

NASOPHARYNGEAL CARCINOMA DURING PREGNANCY

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SUMMARY

Objective: Nasopharyngeal carcinoma, particularly during pregnancy, rarely comes to medical attention before it spreads to the regional lymph nodes.

Case Report: We report a 26-year-old Taiwanese woman who suffered from persistent headache and purulent nasal discharge during mid-pregnancy. Magnetic resonance imaging examination showed a large soft tissue mass measuring 3 × 2 × 2 cm in the left nasopharynx at 31 weeks of gestation. Punch biopsy of the tumor was done, and the histopathologic report revealed poorly differentiated, non-keratinizing type of squamous cell carcinoma (T4N2M0). A female infant weighing 1,790 g was delivered by cesarean section at 33 weeks of gestation with Apgar scores of 5 and 8 at 1 and 5 minutes, respectively. The patient received chemotherapy and radiation therapy after delivery. She was disease-free for 3 years. Subsequently, the patient delivered a second healthy infant weighing 3,084 g in a consecutive pregnancy, with a 3-year birth interval. Her first and second child showed normal psychomotor development at 3 years and 6 months of age, respectively.

Conclusion: The possibility of rare nasopharyngeal carcinoma should be considered in any pregnant woman with presenting symptoms of persistent headache and abnormal nasal discharge, and a detailed thorough investigation is indicated. Successful pregnancy outcome can be achieved after tailored use of a combination of chemotherapy and radiotherapy. [*Taiwan J Obstet Gynecol* 2007;46(4):423–426]

Key Words: chemotherapy, nasopharyngeal carcinoma, pregnancy, radiation therapy

Introduction

Nasopharyngeal carcinoma (NPC) is a rare tumor in the United States and Western Europe, with an incidence of 0.5 to 2 per 100,000 [1]. In contrast, NPC is far more common in southern China where incidence rates as high as 25 to 50/100,000 per year have been reported [2]. NPC has a bimodal age distribution. A small peak is observed in late childhood, and a second peak occurs in people aged 50–60 years, and male to female ratio ranges from approximately 2:1 to 3.5:1 [1]. The scarcity and deep-seated location of NPC often delays diagnosis and presents with an advanced-stage tumor at diagnosis. The etiology of NPC suggests at least three

major factors: environmental factors [3], viral infection (EB virus), [4] and genetic factor (deletion of 3p and 16q, heredity, molecular pathogenesis) [5].

Cancer complication is approximately 1 per 1,000 pregnancies [6] and is rarely found as nasopharyngeal cancer [7–9]. The evaluation and treatment of pregnant women with cancer are generally similar to those of nonpregnant women with a few exceptions. The risks associated with chemotherapy or radiation therapy depend on the gestational age and the dosage of antineoplastic agents and radiation dose. This report describes a pregnant woman in which advanced-stage NPC was diagnosed, and two successful pregnancy outcomes were achieved after tailored use of a combination of chemotherapy and radiotherapy.

Case Report

A 26-year-old Taiwanese primigravida received regular antenatal care at a local hospital. Unfortunately, she

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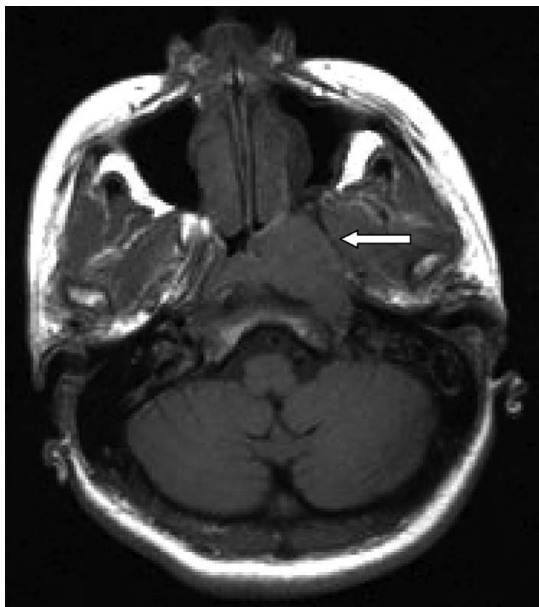


Figure 1. Axial T1-weighted image demonstrates a large iso-intense signal intensity tumor (arrow) measuring $3 \times 2 \times 2$ cm in the left nasopharynx.

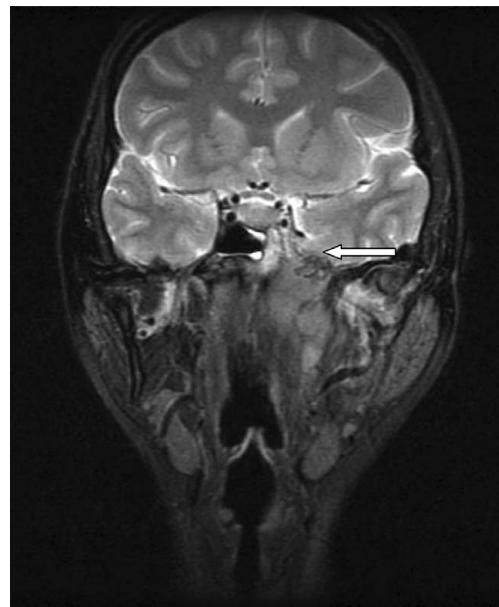


Figure 2. Coronal T2-weighted image depicts skull base tumoral invasion, which is of moderately low signal intensity (arrow).

suffered from nasal discharge and headache, especially in the left parietal area 3 months prior to admission. Initially, she visited a neurologist at a tertiary care hospital for further evaluation. Brain computed tomography was performed, revealing a negative finding. The impression was that of common cold with rhinitis, and she received medication at that time. She was referred to our emergency department because of persistent headache, and paranasal sinusitis was suspected owing to purulent nasal discharge. However, a large nasopharyngeal mass was noted after nasopharyngoscopic examination. Punch biopsy of the tumor was done, and the pathologic report revealed squamous cell carcinoma that was poorly differentiated and of the non-keratinizing type. Because of the intractable headache and pregnant state, she was admitted for tumor survey. Magnetic resonance imaging (Figures 1 and 2) revealed a large mass $3 \times 2 \times 2$ cm in the left nasopharynx, loss of fat signal intensity over the petrosal apex of the left temporal bone and left-side pterygoid process of the sphenoid bone, bone destruction of the skull base by the tumor, and minimal soft tissue over the left parasellar region; and intracranial invasion was considered to be present. Under the impression of advanced-stage NPC (T4N2M0), a radiation oncology doctor was consulted and combined chemoradiotherapy was suggested. She underwent elective cesarean section at 33 weeks' gestation, and a female infant weighing 1,790 g was delivered with Apgar scores of 5 and 8 at 1 and 5 minutes, respectively. Six days after delivery, chemotherapy with cisplatin 60 mg/m^2 at

day 1 and 5-fluorouracil $2,500 \text{ mg/m}^2$ plus leukovorin 250 mg/m^2 at day 8 repeated every two weeks was given for five courses smoothly. Radiation therapy was performed by intensity-modulated radiation therapy with dose 7,000 cGy divided into 35 fractions delivered in 7 weeks by 6 MV photon beam from a linear accelerator. Complete regression of the tumor was observed by nasopharyngoscopy and computed tomography scan 3 months after radiotherapy. She received regular follow-up and tumor survey during the next 3 years, with no evidence of tumor recurrence. Subsequently she conceived again and received antenatal care at our institution. She underwent repeat cesarean section, and a healthy male infant weighing 3,084 g was delivered with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively, with a 3-year birth interval. She was discharged in stable condition. Furthermore, she received restaging work-up in September 2006, and all surveys, including tomography of nasopharynx, whole body bone scan, abdominal sonography and chest X-ray, showed no evidence of tumor recurrence. Her first and second child showed normal psychomotor development at 3 years of age and 6 months of age, respectively.

Discussion

The incidence of malignancies during pregnancy has increased in recent decades. The most common malignancies associated with pregnancy are cervical, breast, melanoma, ovarian and hematologic cancers (leukemia

and lymphoma) [6], but NPC is rarely found during pregnancy. NPC occurs with a high frequency in Chinese people, especially in those from the southern provinces of China and Taiwan [10]. The incidence of NPC in Taiwan is 8.3/100,000 in the male and 3.5/100,000 in the female population [11]. It has been the sixth leading malignant tumor for women in Taiwan since 1983. The histopathologic type of more than 90% of patients is undifferentiated or non-keratinizing squamous carcinoma and is diagnosed at a mean age of around 45 years.

NPC originates in the fossa of Rosenmuller. This is an occult site, and patients often remain asymptomatic for a prolonged period. The most common presenting nasal symptoms include bleeding, obstruction and discharge (77.5%), ear symptoms including deafness and tinnitus (73%), headache (61%), and neck swelling (60%). The clinical triad of a neck mass, nasal obstruction with epistaxis, and serous otitis media occurs infrequently. Bone erosion into the skull base with or without cranial nerve impairment is common at diagnosis. In a study, skull base invasion was seen in 63% of the 150 patients at presentation [12]. Cranial nerves III to VI are most commonly affected. In contrast to other epidermoid cancers of the head and neck, NPC has a greater tendency for early metastatic spread [1].

Adverse prognostic features include cranial nerve palsies, involvement of the paranasopharyngeal space, advanced age, male sex, and involvement of the lymph nodes. The prognosis is worse with distal lymph node involvement proceeding from the upper cervical chain to the middle and lower cervical chain.

Yan et al [7] reported 27 cases of NPC in which the patients were found either to be pregnant during treatment or to have given birth to children after radiotherapy. Nine patients were discovered to be pregnant during treatment (the concurrent group), and 18 patients became pregnant during their follow-up period after radiotherapy (the subsequent group). In the concurrent group, only one patient survived for more than five years without any evidence of tumor recurrence. All the other patients died within one and a half years after radiation. In the subsequent group, 83% (15/18) of patients were living and disease-free for 5 years or more after therapy. Wong et al [8] reported a case in which NPC was diagnosed at 21 weeks' gestation, and the patient received irradiation treatment with the use of 6 million electron volts photon beam from the linear accelerator. The total dose to the nasopharynx was 6,250 cGy in 29 fractions over 6.5 weeks and to the neck in 3,920 cGy in seven fractions over 6 weeks. Fetal growth was assessed biweekly by ultrasound. Normal

fetal growth was observed throughout the pregnancy, and the baby weighing 3,700 g was delivered at 38 weeks' gestational age by cesarean section.

Lin et al [13,14] reported that concurrent chemoradiotherapy is superior to radiotherapy alone for low-risk patients. Adding neoadjuvant and/or adjuvant chemotherapy would be a reasonable approach for high-risk patients. However, chemotherapy or radiation therapy during pregnancy is a challenge to the obstetrician. For NPC, major regimens of chemotherapy are cisplatin and 5-fluorouracil. Cisplatin (risk factor D_M) is an anti-neoplastic used in the treatment of various cancers. This agent produces a chromosomal aberration in normal cell in the tissue culture and is teratogenic and embryotoxic in mice. It is also a transplacental carcinogen in rats, producing tumors in the liver, lung, nervous system, and kidney of adult offspring, probably the result of DNA damage in fetal rat tissues. Only a few cases of cancer in pregnancy that used cisplatin in anti-neoplastic therapy have been reported. Sensorineural deafness with undetermined cause was reported in one of the seven cases. Green et al [15] reported that no congenital malformation was observed in seven liveborn offsprings treated with cisplatin during childhood or adolescence.

Fluorouracil is embryotoxic and teratogenic in mice, rats, and hamsters when given parenteral doses equivalent to the human dose. Multiple fetal defects were observed during systemic therapy in the first trimester [16]. Breast cancer during pregnancy using fluorouracil in antineoplastic therapy have been reported. Giacalone et al [17] reported the outcomes of pregnancies in 20 women with breast carcinoma who were treated with antineoplastic agents; the outcomes included two spontaneous abortions in the first trimester, one intrauterine fetal death in the second trimester, and 17 live births, one of whom died after 8 days. The 16 surviving children developed normally at a mean follow-up of 42.3 months. We recommend that cisplatin and fluorouracil use be avoided in the first trimester.

In general, the radiation effects include lethality, malformations, mental retardation, and cancer induction [18]. According to the International Commission on Radiological Protection publication and the Centers for Disease Control and Prevention [19,20], the dose-response relationships for mental retardation among those irradiated at week 8–15 or 16–25 postconception were initially reported as linear. A more recent analysis has evaluated whether the data are supportive of a threshold using several different models. All the models that provided a good fit to the data indicated a threshold for mental retardation for irradiation at week 8–15 and 16–25 postconception. Besides, the

results for school performance were similar to those for IQ. An association between radiation dose and poorer school performance was seen for those exposed at week 8–15 and 16–25 postconception, with the stronger trend among those in the week 8–15 group. During the mid-fetal period, small head size and mental retardation can often be seen in those with doses exceeding 50 cGy. Small head sizes were seen in two of 30 and two of 44 children exposed *in utero* to doses below 10 cGy and between 10 and 50 cGy, respectively. Mental retardation was observed in 2% for exposures up to 49 cGy.

In conclusion, the possibility of rare NPC should be considered in any pregnant woman with the presenting symptoms of persistent headache and nasal discharge, and a detailed thorough investigation is indicated. Successful pregnancy outcome can be achieved after tailored use of a combination of chemotherapy and radiotherapy.

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