. Subsequent adjuvant chemotherapy of three cycles of cisplatin-fluorouracil was completed in December 2015.

During a follow-up visit in July 2017, multiple enlarged cervical lymph nodes were detected. Magnetic resonance imaging and PET-CT scans of the neck and nasopharynx in July 2017 (Figure 2) showed prominent soft tissue lesions with hypermetabolism over the anterior nasal cavity, left nasopharynx, left tonsil, and bilateral cervical lymph nodes. Subsequent upper endoscopy detected corresponding friable soft tissue masses in the left nasal cavity, as well as a left nasopharyngeal mass involving

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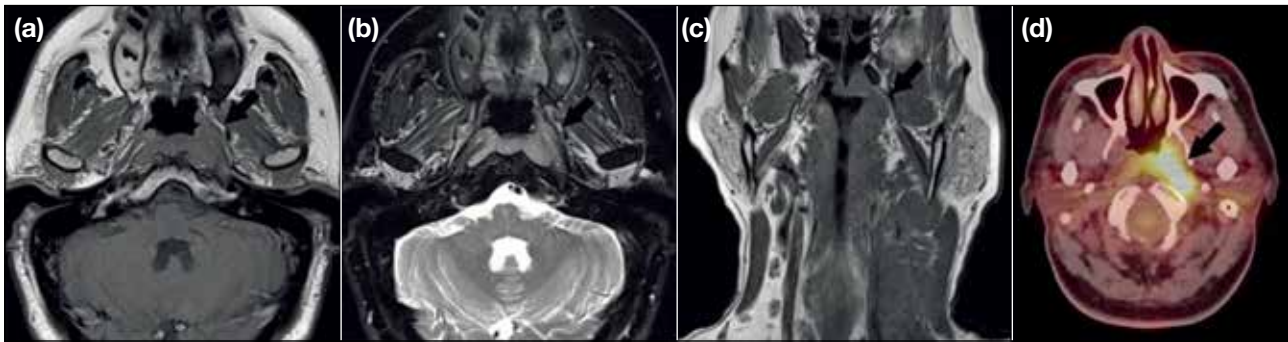
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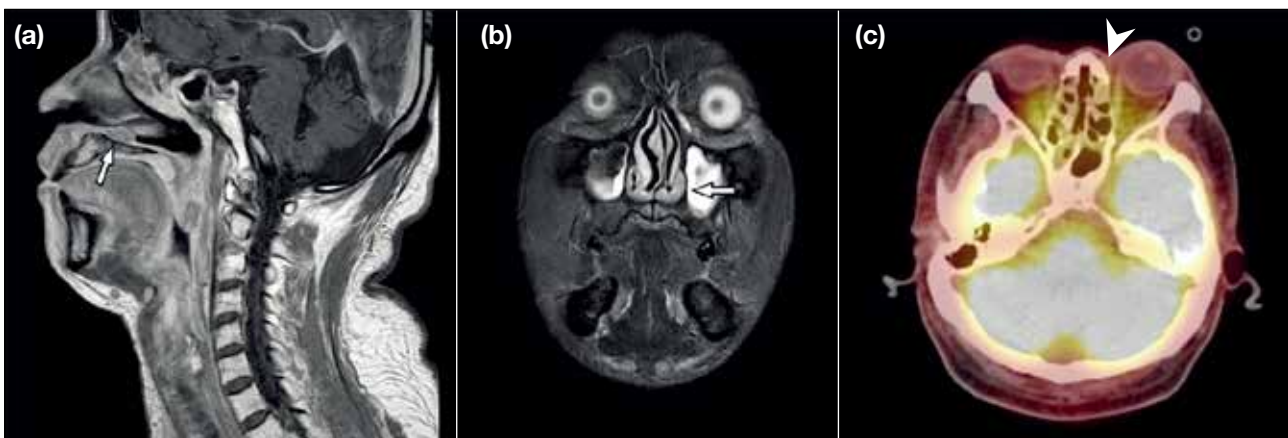
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**Figure 1.** (a-c) Magnetic resonance imaging (MRI) and (d) positron emission tomography-computed tomography (PET-CT), June 2015 (initial staging). PET-CT and MRI showing a hypermetabolic tumour at left nasopharynx with involvement of the left parapharyngeal space, pterygoid base, and prevertebral muscles, corresponding to newly diagnosed nasopharyngeal carcinoma (arrows). Multiple hypermetabolic left cervical and supraclavicular lymph nodes were also detected. Initial tumour staging was cT3N2.



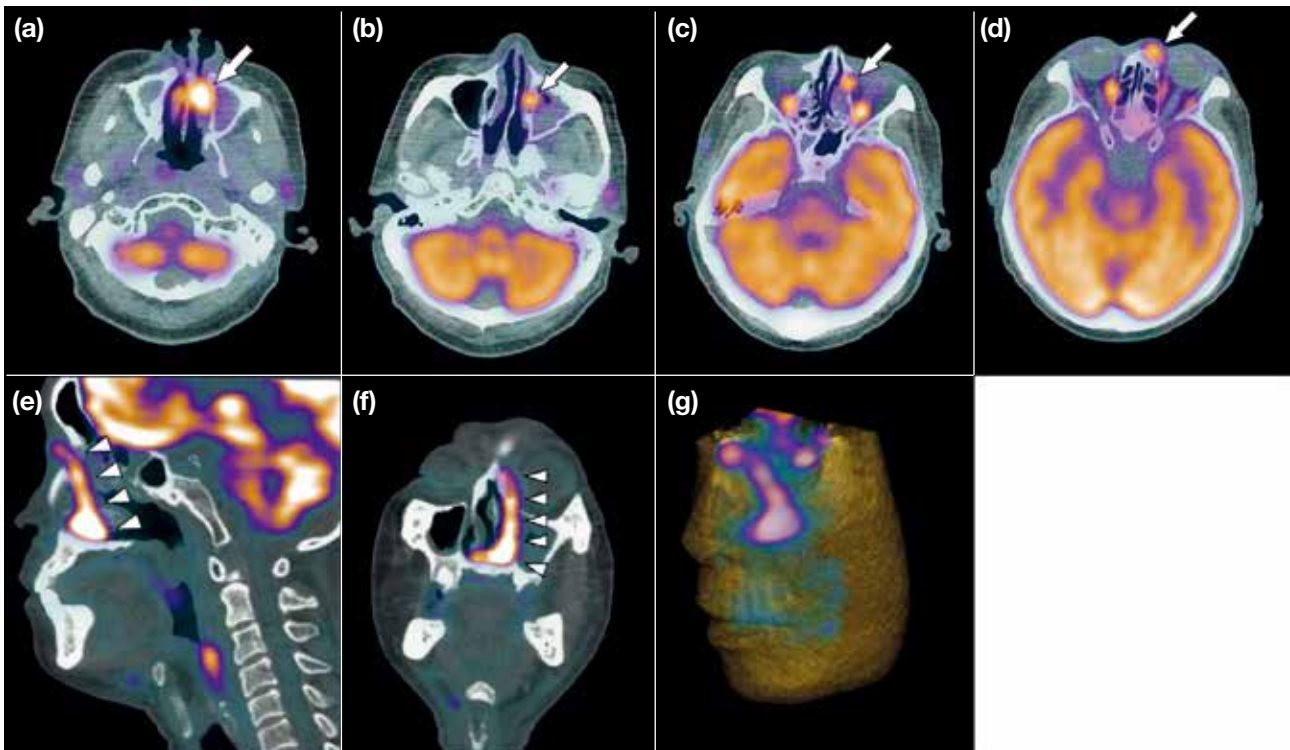
**Figure 2.** (a, b) Magnetic resonance imaging (MRI) and (c) positron emission tomography-computed tomography (PET-CT), July 2017 (first recurrence). Selected images showing a prominent soft tissue lesion over the anterior left nasal cavity on MRI with corresponding hypermetabolism detected on PET-CT (arrows), compatible with biopsy-proven nasopharyngeal carcinoma recurrence. Although soft tissue signal is seen along the left nasolacrimal duct, no associated increased activity was detected at the left nasolacrimal duct or left orbital region (arrowhead) at this time.

the left roof, lateral wall, and left choana. Biopsy of both masses confirmed recurrent undifferentiated NPC.

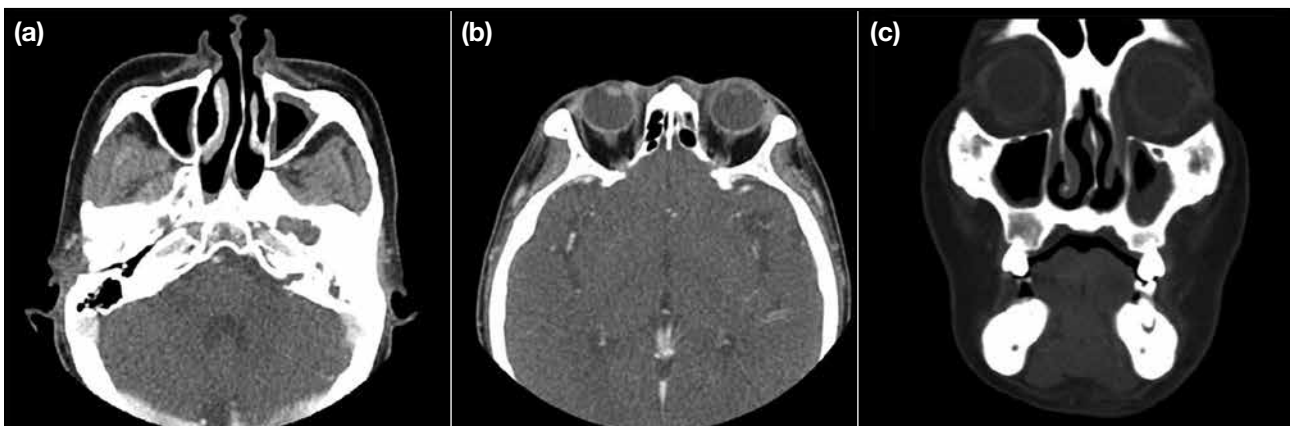
The patient declined surgery or repeat radiotherapy so second-line chemotherapy was offered. A total of five cycles of gemcitabine-cisplatin were given, switched to gemcitabine-carboplatin for two more cycles due to hearing loss. The patient showed an initial partial response. Serologically, Epstein-Barr virus (EBV) DNA titre in February 2018 had reduced to an undetectable level from a pretreatment baseline of 765 copies/mL. Follow-up CT in March 2018 showed a less conspicuous soft tissue thickening at the left nasopharynx and oropharynx with interval resolution of the nasal floor soft tissue lesion. Bilateral cervical lymphadenopathy also showed interval shrinkage.

However, the EBV DNA titre showed a rebound level of 52 copies/mL in November 2018, suspicious of disease progression. The patient also complained of a new 1.5-cm firm mass at the left nasal bridge just medial to the left orbit and enlarging over the last month. The patient was referred to our centre for PET-CT to determine disease progress.

Follow-up PET-CT in December 2018 (Figure 3) revealed a markedly hypermetabolic tumour centred at the anterior floor of the left nasal cavity with involvement of the nasal septum and right anterior nasal cavity. The hypermetabolism showed further superior extension along the left nasolacrimal duct that was mildly expanded by soft tissue, and reached a soft tissue prominence at the left side of the nasal bridge, compatible with the



**Figure 3.** Positron emission tomography–computed tomography, December 2018 (second recurrence). Serial axial cuts from nasal cavity level to orbital level (a-d) showing a markedly hypermetabolic tumour at the anterior floor of the left nasal cavity with further superior extension along the left nasolacrimal duct (arrows). On coronal, sagittal, and three-dimensional reformatting of images (e-g), the course of hypermetabolic soft tissue was shown extending along the left nasolacrimal duct and reached the soft tissue prominence at the left side of the nasal bridge (arrowheads), compatible with the clinically detected periorbital mass. This was suggestive of biopsy-proven nasal cavity nasopharyngeal carcinoma directly extending into the left orbit through the inferior nasal meatus and nasolacrimal duct.



**Figure 4.** Computed tomography neck, March 2019 (progress scan). Axial cuts at (a) nasal cavity and (b) orbital levels and (c) coronal reformatting showing interval shrinkage of the soft tissue mass at the anterior floor of the left nasal cavity and left side of the nasal bridge following palliative chemotherapy, corresponding to clinical findings.

clinically detected periorbital mass. This was suggestive of the biopsy-proven nasal cavity NPC showing direct extension into the left orbit through the inferior nasal meatus and nasolacrimal duct. Hypermetabolic nodal

lesions were also noted at bilateral parotid, submental, and upper cervical regions, likely representing nodal recurrence. Overall imaging features were compatible with disease progression.

In view of disease progression, the patient was offered palliative chemotherapy with capecitabine. The medial orbital mass showed progressive flattening on subsequent clinical follow-ups and showed interval resolution on follow-up CT after 3 months (Figure 4).

## DISCUSSION

Although skull base infiltration of NPC through the neuroforamen or potential spaces is a well-known phenomenon, orbital infiltration is uncommon. It has been reported by Luo et al<sup>2</sup> and Colaco et al<sup>3</sup> that the most common pathway for NPC infiltration into the orbit is via the pterygopalatine fossa and inferior orbital fissure, followed by via ethmoid sinus and sphenoid sinus, reaching the orbital apex. Common orbital metastatic tumours often present with a rather abrupt onset of diplopia, blurred vision, pain, and occasionally a visible lump. Examination may disclose proptosis, displacement of the globe, blepharoptosis, and a visible or palpable mass.<sup>4</sup> NPC infiltration of the anteromedial corner of the orbit, probably through the nasolacrimal duct, is a rare phenomenon with only a few reported cases.

In our patient, known anterior nasal cavity tumour recurrence was biopsy-proven. On three-dimensional reformatting of images, hypermetabolic soft tissue was clearly shown extending along the nasolacrimal duct, connecting the hypermetabolic anterior nasal cavity mass and medial orbital mass. This is evidence of the possible NPC invasion route to the anterior orbit through the nasolacrimal duct. A similar case was reported by Amrith<sup>5</sup> of a 59-year-old woman with NPC recurrence at the anterior nasal cavity who reported left orbital swelling with bloody tears. On follow-up CT, a soft tissue lesion was seen infiltrating bilateral nasolacrimal ducts from nasal cavity masses, connected superiorly to the anteromedial mass in the left orbit. Biopsy of the orbital mass was compatible with NPC recurrence. Amrith<sup>5</sup> also reported another case of recurrent NPC in a 33-year-old man 4 years after initial radiotherapy. He presented with a medial orbital mass and tearing. On CT scan, bilateral lacrimal sac masses were seen with extension into bilateral nasolacrimal ducts. Subsequent biopsy of the orbital mass confirmed it to be recurrent NPC.

Among few other reported cases of NPC recurrence involving the nasolacrimal duct and lacrimal sac, there have often been accompanying symptoms related to tearing, including epiphora and bloody tears, resembling a lacrimal sac tumour.<sup>5-7</sup> These symptoms

may be due to obstruction of the nasolacrimal duct and precede the occurrence of medial orbital mass. Prompt investigation such as early progress PET-CT or EBV DNA titre screening may help early detection of tumour progression.<sup>8</sup> Early initiation of second-line or palliative treatment may still offer symptomatic relief as in our patient.

It has been shown by Li et al<sup>9</sup> that the probability of NPC invasion into structures further away from the nasopharynx, such as the paranasal sinuses or orbital apex, is significantly higher in recurrent disease than in primary disease. One possible explanation suggested by the authors is that tumour cells of subclinical lesions in low-dose radiotherapy areas receive mostly sublethal damage and survive, then continue to split and lead to tumour recurrence; another explanation is that patients susceptible to NPC are prone to recurrence, but the normal structure of the areas adjacent to the nasopharynx have been destroyed by high-intensity rays during the first treatment, with the local blood supply reduced and unfavourable for tumour growth, so the tumour relocates and occurs far away from the nasopharynx. Whichever the case, close attention should be paid when examining follow-up studies, not only at the primary tumour site at the nasopharynx, but at marginal irradiation zones peripheral to the nasopharynx where recurrence may also occur.

## CONCLUSION

We report a patient with NPC recurrence with an uncommon presentation that involved orbital metastasis from the nasal cavity through the nasolacrimal duct. Radiological evidence was revealed on a PET-CT scan. Careful correlation with early clinical symptoms and radiological findings may allow early detection of uncommon tumour recurrence. Subsequent early initiation of second-line or palliative treatment may improve treatment results and enhance patient care.

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