

## Squamous Cell Papilloma in a Student Aviator

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**BACKGROUND:** Although oropharyngeal squamous cell papilloma (OSCP) is not uncommon in the general population, reports of OSCP in aviators are rare. This case report serves as a call for flight surgeons to consider all oropharyngeal pathology as a potential source of airway compromise during flight, and highlights regional risk factors for developing malignancies of the oropharynx.

**CASE REPORT:** A 24-yr-old male foreign national student aviator from a central Asian country was at Fort Rucker for flight training. He presented to the clinic with a chief complaint of sore throat and cough for 2 d. He was afebrile but reported a history of a "throat" mass which was previously evaluated by a U.S. military otolaryngologist. Said mass was approximately 0.5 cm × 0.5 cm, irregular appearing, inflamed, and protruding from the inferior aspect of the right tonsil. Previous biopsy report revealed a squamous cell papilloma and, after consideration of the pilot's training program, active surveillance of the lesion was mutually agreed upon until the student's training had concluded and definitive excision was performed.

**DISCUSSION:** A robust history and physical exam including an occupational, social, and environmental exposure history is crucial to diagnosis. Foreign national patients often have unique backgrounds that merit consideration when developing a differential diagnosis, assessment, and plan. In the field of Flight Medicine, a patient's occupational demands are essential to his or her care. In particular, any potential obstruction of the airway during flight must be considered, even if a pathology does not represent an immediate threat to the pilot's health.

**KEYWORDS:** oropharyngeal lesion, squamous cell, papilloma, oral mass, human, HPV.

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Oropharyngeal squamous cell papilloma (OSCP) is the most common papillary lesion of the oral mucosa, representing 2.5% of all oral lesions.<sup>7</sup> It is a noncontagious, benign overgrowth of well-stratified cells, generally < 10 mm in its largest dimension. OSCP typically lacks any histopathological signs of malignancy, including immature basaloid cells, nuclear pleomorphism, or atypic mitotic figures.<sup>1,7,16</sup> The lesion is commonly inflamed and is associated with *Candida* in up to 10% of cases. It is more common in men than women, and sometimes associated with human papilloma virus (HPV) infection.<sup>1,7,16</sup>

OSCP must be differentiated from malignant lesions, which can have deadly consequences if diagnosed late in their disease course. Head and neck cancers affect up to 560,000 patients per year worldwide, causing 380,000 deaths.<sup>4</sup> Of these, squamous cell carcinoma (SCC) and its variants are most common. Risk factors for SCC include HPV infection, use of tobacco products, alcohol use, and consuming betel, as well as environmental exposures related to a highly active outdoor lifestyle, exposure to arid or other harsh, sediment rich environments, or living in cities or other regions with high particulate pollution.<sup>6</sup>

Although strongly associated with head and neck SCC, the above risk factors have not been associated with the development of OSCP.<sup>13</sup>

HPV-positive OSCP is more frequently seen in patients who have had a higher number of sexual partners and/or engage in sex without protection.<sup>3,15</sup> Additionally, HPV-positive OSCP may be seen in infants whose mothers were infected with genital HPV, as the viral infection can be acquired during childbirth.<sup>15</sup> Benign papillomas associated with HPV infection have higher rates of malignant transformation to SCC, independent of risk factors traditionally associated with squamous cell carcinoma.<sup>6</sup> HPV vaccination is an important preventive health measure to decrease the incidence of genital warts (benign), reproductive organ cancers, and head and neck malignancies.<sup>5,11</sup>

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Oropharyngeal lesions represent a unique risk to aviators, whether benign or malignant. The possibility of airway obstruction has been previously reported during anesthesia induction,<sup>2</sup> and it follows that airway obstruction during flight could represent a very serious risk to the pilot, potentially leading to loss of consciousness, loss of control of the aircraft, and/or compromise of the mission.

## CASE REPORT

The patient was a 24-yr-old male foreign national student aviator in training to fly UH-60 helicopters. He presented to the clinic for evaluation of a sore throat and cough for 2 d. He reported that swallowing was painful and that he felt subjectively feverish overnight. However, he was afebrile, tolerating food and fluids, and was able to breathe easily through his nose and mouth. During continued review of his concerns, this student pilot stated that he felt a lump in the back of his throat. He shared that several months ago he was seen by a U.S. healthcare provider who noted a small mass on his right tonsil.

The patient denied any significant past medical, surgical, or behavioral health history. Specifically, he denied any sexual history. He reported no history of alcohol consumption and limited tobacco consumption (less than 100 cigarettes in his lifetime, with the last cigarette being 4 mo ago). The patient's temperature in the clinic is 98.9°F and he denied receiving antipyretics or other medical therapy prior to this visit. His remaining vital signs were unremarkable.

A physical exam was negative for adventitious breath sounds, facial pain, or tonsillar exudates. Minimal and non-painful cervical lymphadenopathy is present, as well as an approximately 0.5 cm × 0.5 cm, irregular appearing, inflamed mass protruding from the inferior aspect of the right tonsil.

Review of the patient's medical record revealed that this mass had been evaluated by otolaryngology 4 mo previously. A biopsy was performed at that time and pathology reported a squamous cell papilloma: there was no evidence of immature basaloid cells, nuclear pleomorphism, or atypic mitotic figures.

Although the patient denied any sexual history, for sake of completeness a panel to rule out sexually transmitted infection (STI) was run with no positive results, although HPV status was not obtained. Suspicion for malignancy was very low at this time given the previous benign biopsy, and follow-up was arranged in 2 wk.

At the patient's follow-up appointment, the lesion has reduced in size to about 0.3 cm × 0.3 cm. It was now smooth and regular in appearance, and the patient's upper respiratory infection (URI) symptoms had resolved. This decrease in size, corresponding to resolution of the patient's URI symptoms, indicated that it was unlikely that a dysplastic change had occurred, effectively ruling out a need for further urgent evaluation. Furthermore, the previous biopsy had indicated a benign lesion. The patient is able to speak clearly, breath easily, Valsalva, and otherwise fulfill the physical and upper respiratory requirements he needed in order to perform as a student pilot. He was

at a point in his training where even relatively noninvasive surgeries would have significantly impeded his progression and threatened his ability to be retained in the flight program given his foreign national status.

Because the lesion was not immediately harmful, the patient was able to perform his duties, and he was available to follow-up for at least 8 more months, so an "active surveillance" approach was adopted. This was discussed with the patient and it was agreed that he would follow up with serial monitoring by Ear, Nose and Throat (ENT), in addition to earlier evaluation if any change in symptoms or appearance of the lesion occurred. Definitive treatment was planned for a future date, after the patient had completed the majority of his training. He was scheduled for follow-up every 4–6 wk and was referred to ENT for excision after his flight training was completed. The patient was able to complete training and his lesion was ultimately excised without complications or sequelae.

## DISCUSSION

The differential diagnosis for an oropharyngeal mass is broad. OSCP may resemble other benign lesions such as condyloma acuminatum, verruciform xanthoma, papillary hyperplasia, or rarely, leukoplakia. Condyloma acuminatum would typically present as a mass with a broader base, "brighter" red color due to lack of keratinization, and overall larger size than a papilloma, which is generally < 10 mm in its largest dimension.<sup>8</sup> Verruciform xanthomas can resemble papillomas, but are more likely to be found on the gingiva and alveolar ridge than other parts of the oral cavity or pharynx.<sup>8</sup> Papillary hyperplasia (also called inflammatory hyperplasia) may resemble a squamous cell papilloma but would have a readily identifiable cause such as poorly fitted dentures or other instrumentation in the mouth. Leukoplakia, although the most common premalignant lesion of the oral mucosa, would likely not be confused for squamous cell papilloma, as it is predominantly white-colored, flat, thin-appearing, and smooth—not exophytic.<sup>17</sup> Focal epithelial hyperplasia represents a subset of OSCP, presenting as multiple squamous papillomas clustered closely together.<sup>8,12</sup>

Gross examination of the patient's lesion (an approximately 0.5 cm × 0.5 cm, irregular-appearing, inflamed mass protruding from the inferior aspect of the right tonsil) was most consistent with squamous cell papilloma. However, given the significant risks of potentially malignant lesions or masses of the head and neck, a diagnostic workup involving referral to otolaryngology for biopsy with possible whole lesion excision and cytology was a reasonable and appropriate initial procedural course of action,<sup>10</sup> and would have been undertaken in this case if the patient had not been seen and biopsied previously. Even if an oropharyngeal lesion is small and clinically resembles a benign growth, malignant lesions must be ruled out: there is no substitute for biopsy to identify and evaluate the potential for an oral malignancy.<sup>10</sup> The size of this patient's lesion was < 10 mm, which is generally considered the lower limit of malignant transformation risk.<sup>6</sup> His smoking history

was not clinically significant ( $< 100$  cigarettes during his lifetime, with the last cigarette 4 mo ago) and, although nonpainful lymphadenopathy can be indicative of cancer, in this case minimal lymphadenopathy in the setting of a URI is not worrisome. The patient hails from central Asia, an area of the world where airway cancers are on the rise in a direct correlation with industrialization.<sup>18</sup> Chewing betel, a nut known to be associated with oropharyngeal cancer, is also a common practice in parts of Asia. A highly active outdoor lifestyle, exposure to arid or other harsh, sediment rich environments (such as areas in central Asia), or living in cities or other regions with high particulate pollution can cause chronic irritation and inflammation of the respiratory tract and lungs, predisposing to malignancy.<sup>6</sup> However, at only 24 yr of age and without any family history of cancer syndromes, airway cancer due to these environmental risk factors alone is extremely unlikely.

Benign papillomas associated with HPV infection have higher rates of malignant transformation to SCC when compared to noninfected lesions, regardless of risk factors traditionally associated with SCC, including the use of tobacco products, alcohol, and consuming betel.<sup>6</sup> Although more research is needed, some authors have posited that high-risk (strains 16 and 18) and low-risk (strains 6, 11, 31, 33, 45, 52, 58, others) HPV strains are mutually exclusive to squamous cell carcinoma and papilloma, respectively.<sup>14</sup>

Three HPV vaccines are licensed for use in the United States: the quadrivalent (covers strains 6, 11, 16, 18), 9-valent (covers additional strains 31, 33, 45, 52, and 58), and bivalent (only covers high-risk strains 16 and 18).<sup>9</sup> Nearly all papillomas are thought to be associated with low-risk HPV strains, particularly 6 and 11.<sup>7</sup> After vaccination, antibodies against HPV are found in both cervical secretions (female only) as well as airway secretions in both sexes.<sup>5,11</sup> It follows that if this patient were to receive the quadrivalent or 9-valent vaccine, he would have increased protection against not only genital and oropharyngeal cancer (associated with high-risk HPV strains), but also against genital warts or the recurrence of an HPV-positive lesion caused by low-risk strains. Although the vaccine is covered by most insurance companies (including TriCare) only up until age 26 (as recommended by the Centers for Disease Control), there is evidence that older patients experience a similar increase in anti-HPV antibodies after vaccination.<sup>5</sup>

While squamous papillomas tend to be slow-growing and do not generally represent a significant or immediate health risk, excision is curative. Ultimately, treatment for OSCP is usually knife excision or laser ablation.<sup>7</sup> Other less common methods of removing these lesions include electrocautery and cryosurgery, and, rarely, intralesional injections of interferon.<sup>7</sup> In the case of our aviator, the flight surgeon was faced with a challenge; not only to determine if this patient's presentation should affect his ability to fly UH- 60 helicopters, but when or even if surgical excision was indicated.

Airway obstruction is possible with oropharyngeal lesions, especially those on the uvula or tonsils. In fact, obstruction has been reported following administration of anesthesia even with small ( $< 10$  mm) papillomas.<sup>2</sup> To our knowledge, no previous

case reports of oropharyngeal lesions in aviators exist, but we believe this should be a serious consideration when assessing a patient's ability to fly. Should a patient's airway become obstructed during flight, especially during "high g" maneuvers, he or she may become panicked, be in danger of losing control of the aircraft, or even lose consciousness. This represents a clear risk of compromise to the mission as well as the pilot's future confidence in flight. It is the responsibility of the flight surgeon to impress upon his or her pilots that if any difficulty breathing were to occur, further evaluation is immediately warranted for the safety of the individual pilot as well as others involved in their mission.

In conclusion, the flight surgeon has a responsibility to consider oropharyngeal pathology a serious concern for his or her aviators—even benign, "harmless" lesions which civilian physicians may not consider worrisome. If a pilot is deemed fit to fly, as was the case with this patient, frequent follow-up is appropriate to ensure that lesions are not progressing. Foreign national patients, in particular, may present with special environmental exposures or cultural history which may put them at risk for certain conditions. The flight surgeon must be well-versed and culturally competent in order to ask his or her foreign-born patients culturally relevant questions in a respectful manner. This case report serves as a reminder for flight surgeons to consider all oropharyngeal pathology as a potential source of airway compromise during flight, and is a call to consider a patient's cultural background when evaluating and treating both foreign-born and American-born patients.

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