1: J Natl Cancer Inst. 1999 Apr 7;91(7):599-604. 

Links

Unknown primary head and neck squamous cell carcinoma: molecular identification of the site of origin.

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BACKGROUND: Unknown primary head and neck squamous cell carcinoma (HNSCC) presents as a cervical lymph node metastasis without identification of the primary tumor, despite thorough diagnostic work-up that includes physical examination, computed tomography, esophagoscopy, laryngoscopy, bronchoscopy, and multiple surveillance biopsies. We investigated whether the site of origin of the primary tumor could be localized in the upper aerodigestive tract mucosa by detection of genetic alterations identical to those found in metastatic lesions. METHODS: Microsatellite analysis was performed on metastatic tumors obtained from 18 patients with unknown primary HNSCC. Histologically benign surveillance biopsy specimens were also analyzed. Patients were followed up to 13 years with continuing surveillance for primary mucosal tumors. Most patients were treated with neck dissection followed by radiation therapy to the affected neck and ipsilateral Waldeyer's ring. RESULTS: In 10 (55%) of the 18 patients, at least one histopathologically benign mucosal biopsy specimen from defined anatomic sites (i.e., most likely sites for an occult primary tumor)

demonstrated a pattern of genetic alterations identical to that present in cervical lymph node metastases. One patient harboring genetic alterations in the base of the tongue and two patients harboring genetic alterations in a tonsillar fossa subsequently developed HNSCC in the identical or adjacent mucosal region; all three of the primary head and neck mucosal tumors that eventually appeared between 1 and 13 years later in these patients had genetic changes identical to those in the benign mucosal biopsy specimens and in the metastatic lymph nodes. CONCLUSIONS: These data support the hypothesis that histopathologically benign mucosa of the upper aerodigestive tract may harbor foci of clonal, preneoplastic cells that are genetically related to metastatic HNSCC and that such mucosal sites are the sites of origin of unknown primary HNSCC. Microsatellite analysis may represent a clinically useful tool for determining such sites