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Letter to the editor

# Oral tongue cancer in a patient with hereditary nonpolyposis colorectal cancer: A case report and review of the literature

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ABSTRACT

Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal dominant disorder characterized by mutations of mismatch repair genes leading to the early development of multiple malignancies. The most common malignancy is colorectal cancer but there is a strong association with malignancies of the ovary, endometrium, small intestine, stomach, skin, brain, and pancreas. We report a case of a 35-year-old female with a history of known HNPCC who presented with adenocarcinoma of the small intestine as well as a synchronous oral tongue squamous cell carcinoma. The patient underwent a combined oncologic surgery involving a hemiglossectomy, selective neck dissection, and partial small bowel resection. Despite the wide range of malignancies seen in patients with HNPCC, no cases of oral cavity cancer have previously been reported. This represents the first case in the literature of oral cavity cancer in a patient with HNPCC.

## Introduction

Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal dominant disorder caused by mutations of DNA mismatch repair genes. It is also known as Lynch syndrome (LS) and these patients have approximately an 80% probability of developing colorectal cancer (CRC) by the age of 65. Patients with LS have an increased risk of developing several extracolonic malignancies as well including most commonly ovarian, endometrium, gastric, small intestine, urological tract, pancreas, brain, and skin [1,2].

The Amsterdam II criteria are a set of diagnostic criteria used to identify patients with LS. In 2004, the National Cancer Institute revised the Bethesda Guidelines which are a set of recommendations to identify patients that should undergo genetic testing for LS. These are both outlined in detail in Tables 1 and 2.

Patients with LS and a mismatch repair mutation are at increased risk for almost any type of solid tumor. However, there are no reported cases of a patient with LS developing oral cavity cancer. We present the first ever documented case of squamous cell carcinoma of the oral tongue in a patient with known Lynch syndrome.

## Patient

At only the age of 35, our patient has an extensive history of cancer. She is a nonsmoker, nondrinker with a known familial gene mutation that was identified after she was diagnosed with T3N0 undifferentiated carcinoma of the colon at age 24. She had a brother and a sister with the same mutation that both passed away from brain cancer at ages 17 and 22 respectively. She completed chemotherapy and radiation but ultimately underwent a right hemicolectomy for persistent disease. She then developed intracystic papillary carcinoma of the breast and underwent a partial mastectomy followed by chemotherapy at age 26. At age 29 she was found to have adenocarcinoma of the colon and underwent a completion colectomy. She developed invasive ductal carcinoma of the contralateral breast and underwent bilateral mastectomy at age 31. At the same time as bilateral mastectomy, a cutaneous squamous cell carcinoma of the forehead was noted and excised. After having a daughter, she had a prophylactic total hysterectomy and bilateral salpingo-oophorectomy at age 32.

She presented to the emergency department with fatigue and worsening of her chronic anemia and was ultimately found to have adenocarcinoma of the jejunum. During the work up of her anemia, she also complained of tongue pain and was noted to have a two-centimeter firm raised lesion to her right lateral oral tongue suspicious for malignancy. Biopsy confirmed invasive squamous cell carcinoma. There was extensive discussion between the two surgical services as well as with the patient and her family regarding the timing, prioritization, and sequential order of the tongue and small bowel resections. The increased risks of resecting both tumors during a simultaneous surgery was felt to outweigh the risks of delaying treatment of either cancer until recovered from the first oncologic surgery. She underwent a rare combined surgery with otolaryngology and surgical oncology services which included a right partial glossectomy, right selective neck dissection, and partial small bowel resection. There were no post-operative head and neck surgical complications. Final surgical pathology revealed well differentiated invasive squamous cell carcinoma with a size of 1.7 cm and a depth of invasion of 7 mm. All surgical margins were negative with the closest margin being 4 mm. Right neck dissection levels I-IV revealed one positive node measuring 2.2 cm with a metastatic focus of 3 mm without extracapsular extension. The case was presented at multidisciplinary tumor board conference as a T2N1 squamous cell carcinoma of the oral tongue to discuss the role of adjuvant treatment for her oral cavity cancer. Given her favorable pathology and unfortunately high likelihood of developing a second head and neck malignancy no further adjuvant treatment was recommended at this time.

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**Table 1**
The Amsterdam II clinical criteria for families with Lynch syndrome.

| Amsterdam II Criteria |
|---|
| • 3 or more relatives with an associated cancer (colorectal, endometrium, small intestine, ureter or renal pelvis)<br>• 2 or more successive generations affected<br>• 1 or more relatives diagnosed before the age of 50 years |

**Table 2**
The revised Bethesda guidelines to identify patients that should be tested for Lynch Syndrome. CRC – colorectal cancer. LS – Lynch Syndrome.

| Revised Bethesda Guidelines |
|---|
| • CRC diagnosed in a patient who is less than 50 years old<br>• Presence of synchronous or metachronous CRC or other LS associated tumors, regardless of age<br>• CRC with high microsatellite instability diagnosed in a patient less than 60 years old<br>• CRC diagnosed in one or more first-degree relatives with a LS associated tumor, with one tumor being diagnosed at less than 50 years of age<br>• CRC diagnosed in two or more first-degree or second-degree relatives with LS associated tumors, regardless of age |

## Discussion

The role of environmental causes of mucosal squamous cell carcinoma of the head and neck are well described. In contrast, the role of genetic factors is less commonly encountered and not as well understood. The familial occurrence of head and neck cancers supports a role of hereditary factors in this disease group. The best described genetic syndromes associated with the risk and prognosis of head and neck cancer include Li Fraumeni, ataxia telangiectasia, xeroderma pigmentosum, Fanconi's anemia, and Bloom syndrome [3,4].

In contrast, Lynch syndrome has not previously been described to have a link to mucosal malignancies of the head and neck. An analysis by Pande et al of 368 patients with a total of 504 types of cancer, there were zero cases of oral cavity cancer. The only cases of head and neck cancer was one case of carcinoma of the sinus cavity and three cases of thyroid carcinoma [2]. Lynch et al published a case report of a patient with LS that was diagnosed with cervical cancer at age 34 and laryngeal squamous cell carcinoma (SCC) at age 60. The son of this patient who was a nonsmoker and nondrinker manifested laryngeal cancer at age 31 [5]. To our knowledge there are no other reported cases of mucosal head and neck cancer in a patient with Lynch syndrome.

It is critical to understand the potential consequences of head and neck cancer in patients with genetic mutations. This is the first reported case of oral cavity cancer in a patient with Lynch Syndrome. Literature review reveals a low overall incidence of any mucosal head and neck malignancies in patients with LS and does not warrant prophylactic screening exams in these patients. However, given their predilection for malignancies, any head and neck symptoms should be taken seriously with a high suspicion until thorough exam proves otherwise.

## Conflicts of interest

No financial disclosures or conflicts of interest.

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