Autopsy Findings of Alveolar Carcinoma Due to Betel Quid Chewing - A Case Report

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Abstract: Over 200,000 cases of head and neck cancer occur each year in India. Out of these 80,000 are diagnosed as oral cancers. Nearly two-thirds of oral cancers are located in the buccogingival sulcus, where the betel quid is kept for long periods in the oral cavity. The location and aetiology of this buccogingival cancer may warrant the term "the Indian Oral Cancer" [1]. Case discussed underneath is of an alveolar carcinoma with destruction of right side of mandible. Metastases had involved cervical lymph nodes, liver and omentum. This so called Indian Oral Cancer has its inherent aetiology, disease behaviour and prognostication which need special attention when dealing with cancers of such type.

Keywords: Head and neck Squamous Cell Cancer (HNSCC), Betel Quid, Buccogingival sulcus, Indian Oral Cancer, Alveolar Carcinoma

1. Introduction

Epithelial carcinomas of the head and neck arise from the mucosal surfaces in the head and neck area. They typically are Squamous cell in origin. The mucosal surface of the entire pharynx is exposed to alcohol and tobacco-related carcinogens. So, it is at risk for the development of a premalignant or malignant lesion [2]. Tobacco smoke contains pyrolysis products, which are generated due to high temperatures at the burning tip. Smokeless tobacco is rich in nitrosamines. The concomitant use of betel quids leads to a 50-fold increase in reactive oxygen species generated [4].

Oral precancerous lesions (PCLs) such as leukoplakia and submucous fibrosis are early indicators of damage to the oral mucosa with transformation rate of 2–12% into frank malignancies [3]. They include cancers of the oral cavities, the pharynx (naso-, oro- and hypopharynx), the larynx and malignancies [3]. They include cancers of the oral cavities, the pharynx (naso-, oro- and hypopharynx), the larynx and the parasinal sinuses.

In India chewing of tobacco accounts for nearly 50% of cancers of the oral cavity and oropharynx in men and over 90% in women [4]. Oral premalignancies are common in betel-nut chewers and 10% of these undergo malignant transformation. In Asia and the South Pacific region too betel-nut (Areca catechu) chewing is closely associated with oral cavity cancers. It is having both independent and synergistic effects with smoking and alcohol drinking. Normally, betel quids are consumed containing areca nut and calcium hydroxide (lime). Areca nut has been declared a known human carcinogen by an IARC Expert Group (2003) [5], [6], [7]. Since practice is in vogue to keep such betel quids for hours in buccogingival sulcus, it is not uncommon to find cases of Alveolar carcinoma in this region.

The alveolus and its accompanying gingiva constitute the dental surfaces of the maxilla and mandible. It extends from the gingivobuccal sulcus laterally to the floor of the mouth and hard palate medially. Posteriorly, the alveolus extends to the pterygopalatine arch and ascending ramus of the mandible, also referred to as the retro molar trigone [3].

2. Literature Survey

Cancer is believed to arise from the acquisition of multiple mutations that cooperate to transform normal cells. HNSCCs arise from the mucosa of the upper aerodigestive tract. Most head and neck cancers do not present with a history of premalignant lesions. Multiple synchronous or metachronous cancers can also be observed. In fact, over time patients with early-stage head and neck cancer are at greater risk of dying from a second malignancy than from a recurrence of the primary disease [3].

Squamous cell head and neck cancers can be divided into well-differentiated, moderately well-differentiated, and poorly differentiated categories. Poorly differentiated tumours have a worse prognosis than well-differentiated tumours [3]. Carcinomas of the oral cavity present as non-healing ulcers, changes in the fit of dentures, or painful lesions. Advanced head and neck cancers in any location can cause severe pain, otalgia, airway obstruction, cranial neuropathies, trismus, odynophagia, dysphagia, decreased tongue mobility, fistulas, skin involvement, and massive cervical lymphadenopathy, which may be unilateral or bilateral. Some patients have enlarged lymph nodes even though no primary lesion can be detected by endoscopy or biopsy. If the enlarged nodes are located in the upper neck and the tumour cells are of squamous cell histology, the malignancy probably arose from a mucosal surface in the head or neck [8].

The degree of aggression is also known to vary between tongue and buccal mucosa cancers. These are explained on the basis of differences in structure and function; tongues being vascular by nature, cancers of this site are highly metastatic as compared with buccal mucosa [3]. Distant metastases are found in <10% of patients at initial diagnosis and are more common in patients with advanced lymph nodal stage; microscopic involvement of the lungs, bones, or liver is more common, particularly in patients with advanced neck lymph node disease [8].

Most head and neck cancers occur in patients older than age 50 years. HPV-related malignancies are frequently diagnosed in patients in their 40s while EBV-related...
nasopharyngeal cancer can occur in all ages, including teenagers [2]. Nasopharyngeal cancer has also been associated with consumption of salted fish.

Epidemiologically HPV related oropharyngeal cancer occurs in a younger patient population and is associated with increased numbers of sexual partners and oral sexual practices. Similar to cervical cancer, HPV 16 and 18 are the commonly associated viral subtypes. Incidence of oropharyngeal cancers is increasing in western countries [8].

Although all neoplastic cells within a cancer presumably arose from a common ancestor, the progeny of this common ancestor continue to evolve. The presence of multiple progeny clones within an individual tumour reflects genetic heterogeneity [9]. HNSCC has high rate of recurrence. This is believed to result from histopathologically benign squamous cell epithelium harbouring a clonal population with genetic alterations. Studies using microsatellite analysis and X chromosome inactivation have verified that metachronous and synchronous lesions from distinct anatomic sites in HNSCC often originate from a common clone.

This evidence confirms that genetically altered mucosa is difficult to cure in the HNSCC patient because it is on the path to tumorigenesis, as predicted by this model. Indeed, HNSCC patients have a 3% to 7% annual incidence of secondary lesions in the upper aerodigestive tract, oesophagus, or lung.

A synchronous second primary lesion is defined as a tumour detected within 6 months of the index tumour. The occurrence of a second primary lesion more than 6 months after the initial lesion is referred to as metachronous. A second primary will develop in the aerodigestive tract of 14% of patients with HNSCC over the course of their lifetime, with more than half of these lesions occurring within the first 2 years of the index tumor. Second head and neck malignancies reflect the exposure of the upper aerodigestive mucosa to the same carcinogens that caused the first cancer [8]. One of the major causes of death was the high incidence of second primary malignancies that jeopardized survival rates most in patients with early-stage disease [10].

Due to the tight attachment between the mucosa and underlying bone, treatment of alveolar SCC often involves treatment of the maxilla or mandible. Of gingival carcinomas, 70% occur on the lower gum. The periosteum of the mandible is a strong tumour barrier, and tumours that abut the bone may often be resected along with the adjacent periosteum only [3].

3. **Method and Approach**

Details and findings of this case were painstakingly explored at autopsy room of Institute of Medical Sciences, BHU, Varanasi. Patient’s personal history, supportive treatment and investigation records were collected. These all facts were analysed retrospectively with existing literature support.

4. **Problem Definition / Case Report**

A 54 year old male presented with complaint of ulcerative lesion over right cheek for two months progressive in size at Institute of Medical Sciences and S.S. Hospital, BHU, Varanasi. There was pain in the gum with loosening of teeth and diffuse swelling around the neck. Patient had history of betel quid chewing for past five years approximately. There wasn’t any history of co-morbid illness. Patient was diagnosed as carcinoma right cheek involving alveolus measuring 6 × 7 cm in size (Figure-1). Right submandibular node was enlarged measuring 7 × 6 cm in extent.

**Figure 1: Extent of spread of carcinoma on clinical Examination**

Computerised Tomographic scan of head and neck showed near destruction of right side of the jaw and extensive right jugular vein thrombosis (Figure-2).
Biopsy examination of right cervical lymph node had evidence of metastatic Squamous Cell Carcinoma. Chest X-Ray was normal. OPG showed mandibular secondaries. Two cycles of chemotherapy with Paclitaxel, Cisplatin and 5-Fluoro Uracil were given with supportive and palliative management. Due to progressive nature of the disease patient couldn’t be saved. Later the body was subjected to medico-legal autopsy in the Dept. of Forensic Medicine, Institute of Medical Sciences, BHU, Varanasi. On external examination, there was mild peri-oral puffing of the face. Opening of the mouth and oral cavity were nearly obliterated due to extensive growth of the carcinoma (Figure-3).

Entire right side of the face was disfigured. Angle of the mouth had shifted extreme towards left side (Figure-4).

Submandibular and cervical lymph nodes enlargements due to metastasis were obvious externally (Figure-6).

Neck dissection confirmed these nodal metastases (Figures-7 and 8).
Superior surface of the liver showed multiple cauliflowers like secondary growths each 1-2 cm in diameter. Similar secondaries were noted on inferior surface of the liver and on the adjacent omentum too (Figures-9 and 10).

Consequently liver was enlarged massively weighing 2200 grams. Peritoneal cavity contained 600 ml of ascitic fluid. Spleen weighed 240 grams and both kidneys weighed 320 grams. Spleen and kidneys both didn’t show any secondaries. After considering these autopsy findings death was attributed to fulminant hepatic failure due to extensive secondary metastases involving the liver with evidence of carcinoma right side of jaw.

5. Results and Discussion

This patient presented with ulcerative lesion on right cheek which were suggestive of pre-malignant changes in oral mucosa. These pre-malignant changes were attributed to the habit of betel quid chewing. Betel quids are normally chewed with areca nut and lime (Calcium Hydroxide) in these parts, a known carcinogen. Such mixture of contents of betel quid is known to increase generation of reactive oxygen species. It is typically Squamous cell in origin from adjacent mucosa. Patient typically presented with pain in gums and loosening of teeth.

As with HNSCCs it was rapidly progressive. In span of about three months it obliterated the oral cavity. Patient had to be shifted on liquid diet via naso-gastric tube. It destroyed Right side of mandible. It typically had submandibular and cervical lymph node metastases. Biopsy report of cervical lymph nodes confirmed Squamous cell nature of these metastases.

Although lungs are commonly involved secondarily, such involvement was not seen in our case. However, liver and adjacent omentum was synchronously involved since these involvements were noted within three months. These cancers have high incidence of second primary malignancies which lead to deaths seen in this case due to extensive liver and omental involvement.

6. Conclusion

From above findings it is obvious that cause of oral cancers in these parts of India is strikingly different. This is mainly due to local practice of betel quid chewing, associated use of tobacco with lime or in form of Gutkha(a powdered tobacco cocktail preparation) or areca nut chewing. Hence, the term Indian Oral Cancer may stand justified.

7. Future Scope

Cancer-related outcomes are influenced by a number of factors and clinicians commonly consider prognostic factors that are not included in the TNM system for decision making in actual patient care [11]. With advances in understanding of cancer biology, we are now faced with a deluge of information on molecular and genetic predictors of prognosis. Human papilloma virus infection in oropharyngeal cancer and Epstein-Barr virus infection in nasopharyngeal cancer are etiological inclusions. Prognostic data of this nature will have to be incorporated into staging systems in order to maintain relevance of any staging system as our understanding of cancer continues to
evolve. Nomograms are well suited to adapt to this need [12](Figure-11).

Figure 11 Nomograms can incorporate multiple prognostic factors [12].

The ability of nomograms to take into account more variables than the conventional TNM staging system also sets up the possibility that a staging system based on nomograms would more accurately stratify patients into groups with similar estimated outcomes than the currently used TNM system [13].

References


Author Profile

Manoj Kumar (India): awarded Associate Professor on Feb 7th, 2014 in Department of Forensic Medicine, Institute of Medical Sciences, Banaras Hindu University and Headship on May 6th, 2014. Did his M.B.B.S from Patna Medical College Hospital, Patna in 1999. Got his MD in Forensic Medicine in 2004 from Institute of Medical Sciences, BHU. He has been actively involved in academic, research and medico-legal work. He has around thirty research papers published till now.

Navin Kumar (India): currently pursuing MD in Forensic Medicine at Institute of Medical Sciences, Banaras Hindu University. He graduated in M.B.B.S from Nalanda Medical College, Patna in 2005. He takes keen interest in academics and research paper works.