Cancer Treatment and Research Communications 9 (2016) 126–130

Contents lists available at ScienceDirect

Cancer Treatment and Research Communications

journal homepage: www.elsevier.com/locate/ctarc

Nasopharyngeal carcinoma in pregnancy: A case series and literature review

Runa Shrestha[a], Vijaya Raj Bhatt[b], Weining Ken Zhen[c], Oleg Militsakh[d], Paul G. Tomich[e], Apar Kishor Ganti[b,f,*]

[a] Department of Medicine, SUNY Upstate Medical University, Syracuse, NY, USA
[b] Division of Oncology-Hematology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, USA
[c] Division of Radiation Oncology, University of Nebraska Medical Center, Omaha, NE, USA
[d] Division of Head and Neck Surgery, Department of Ot olaryngology, University of Nebraska Medical Center, Omaha, NE, USA
[e] Division of Maternal-Fetal Medicine, University of Nebraska Medical Center, Omaha, NE, USA
[f] Department of Internal Medicine, Veteran's Affairs Nebraska-Western Iowa Health Care System, Omaha, NE, USA

ABSTRACT

Nasopharyngeal carcinoma (NPC) in pregnancy presents a therapeutic challenge due to its rarity. We report our management approaches in three such patients. A 37-year-old woman was diagnosed with stage III (T1N2M0) NPC at 18 weeks of gestation. She was treated with antepartum induction chemotherapy and postpartum chemoradiation. She delivered a healthy infant at 37 weeks and is in remission at 2 years. Two other patients (ages, 30 years and 20 years) were diagnosed with stage IVB and III NPC at 27 and 31 weeks of gestation respectively. Both the patients elected to wait until delivery and were subsequently treated with chemoradiation followed by adjuvant chemotherapy. The patients are in complete long-term remission. Thus antepartum induction chemotherapy after the first trimester followed by postpartum chemoradiation may be effective for NPC in pregnancy. This helps avoid radiation induced feto-toxicity. Patients who present in later pregnancy may delay therapy until after delivery.

Introduction

The overall incidence of cancer in pregnancy is about 1 in 1000 pregnant women, with cervical and breast cancers being the most common [1]. However, as more women defer pregnancy to the later part of life, the incidence of cancer in pregnancy may be expected to increase. The use of computed tomography scans, radiation therapy and several chemotherapy regimens may have the potential of feto-toxicity [2–4]. In addition, pregnancy is associated with the increase in plasma volume and body weight, thus possibly resulting in lower plasma steady-state concentration, lower plasma half-life and high clearance rate of chemotherapeutic agents [5,6]. The modality of treatment of cancer in pregnancy should be based on the available clinical evidence for the stage of the cancer and also on the gestational age of the fetus. The rarity of pregnancy-related malignancies results in lack of evidence-based management of such cancers. In the past, the treatment option for a cancer diagnosed in pregnancy was frequently an early delivery rather than definitive therapy during pregnancy.

Nasopharyngeal carcinoma (NPC), endemic in Southern China and Taiwan, particularly in men, is a rare cancer in US with an estimated incidence of 0.5–2 per 100,000 population [7]. NPC can arise from a clinically occult site, fossa of Rosenmuller, which accounts for a prolonged asymptomatic period and advanced stage at diagnosis. NPC is a radiosensitive cancer; therefore, radiation therapy is the standard component of therapy for non-metastatic disease. The National Comprehensive Cancer Network guidelines recommend concurrent chemoradiation for Stage II-IV, and radiation alone for Stage I NPC [8]. The current treatment standard for locally advanced NPC includes concurrent chemoradiation with high-dose cisplatin (100 mg/m^2 on days 1, 22 and 43 of radiation) followed by adjuvant chemotherapy with cisplatin (80 mg/m^2 on day 1) and 5-fluorouracil (1000 mg/m^2/d on days 1–4) administered every 4 weeks for three cycles [9,10]. However, this approach is associated with significant toxicity and in the landmark SWOG study, only 73% of patients in the combined modality arm were able to complete recommended therapy [9].

This approach could be even more problematic in NPC during pregnancy because of the fetal toxicity associated with radiation. There are only few reported cases of NPC diagnosed in pregnancy, thus making the decisions empiric and difficult. Here we report three cases of NPC diagnosed during the second and third trimesters of pregnancy

* Correspondence to: Department of Internal Medicine, Division of Oncology-Hematology, University of Nebraska Medical Center, 987680 Nebraska Medical Center, Omaha, NE 68198-7680, USA.
E-mail address: aganti@unmc.edu (A.K. Ganti).

http://dx.doi.org/10.1016/j.ctarc.2016.09.006
Received 18 July 2016; Received in revised form 27 September 2016; Accepted 28 September 2016
2468-2942/ Published by Elsevier Ltd.

Table 1
Outcomes of nasopharyngeal carcinoma (NPC) in pregnancy.

Reference	Number of patients	Stage of NPC	Gestation Age (weeks)	Antepartum Therapy	Post-partum therapy	Outcome at last follow-up	Fetal birth weight (gm)/Apgar at 1 and 5 min
Present Cases	1	III	18	Induction chemotherapy	ChemoRT	Alive at 2 years	4907/4 and 7
	1	IV	27	None	ChemoRT, then additional chemotherapy	Alive at 13 years	2550/8 and 9
	1	III	31	None	ChemoRT, then additional chemotherapy	Alive at 12 years	1953/NA
Yan et al. [25]	9 Concurrent	I–IV	4–36 weeks	RT (n=4)	RT (n=6)	5-year OS 11%	NA
	18 Subsequent	I–IV	NA	NA	RT (n=18)	5-year OS 83%	NA
Star et al. [36]	1	IV	Symptoms at 16 weeks; diagnosed at 32 weeks	None	4 Cycles of chemo and RT	OS of 6 months	1750/5 and 7
Wong et al. [37]	1	III	21 weeks	RT[a]	None	NA	3700/normal
Lin et al. [38]	1	IVA	31 weeks	None	ChemoRT[b]	Alive at 3 years	1790/5 and 8

RT – radiation therapy.
NA – not available.
OS – overall survival.
[a] The dose of radiation to the nasopharynx was 6250 cGy given in 29 fractions over 6.5 weeks and the neck was 3920 cGy given in 7 fractions over 6 weeks.
[b] Cisplatin 60 mg/m² on day 1, 5-FU 2,500 mg/m² on day 8, every 2 weeks for 5 cycles. Intensity-modulated radiation therapy with dose 7000 cGy divided into 35 fractions delivered in 7 weeks by 6 MV photon beam from a linear accelerator.

and our management approach in these patients.

Case presentations

The details of each patient are described in Table 1. The first patient was a 37-year-old Caucasian woman, who presented with a 4-month history of right ear fullness and hearing loss at 18-week pregnancy. She had also noticed firm left-sided neck mass. She was evaluated by an otolaryngologist who found right sided serous otitis media and bilateral cervical lymphadenopathy. A flexible nasopharyngoscopy showed enlarged right adenoid and obstruction of right eustachian tube orifice. Biopsies of right adenoid showed undifferentiated carcinoma with lymphoid stroma (lymphoepithelial carcinoma), which was positive for keratin (AE1/3), negative for CD3 and CD20 and positive for Epstein-Barr virus by in situ hybridization.

A magnetic resonance imaging (MRI) of the neck without contrast confirmed prominent adenoid tissue, slightly asymmetric, with the right side larger than the left. The anterior-posterior dimension of the right adenoid was approximately 2 cm. There was prominent bilateral cervical lymphadenopathy. The largest lymph node on the left, deep to the sternocleidomastoid muscle, which was thought to possibly represent a confluent nodal mass, measured 4.5 cm x 3.5 cm x 1.5 cm. In addition, there were a cluster of lymph nodes on the right side, deep to the sternocleidomastoid muscle, with overall dimensions of 3.8 cm×2.3 cm×1.1 cm. She was diagnosed with Stage III (T1N2M0) undifferentiated nasopharyngeal carcinoma. After multidisciplinary discussion, she was started on induction chemotherapy with cisplatin 80 mg/m^2 on day 1 and infusional 5-fluorouracil 1000 mg/m^2 over 24 hours daily on days 1–4. Antiemetic prophylaxis included aprepitant and ondansetron. Following the first cycle of chemotherapy, she had partial improvement in hearing, and partial resolution of cervical lymphadenopathy. Apart from grade 1 nausea, she tolerated the therapy well, but lost about 2-lb weight during the first cycle. She was closely followed by a dietician and an obstetrician. The chemotherapy regimen was repeated every 28 days for a total of 4 cycles. This was done in order to minimize the duration between the end of chemotherapy and start of radiation, and allowing delivery as close to term as possible. At 37 weeks and 4 days of gestation, the patient presented in active labor, with spontaneous rupture of membranes. Estimated fetal weight on ultrasonography was 4900 g. The patient elected for and underwent primary low-transverse cesarean section of a viable male infant with a weight of 4907 g and Apgar scores of 4 and 7 at 1 and 5 min respectively. Her post-partum course was uncomplicated.

MRI neck performed postpartum, revealed a marked interval decrease in the mucosal lesion within the nasopharynx, and an improvement in cervical lymphadenopathy. There were several small lymph nodes throughout the bilateral deep cervical chain. The largest lymph node was within the left suprahyoid neck and measured 2.5 cm in long axis dimension. Approximately 2 weeks following the delivery, the patient was started on concurrent chemoradiation with cisplatin 100 mg/m^2 on day 1. This was complicated by the development of significant depression, gram-negative bacteremia with *Enterobacter cloacae*, renal dysfunction, anorexia, and 9-lb weight loss. She completed only one dose of cisplatin due to renal dysfunction and received 5600 of initially planned 6600 cGy to nasopharynx and bilateral neck lymph nodes in 28 fractions. An integrated 18F-fluorodeoxyglucose positron emission tomography and computed tomography scan of skull to mid-thigh 14 weeks after the completion of therapy showed only a mild diffuse increased radiotracer uptake seen in the nasopharyngeal region most likely physiologic in nature or post-treatment changes. At last follow-up, 2 years from the initial diagnosis, the patient continues to remain in clinical remission. She has not experienced any significant late toxicities of the radiation or chemotherapy. The baby appears to be growing appropriate for age without any obvious adverse effects as well.

The second patient, a 30-year-old woman, was diagnosed with