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Original article

Pregnancy associated nasopharyngeal carcinoma: A retrospective case-control analysis of maternal survival outcomes

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ABSTRACT

Background: Pregnancy-associated nasopharyngeal carcinoma (PANPC) has been associated with poor survival. Recent advances in radiation technology and imaging techniques, and the introduction of chemotherapy have improved survival in nasopharyngeal carcinoma (NPC); however, it is not clear whether these changes have improved survival in PANPC. Therefore, the purpose of this study was to compare five-year maternal survival in patients with PANPC and non-pregnant patients with NPC.

Methods: After adjusting for age, stage and chemotherapy mode, we conducted a retrospective case-control study among 36 non-metastatic PANPC patients and 36 non-pregnant NPC patients (control group) who were treated at our institution between 2000 and 2010.

Results: The median age of both groups was 30 years (range, 23–35 years); median follow-up for all patients was 70 months. Locoregionally-advanced disease accounted for 83.3% of all patients with PANPC and 92.9% of patients who developed NPC during pregnancy. In both the PANPC and control groups, 31 patients (86.1%) received chemotherapy and all patients received definitive radiotherapy. The five-year rates for overall survival (70% vs. 78%, $p = 0.72$), distant metastasis-free survival (79% vs. 76%, $p = 0.77$), loco-regional relapse-free survival (97% vs. 91%, $p = 0.69$) and disease-free survival (69% vs. 74%, $p = 0.98$) were not significantly different between the PANPC and control groups. Multivariate analysis using a Cox proportional hazards model revealed that only N-classification was significantly associated with five-year OS.

Conclusion: This study demonstrates that, in the modern treatment era, pregnancy itself may not negatively influence survival outcomes in patients with NPC; however, pregnancy may delay the diagnosis of NPC.

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Nasopharyngeal carcinoma (NPC) is a highly endemic disease with an unbalanced distribution, and has a high incidence in Southern China and the surrounding regions [1]. Pregnancy-associated nasopharyngeal cancer (PANPC) has been defined as NPC diagnosed during pregnancy or within one year of delivery [2], and presents both diagnostic and therapeutic dilemmas. Pregnancy complicated by cancer is a relatively rare phenomenon with an incidence of 0.02–0.1% [3]. With the recent trends for women delaying pregnancy into later reproductive years [4] and the higher incidence of NPC in individuals over the age of 30 [5], physicians can expect to see increased numbers of cases of PANPC in the future.

There is no difference in the survival rates of pregnant and non-pregnant patients in some types of cancer [6,7]. However, previous case reports and small sample studies performed in the 1980s and 1990s indicated that patients with PANPC have a much poorer prognosis than female patients with NPC [8,9]. As a result of the development of diagnostic and therapeutic techniques and the introduction of chemotherapy, the management of NPC has been revolutionized and the 5-year relative survival rates have improved from approximately 50–75% in the last 10 years

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[10,11]. Nevertheless, it remains unclear whether patients with PANPC still have a poorer prognosis than patients with NPC. Furthermore, previous reports have suggested that patients with PANPC tend to present at a more advanced stage [8,9,12]. Therefore, the survival of patients with PANPC needs to be investigated and compared with non-pregnant patients of the same stage who receive the same treatment. However, as previous studies were limited by the rarity of PANPC, they were hindered by relatively small sample sizes and lack of control groups.

On the basis of this premise, we conducted a retrospective case-control study to compare the rates of overall survival (OS), distant metastasis-free survival (DMFS), local relapse-free survival (LRFS) and disease-free survival (DFS) in patients with PANPC and non-pregnant patients with NPC.

Materials and methods

Patients

This retrospective study was approved by the institutional review board, and the requirement to obtain informed consent was waived. This case-control study was designed to compare female patients with PANPC with non-pregnant age-, stage- and chemotherapy-matched controls who were diagnosed and treated at our institution between June 2000 and November 2010. In total, 36 patients with PANPC and 36 age-, stage- and chemotherapy-matched female patients with NPC who were not pregnant were identified from our institution registry. Data were obtained from the patients' charts and the institution registry. Patients who developed clear symptoms of NPC, especially a cervical mass, during pregnancy but whose diagnostic workup was delayed until after delivery were considered to have developed cancer "during" pregnancy, in contrast to the patients who developed clear symptoms within 1 year after delivery. Pathological diagnosis was confirmed in all individual cases. The data collected included age, family history, pregnancy status, weeks of gestation, number of weeks postpartum, symptoms at presentation, diagnostic imaging, biopsy findings and NPC seromarkers. Details of the radiotherapy and chemotherapy treatment, date of death (if applicable), date of relapse and site(s) of relapse were obtained for all patients.

Treatment

The final decisions regarding treatment strategy, pregnancy management and the use of chemotherapy were based on clinical stage, the physician's discretion and patient choice. None of the patients underwent treatment during pregnancy.

Radiotherapy

All patients were treated with definitive-intent radiotherapy in the form of two- dimensional conventional radiotherapy (2D-CRT) or intensity-modulated radiotherapy (IMRT). All patients were treated with one fraction daily for 5 days per week.

Table 1
Patient and tumor characteristics.

Characteristic	Non-PANPC *n* = 36 *n* (%)	PANPC *n* = 36 *n* (%)	*P*-value*
Age at diagnosis, *y*			NS
⩽30	21 (58.3)	21 (58.3)	
>30	15 (41.7)	15 (41.7)	
Family history			NS
Positive	11 (30.6)	12 (33.3)	
Negative	25 (69.4)	24 (66.7)	
WHO histologic type			NS
I	1 (2.8)	0	
II	1 (2.8)	0	
III	34 (94.4)	36 (100)	
Stage†			NS
I	0	0	
II	6 (16.7)	6 (16.7)	
III	21 (58.3)	21 (58.3)	
IV	9 (25.0)	9 (25.0)	
Symptom			NS
BSND	18 (50.0)	22 (61.1)	
Cervical mass	18 (50.0)	18 (50.0)	
Headache	7 (19.4)	9 (25.0)	
Tinnitus	11 (30.6)	5 (13.9)	
Others	21(58.3)	10 (27.8)	
Seromarkers			NS
VCA-IgA+	31 (86.1)	34 (94.4)	
EA-IgA+	20 (55.6)	22 (61.1)	
Unknown	3 (8.3)	2 (5.6)	
RT technique			NS
2D-CRT	28 (77.8)	28 (77.8)	
IMRT	8 (19.4)	8 (19.4)	
Afterloading	2 (5.6)	4 (11.1)	
Chemotherapy			NS
Concurrent chemoradiotherapy	13 (36.1)	13 (36.1)	
Neoadjuvant + concurrent chemoradiotherapy	8 (22.2)	8 (22.2)	
Neoadjuvant chemotherapy + radiotherapy	8 (22.2)	8 (22.2)	
Concurrent chemoradiotherapy + adjuvant	2 (5.6)	2 (5.6)	
No chemotherapy	5 (13.9)	5 (13.9)	

WHO, World Health Organization; BSND, blood-stained nasal discharge; RT, radiotherapy; 2D-CRT, two-dimensional conventional radiotherapy; IMRT, intensity-modulated radiotherapy. NS, not significant.

* PANPC vs. non-PANPC; chi-square or Fisher's exact tests.

† The 7th American Joint Commission on the Cancer staging system.

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