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Human Papilloma Virus Associated Oropharyngeal Cancer in Pregnancy: Diagnostic and Management Challenge

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Abstract

Human papilloma virus (HPV) associated head and neck cancer is a relatively new entity causing significant disease burden to otherwise healthy, young individuals. We describe the first case to our knowledge of HPV positive oropharyngeal cancer arising in a young pregnant woman. We discuss the implications of pregnancy on limiting management and treatment options and the need for timely multidisciplinary input. The case demonstrates how HPV squamous cell carcinoma is affecting a younger demographic and if not considered, can present as a diagnostic challenge. p-16 positive neck lymphadenopathy should be included in the differential diagnosis of a neck mass in a young patient. The case also illustrates the need for approved management guidelines in such a challenging clinical scenario.

Keywords: Head and neck neoplasms; Carcinoma; Squamous cell; Human papilloma virus 16; Pregnancy

Introduction

Human papilloma virus (HPV) associated oropharyngeal cancer is currently attracting a lot of interest, as its prevalence increases across western countries and the disease affects young, previously healthy individuals. Head and neck squamous cell carcinomas (SCCs) have traditionally been seen in older populations and are associated with significant tobacco and alcohol consumption.

Recent studies have shown what has been described as an epidemic of HPV oropharyngeal cancers in younger populations [1]. HPV SCCs are estimated to make up around 70-80% of all oropharyngeal cancers [1-3]. We are seeing a new subset of patients presenting in their thirties and forties with well-advanced head and neck tumors rarely seen in this population before. We present here the first case of HPV oropharyngeal SCC arising in a pregnant woman.

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Case Report

A 30-year-old female presented to the emergency department with a rapidly increasing, large right-sided neck lump. She was febrile with a level II neck mass, erythematous and warm to touch. She had trismus with an otherwise patent airway. Clinically the oropharynx was unremarkable. She was a non-smoker and did not drink alcohol. There was no other significant medical history.

Computed tomography (CT) (Fig. 1) showed large lobulated, cystic appearing, right neck lymphadenopathy with low Hounsfield unit (HU) of 30 - 35; also noted was right tonsillar enlargement without any imaging evidence of tonsillitis or peritonsillar abscess. The appearance was atypical for infection as there was no fat stranding or inflammatory change seen in the right neck in spite of large size of the nodes. She underwent incision and drainage under otolaryngology and pus samples grew *Streptococcus pneumonia*. She was treated with intravenous antibiotics and improved clinically.

Twelve months later she presented with a neck mass at the same location on the right neck. This had increased in size over a 2-week period and there was no improvement on oral antibiotics. She was 31 + 1 pregnant at the time (G3P1T1) and her pregnancy to date had been uncomplicated. She was referred to otolaryngology.

Clinically she was afebrile with large level II/III mass neither fluctuant nor erythematous. The airway was uncompromised. On examination, the right tonsil was enlarged without inflammation or exudate. Nasal endoscopy and blood inflammatory markers were normal. Serology indicated previous Epstein-Barr virus infection. Ultrasound showed no drainable collection and core biopsy of the mass revealed a poorly differentiated SCC of basaloid variant. Subsequent magnetic resonance imaging (MRI) (Fig. 2) found solid right neck lymphadenopathy, predominantly in levels II, III and V with small necrotic areas. A right oropharyngeal mass suggested a tonsillar primary. The imaging was performed without gadolinium

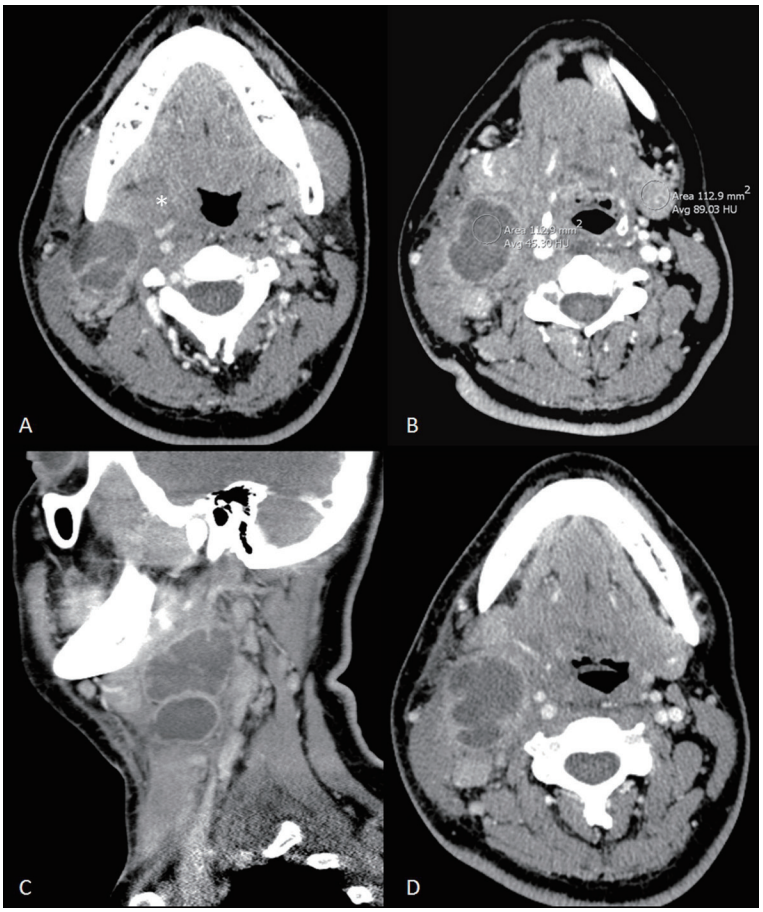

Figure 1. Contrast enhanced CT of the neck demonstrates right level II/III cystic appearing lymphadenopathy with peripheral enhancement and low HU of 31 in comparison to normal node of 89 HU in left IB location (B). Also note right tonsillar enlargement (*).

because of patient's pregnant status.

At 33 weeks into her pregnancy, the patient underwent tonsillectomy and panendoscopy. Histology of the right tonsil confirmed SCC of basaloid variant, with immunoperoxidase staining positive for HPV p-16, giving the diagnosis of T1N2b SCC right tonsil, HPV p-16 positive.

In consultation with obstetrics, the decision was made to induce labor at 34 weeks so that full staging CT and positron emission tomography (PET) workup could be completed and chemoradiotherapy could be commenced as a priority.

Discussion

HPV oropharyngeal SCCs (OPSCCs) arise from chronic HPV infection of the oral cavity, the most prevalent strain being p-16. The primary tumor is of the palatine tonsils or base of tongue and disease is linked to risky sexual activity and cigarette use [1, 2, 4-6]. Infection is thought to occur via local transmission of the HPV virus.

HPV OPSCCs commonly present as locally advanced disease with secondary lymph node metastases and a small or inconspicuous primary (T1-2, N2-3). Lymph nodes are often large and cystic in nature [1, 6]. On MRI, HPV positive nodes are large, cystic and demonstrate high T2 signal with a well-defined hypointense rim. On post contrast images, they usually demonstrate smooth rim enhancement and have low HU like our patient had an HU of 31. p-16 positive neck lymphadenopathy is indistinguishable from lymphoma or suppurative lymphadenitis on clinical grounds alone. Treating clinicians must be aware of this increasing new trend to avoid delay in the diagnosis. HPV OPSCC has a cure rate of > 90% if picked up early [1, 6, 7]. Initial clinical presentation and CT of our patient raises the possibility that the first episode may have been a cystic p-16 positive lymphadenopathy with tonsillar primary. Young age and possible secondary infection complicated things further, hence delaying the diagnosis.

Whilst women are less commonly affected by oral HPV than men (1:3), it is important to recognize that HPV OPSCC is arising in women of childbearing age. As prevalence continues to increase, with it estimated to overtake that of cervical cancer by 2020 [2], we will inevitably be seeing more patients presenting during pregnancy. This will bring on new challenges in directing investigation and treatment when weighing up risks to the mother and baby. For this reason, we feel there is a need for defined management of HPV OPSCC during preg-

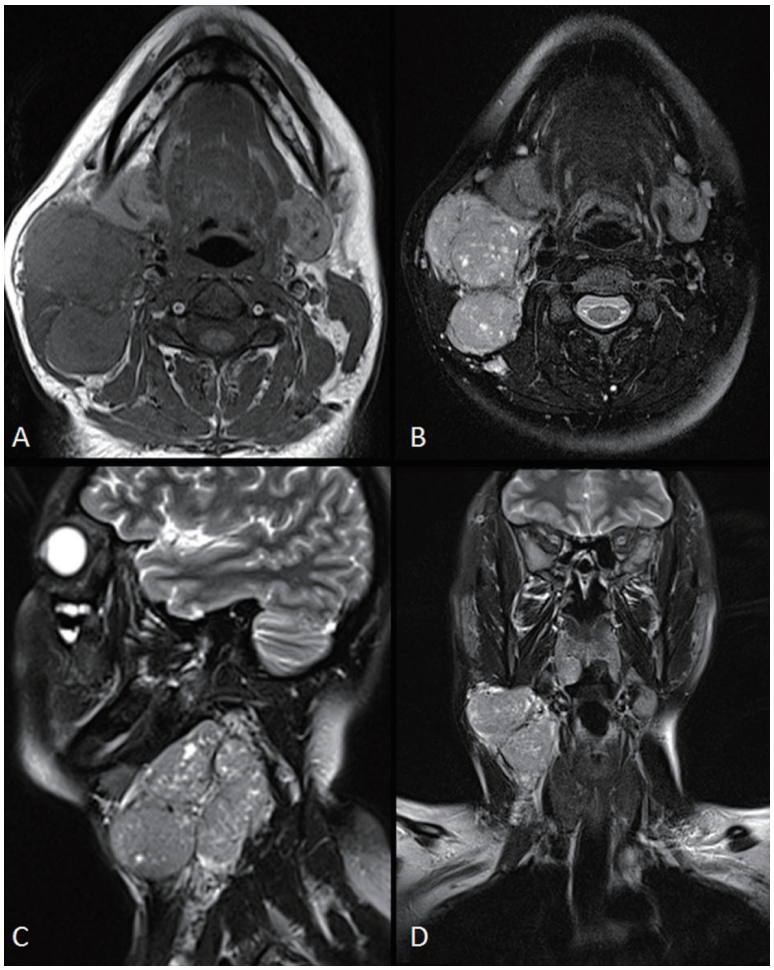

Figure 2. T1 W axial MR image (A) shows large solid mass in right level II/III location. Note marked heterogeneity of these lymph nodes on T2 W images (B to D).

nancy.

In pregnant patients, staging workup involving CT should be avoided and PET is contraindicated. Similarly MRI can be performed as the only relatively safe modality but gadolinium is avoided; this makes the study suboptimal for assessment of nodes. Safety of MRI in first trimester is still questionable [8, 9].

Chemotherapy agents commonly used with proven efficacy in HPV OPSCC include cisplatin, 5-fluorouracil and doxetaxal. Such regimes combining chemoradiotherapy are associated with significant toxicity [1, 6] and are detrimental to the fetus. Radiation should not be given during any stage of pregnancy [10].

Current guidelines exist for management of Hodgkin's lymphoma and breast, cervical and ovarian cancers during pregnancy. The mainstay of therapy is balancing the health of the mother and the fetus. We expect guidelines for treatment of pregnant women with HPV OPSCC would follow a similar principal.

With the introduction of the quadrivalent HPV vaccine to the National Immunization Program in Australia in 2006 for females, and most recently adolescent males in July 2012, we hope to see a decrease in HPV related OPSCC. Its efficacy against oropharyngeal disease, however, is yet to be established.

As the prevalence of head and neck HPV SCC continues to rise, we are likely to see more young women presenting during pregnancy. This poses a diagnostic and management challenge. p-16 positive neck lymphadenopathy should be included in the differential diagnosis of a neck mass in a young patient.

This case also illustrates the need for approved management guidelines in such a challenging clinical scenario.

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