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Enduring the Aftermath: A 16-Year Case Study of Radiotherapy Side Effects in Nasopharyngeal Cancer

Abstract – Nasopharyngeal carcinoma (NPC) is a common malignancy in Malaysia, typically affecting men; however, cases in women, especially during the postpartum period, are rare. This report describes a 33-year-old woman diagnosed with advanced non-keratinizing squamous cell carcinoma of the nasopharynx (T4N3M0, Stage III) postpartum. She underwent 3D-conformal radiotherapy (3D-CRT) with concurrent Cisplatin chemotherapy, followed by additional chemotherapy for residual disease. Despite achieving 16 years of disease-free survival, she developed multiple late complications, including xerostomia, trismus, osteoradionecrosis, and cerebrospinal fluid rhinorrhoea with recurrent infections, which significantly impaired her quality of life. This case highlights the long-term survivorship and chronic sequelae associated with 3D-CRT in NPC, and suggesting that newer techniques such as intensity-modulated radiotherapy (IMRT) may offer improved precision and potentially reduce such complications.

Keywords – nasopharyngeal carcinoma, 3D-CRT, IMRT, survivorship

1 INTRODUCTION

Nasopharyngeal carcinoma (NPC) is relatively a rare cancer globally [1] but endemic in China and Southeast Asia [2]. In Malaysia, it ranked the sixth common cancer among male, peaked among Chinese ethnic between 60 and 64 years old. Notably, up to 76.0% were diagnosed late at advanced stages of disease (Stage III or Stage IV) [3]. Several risk factors are associated with the increase incidence of NPC, such as Epstein-Barr virus infection, consumption of fermented and preserved food, genetic predisposition, smoking, use of alcohol and occupational exposure to smoke or dust [4].

Concurrent chemoradiotherapy (CCRT) served as the mainstay of treatment for advanced NPC. 3D-conformal radiotherapy (3D-CRT) with concurrent administration of platinum agents are associated with high local control rates [5]. Conversely, patients must endure significant early and long-term side effects from the treatment, which pose substantial challenges to lifelong care and significantly impact on the quality of life for both patients and their caregivers [6].

This case is particularly notable as the patient was a young female without any identifiable pre-existing risk factors and was diagnosed during her postpartum period. It illustrates the challenges of disease course, treatment, and complications.

2 MATERIALS & METHODS

This is a retrospective case study. Clinical data were collected via review of the patient's medical records. All patient information was anonymized to ensure confidentiality.

3 CASE PRESENTATION

This case reports a 33-year-old Malay woman who suffered from epistaxis, persistent headache and hearing loss during postpartum period in 2009. Biopsy of the tumour in left nasopharynx confirmed non-keratinizing squamous cell carcinoma. CT scans revealed an extensive mass in the nasopharynx extending to the cavernous sinuses, with bilateral nodal involvement (>6cm) and no distant metastasis (T4N3M0, Stage III). She was treated with 3D-CRT, 66Gy/33 fractions delivered to neck, right and left lateral facial, 26 Gy/13 fractions to the anterior nose and 56 Gy/25 fractions to the anterior neck, with concurrent Cisplatin 30mg/m^2. However, PET CT scan post treatment revealed residual disease, necessitating another 6 cycles of Cisplatin and Fluorouracil.

Following completion of CCRT, the patient's functional status showed marked improvement, progressing from ECOG performance status 3 to ECOG 1. Nonetheless, despite this recovery, she subsequently experienced multiple late complications, particularly affecting the oral cavity. These included severe xerostomia, gingivitis, gum

atrophy, and extensive dental caries. Progressive dental deterioration led to multiple tooth extractions, which were complicated by chronic mandibular pain and difficulty in chewing, eventually leading her to only tolerate soft diet. In 2014, she required total teeth extraction, after which she developed temporomandibular joint stiffness and osteoradionecrosis (ORN) of the mandible. The ORN caused persistent pain and restricted mouth opening, significantly impacting her nutrition and quality of life, and necessitated long-term morphine therapy for pain control and functional comfort.

Additionally, she developed persistent headache and rhinorrhoea, which was confirmed by a CT scan of brain and neck as cerebrospinal fluid (CSF) rhinorrhoea due to base of skull destruction, leading to communication with cerebrospinal space. At the same time, she suffered from recurrent otitis media, causing a decline in her hearing. A left grommet tube was inserted in 2019, but her hearing remained significantly impaired. During this period, she also faced significant mental challenges, especially depression, for which she required psychiatrist's intervention and follow-up.

Over the subsequent decade, she underwent multiple biopsies and scans for suspected recurrence, all results remained negative. She was disease-free for 16 years but continued to endure significant long-term effects of 3D-CRT.

4 DISCUSSION

Pregnancy complicated by malignancies is relatively rare but the incidence of cancer during pregnancy has increased in recent decades. Among these, NPC is comparatively rare during pregnancy, especially when compared to other female-related cancers such as cervical, breast, ovarian and those haematological malignancies [6]. In this case study, the patient was diagnosed during the postmortem period with stage III disease. Pregnancy-associated nasopharyngeal carcinoma has been linked to poorer survival outcomes, largely because of delays in diagnosis and treatment. Symptoms may be overlooked or misattributed during pregnancy, which can hinder timely intervention [8].

Despite the patient achieving survival of more than a decade post-treatment, she continued to experience significant long-term side effects that greatly impacted her quality of life. She suffered severe dental issues, including tooth decay which led to necessitated total teeth extraction and persistent mandibular pain due to ORN. The relationship between radiotherapy and ORN is well-defined, but the role of pre-radiotherapy dental extractions remains debatable.

Some studies recommended that pre-radiotherapy dental extractions may increase the risk of ORN and do not encourage tooth extraction before starting treatment [9]. Conversely, some research proposed that decayed teeth may need to be extracted before initiation of radiotherapy in the affected area but must allow at least 7 to 21 days for wound healing [10].

In terms of CCRT, although 3D-CRT was once standard modality, it has now been largely supplanted by intensity-modulated radiotherapy (IMRT) due to its superior precision and less toxicity profile. Numerous studies have demonstrated the superiority of IMRT over 3D-CRT in the treatment of NPC. A study was conducted in Japan to compare the locoregional control and progression-free survival rates between the groups of patients treated by IMRT and 2D /3D-RT. The results showed that patients treated with IMRT had higher 5-year rate of overall survival and less late toxicities of grade 2 or higher [11]. Another study showed similar findings that 2D/3D-RT had higher frequencies of both acute and late toxicities than IMRT populations. However, there is no statistical difference between IMRT and 2D/3D-RT in term of death. [12]

5 CONCLUSION

This case underscores the long-term sequelae experienced by a female NPC survivor treated with 3D-CRT 16 years ago. The tolerability of induction chemotherapy and radiotherapy remains controversial, necessitating a case-by-case approach to treatment indications and timing. While aggressive multimodal therapy shows better survival outcome, its enduring side effects may continue to impact the patient's life. This emphasizes the dual burden of advanced NPC and its treatment—highlighting the need for integrated survivorship care that addresses long-term physical, psychological, and social challenges.

ACKNOWLEDGEMENT

We acknowledge the oncology and radiotherapy teams for their support in the management and follow-up of this case.

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Figure 1. Repeated PET-CT scan post 3D-CRT. There was increased FDG accumulation in the nasopharynx, indicating residual disease which necessitated another 6 cycles of Cisplatin and Fluorouracil.