

A case of nasopharyngeal carcinoma and precious pregnancy

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SUMMARY

Cancer during pregnancy is a rare condition. We report here a case of a lady diagnosed with nasopharyngeal carcinoma (NPC) at University of Malaya Medical Centre during her first pregnancy conceived via In Vitro Fertilisation (IVF). A multidisciplinary (MDT) meeting among Oncology, Obstetrics, Rheumatology and Otolaryngology teams was conducted to discuss her treatment options. She opted for treatment with Complementary and Alternative Medicine (CAM). This case illustrates the unique challenges in the oncological management of a patient diagnosed with NPC during pregnancy. It also serves as a reminder that the use of CAM in cancer patients is prevalent. It is important for doctors to inquire about use of CAM and to be well-informed about it. Transparent communication and taking cognizance of the goals and concerns of the patients are essential in delivering patient-centred care.

CASE REPORT

A 33-year-old Chinese school teacher presented in March 2019 at University of Malaya Medical Centre (UMMC) with a 3-month history of unilateral right otitis media which did not improve with antibiotics. She had a background of systemic lupus erythematosus (SLE) which was well controlled on Azathioprine 75mg OD and Hydroxychloroquine 400mg OD. She was diagnosed with primary infertility and had been desperately trying to conceive for the last 5 years, with two previous failed IVF attempts. Our patient and her partner were delighted with the news of their 10-week pregnancy. This news occurred at a similar time-point with her presentation of unilateral otitis media.

She initially presented to a private hospital where she underwent a series of investigations. Nasoendoscopy showed exophytic mass arising from the right fossa of Rosenmuller (FOR). A biopsy was done which showed non-keratinizing squamous cell carcinoma, differentiated subtype. After she was diagnosed with nasopharyngeal carcinoma (NPC), she was referred to UMMC, a public tertiary referral centre. At this point, she was 13 weeks into her pregnancy.

Imaging studies included magnetic resonance imaging (MRI) of the head and neck which showed a soft tissue lesion at the right FOR extending slightly across the midline (Figure 1a). The adjacent parapharyngeal spaces, pterygoid muscles, and

skull base were preserved with sub-centimetre cervical lymph nodes. Her pregnancy limited staging investigations but a chest X-ray (with abdominal shielding) and ultrasound of the abdomen did not reveal metastatic lesions. Staging at the point of diagnosis was T2N0M0. We conducted a multidisciplinary (MDT) meeting between Oncology, Obstetrics, Rheumatology and Otolaryngology teams to discuss her treatment options.

Treatment options discussed were the following:

1. Primary radiotherapy (RT) with curative intent to be delivered in her second trimester. Adequate abdominal shielding is needed to reduce risks of mental retardation, malformation, childhood cancer, miscarriage, preterm labour, and cataracts to the fetus (most likely <5%).¹
2. Neoadjuvant chemotherapy as a holding measure that would be scheduled to start in 2nd trimester, after 16 weeks period of gestation (post organogenesis) and RT after delivery. There are also risks to the mother (infection, bleeding) and fetus (malformations, intrauterine growth retardation, malformations).
3. Termination of pregnancy with either medical or surgical methods.

The patient and her partner opted for primary radiotherapy. A planning meeting was held between physicists, dosimetrist, and clinical oncologists to discuss and plan the details and logistics of radiotherapy delivery. Our team conducted a literature review on technical considerations of radiotherapy planning for NPC patients in pregnancy which revealed that the total fetal dose recommendation is less than 0.1Gy for the entire treatment. ¹ We decided to employ a cost-effective method using Cerrobend for abdominal shielding. As collimator scatter was the main contributor of peripheral dose, we reduced it with a custom-built Cerrobend shield placed beneath the collimator head, reducing the fetal dose by a factor of 3.5. Initial anthropomorphic study (Figure 2a) with volumetric modulated arc therapy (VMAT) using diode found total dose to be 0.07Gy at fundus (without abdominal shielding). A rectangular portable Cerrobend shielding screen was custom made to reduce scattered dose during gantry positions of 90 degrees and 270 degrees (Figure 2b). Radiotherapy of 70Gy 33 Fractions in 6.5weeks was planned to be delivered using volumetric modulated arc therapy (VMAT).

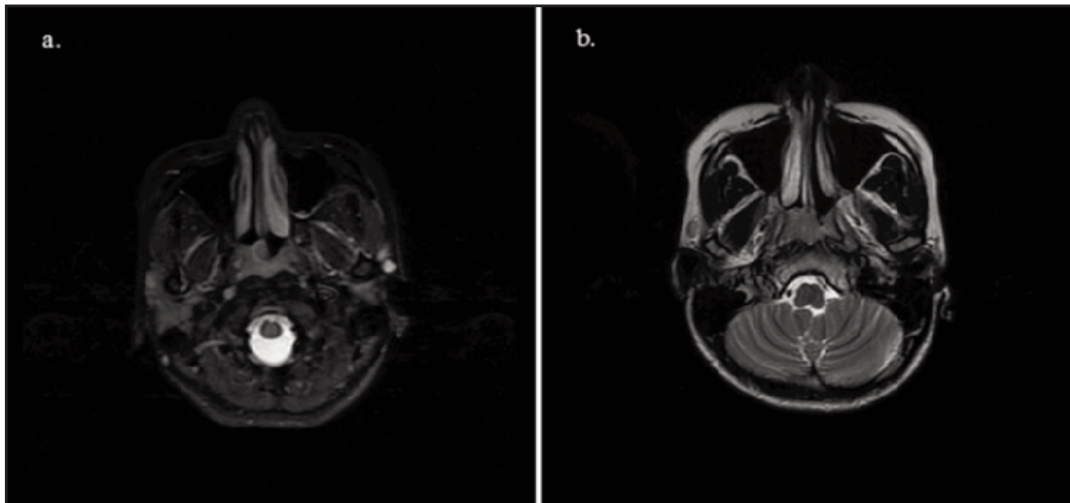


Fig. 1: (a) Axial MRI showing nasopharyngeal carcinoma at the right Fossa of Rosenmuller, at diagnosis. (b) Axial MRI showing nasopharyngeal carcinoma 3 months.

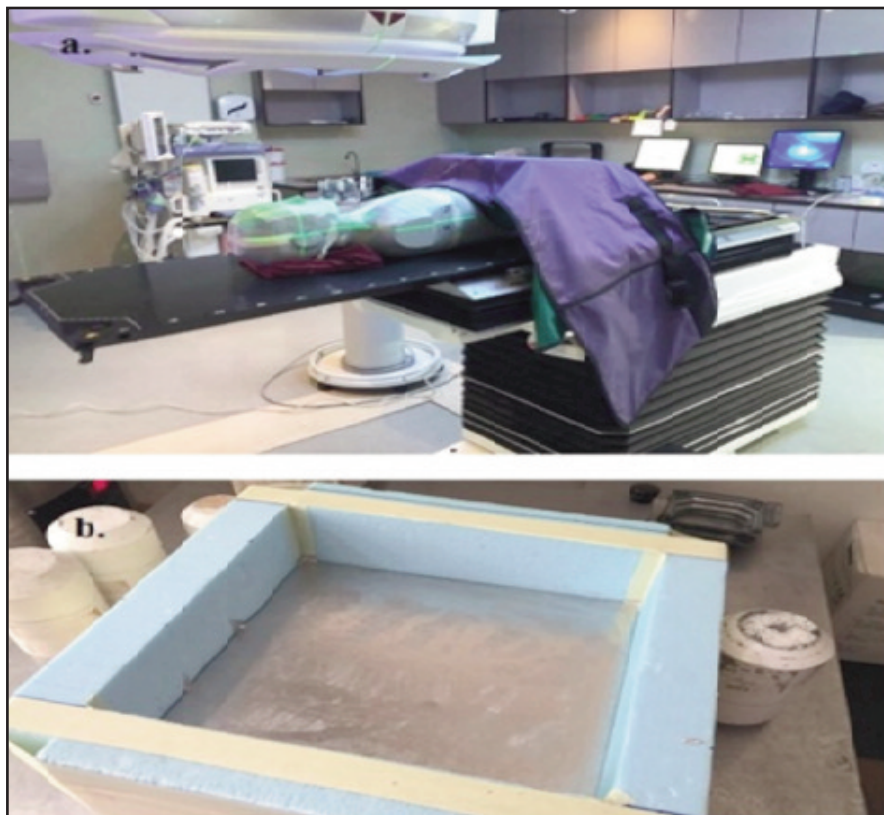


Fig. 2: (a) Anthropomorphic study using diode in VMAT (b) Moulding for Cerrobend as abdominal shielding.

Computed tomography (CT) simulation was scheduled with treatment planned to start in her second trimester. Patient was also assessed and supported by a clinical psychologist throughout her decision-making process. The patient and her partner also sought further opinions from another private hospital in Malaysia as well as Singapore. Similar treatment options were advised.

However, after some deliberation, our patient subsequently declined oncological management. She investigated various alternative therapies and was recommended Yuan Shi Dian (YSD) (Origin Point Therapy) by a close friend. She chose to proceed with YSD despite our explanation that there is no scientific evidence supporting the use of YSD in the treatment of NPC, with a real risk of disease progression.

They went abroad to Taiwan for Yuan Shi Dian (YSD) treatment. YSD's concept is aimed at replenishment of internal and external heat sources coordinated with appropriate exercise, proper rest, and a good state of mind to achieve self-healing. They went through an 18-day program with an emphasis on lifestyle modification to boost body recovery. Her diet consisted of "heaty food" (mainly ginger, spices, pepper, avoiding fruits) and 1.5 hours of daily exercise. Upon returning to Malaysia, she continued with YSD treatment and updated her YSD practitioners in Taiwan via phone, reporting on her meals and physical activities. Despite being discouraged by her YSD practitioners; she was compliant with her hospital appointments. Our team continued monitoring her NPC. We arranged for a follow-up MRI Head and Neck, which showed marginal enlargement of her NPC 3 months after diagnosis (Figure 1b). She opted to continue with YSD treatment until delivery.

She subsequently disengaged with us but kept her obstetrics appointments in our hospital. She delivered a healthy baby at 38 weeks but opted for oncological care in a different hospital. Post-delivery, she received induction chemotherapy with a plan of subsequent chemo-radiotherapy, 11 months after initial diagnosis.

DISCUSSION

Principles of Oncological Management of NPC in pregnancy Radiotherapy (RT) and concurrent chemo-radiation therapy (CCRT) are currently the primary treatments for NPC as the tumour is radio- and chemo-sensitive and is often located at anatomical locations where surgery may not be feasible. When treated with RT, over a 90% 5-year survival rate can be achieved in patients with early-stage NPC. Potential radiation effects to the fetus include lethality, malformations, mental retardation, and cancer induction.¹ Hence, fetal dose estimation and fetal dose reduction are crucial in the radiotherapy planning of cancer patients in pregnancy. The resulting dose to the fetus is dependent on the total radiation dose, the distance between the target lesion and the fetus, leakage from equipment, scattered radiation from collimator and beam modifiers, and the radiation scattered within the patient.¹ Shielding protects the fetus from scattered dose in the room and increases the distance from the target to the fetus.¹ It also reduces the radiation scattered within the patient that is received by the fetus.¹ In general, studies suggest that radiotherapy is to be done after 16 weeks of gestation with adequate shielding. A retrospective case-control analysis done by Cheng YK et al. demonstrated no statistically significant difference in overall survival, distant metastasis-free survival, loco-regional relapse free survival and disease-free survival between pregnancy-associated NPC patients and non-pregnant patients with NPC (control group).² In both groups, 81% had received chemotherapy (Neoadjuvant, concurrent and/or adjuvant chemotherapy according to the Oncologist's discretion) and all patients had received definitive radiotherapy (IMRT or 2D-CRT).²

Our patient's history of SLE can potentially increase her risk of radiotherapy toxicity. We consulted her rheumatologist for input on her SLE during our multi-disciplinary discussion. Given her SLE is mild, with minimal organ involvement, the consensus was that benefit derived from radiotherapy

outweighs its potential toxicities. This information was conveyed to the patient when she was counselled for treatment.

Data on the effect of chemotherapy on fetus are limited due to the rarity of cancer-pregnancy conditions and ethical issues pertaining to clinical trials involving humans. For NPC, the main chemotherapeutic agent is Cisplatin which produces chromosomal aberrations in normal cells and is teratogenic in mice.² In general, chemotherapy is not recommended during the first trimester when organogenesis is taking place.²

CAM Use in Cancer Patients

Complementary and alternative medicine (CAM) refers to various medical and healthcare systems, practices, and products that are not considered part of conventional medicine. It is important to note that the existing randomized controlled trials on CAM use in NPC are in the context of its role as adjunctive therapy to Oncological treatment. In response to WHO's strategy, the Traditional and Complementary Medicine Division (T&CMD) in Malaysia developed its own Traditional and Complementary Medicine (T&CM) Blueprint in 2017 to allow stakeholders, mainly CAM users to access T&CM in a safe manner by promoting evidence-based practice.³ This organization collaborates with the WHO in providing education, clinical training and regulation on T&CM. Under the Ministry of Health, the National Cancer Institute has established a T&CM unit on site, and it has been operating since 2013. The T&CM unit provides acupuncture, herbal remedies and massages as supportive symptom control measures rather than a substitute to conventional disease modifying treatments. In addition, this division holds health events and lectures to educate the public on utilizing T&CM in cancer patients in a safe and effective manner.

An important milestone was achieved in 2016 with the enforcement of T&CM Act 2016 (Act 775) for regulation of its industry to ensure safe and quality service is delivered.⁴ This registry acts akin to the General Medical Council for monitoring purposes. Under Act 775, a fine of up to RM 50,000, or jail sentence for 3 years can be charged to practitioners who are not registered.⁴

The use of CAM may be prompted by various factors including one's cultural beliefs, fear of side effects of conventional treatment, need for personal control, and lack of communication with doctors. A cross-sectional study done in Malaysia showed that nutritional supplements, herbal products, and multivitamins were the most frequent CAM used by cancer patients.⁵ Other forms of CAM used included traditional Chinese and Malay medications, light therapy and ozone therapy.⁵ Although a large percentage (14.5 - 91%) of cancer patients use CAM, studies suggest that approximately 60% of cancer patients do not disclose their use of CAM to their doctor.⁵ Reasons given for non-disclosure include the perception that it is not important for doctors to know, the question was not asked, doctors have minimal knowledge on CAM, fear of disapproval and fear of termination of conventional therapies.⁵ Failure to elicit information or to encourage discussion on patients' concerns inhibits rapport and contributes to non-disclosure. Having

these discussions may uncover essential information about unrecognised interactions between conventional drugs and CAM agents and may be an opportunity to educate patients on this.

It is imperative that further studies are done to investigate interactions between CAM and conventional oncological therapies as well as the safety and potential adverse effects of CAM. There remains a dire need for conventional medical practitioners to be provided with guidance on how best to manage patients who opt for CAM and to be equipped with basic knowledge of CAM and its interactions with conventional therapies.

CONCLUSION

We report a rare case of nasopharyngeal carcinoma in pregnancy in which the patient opted for CAM during pregnancy followed by conventional oncological treatment post-delivery. Awareness that CAM use is prevalent among cancer patients should prompt oncologists to elicit this information during patient encounters. Understanding the basic principles of oncological management during pregnancy is imperative in minimising maternal and fetal risk.

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