

## Quadruple cancer, including triple cancers in the head and neck region

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Multiple primary tumors are not rare: they are encountered in 3–5% of malignant tumors. They are particularly frequent in the head and neck [20]. They are most often met with secondary malignant tumors; triple tumors occur in only 0.5%, quadruple tumors in 0.3% of malignant tumors. The possibility of developing a second metachronous cancer 5 years after undergoing treatment of the initial head and neck cancer is approximately 22%.

Multiple metachronous tumors often appear 3–4 years after the observation of the primary tumor, or even after 5–10 years in the case of laryngeal tumors.

The frequency of multiple primary tumors in the head and neck region supports the “field cancerization” theory, according to which the inducing agents (primarily smoking and alcohol consumption) can initiate the tumorous degeneration at a number of sites in the oropharyngeal region.

The authors report on a case in whom surgery for bladder tumor was followed 101 months later by tumor development in the region of the head and neck: 3 such tumors were treated within a period of 21 months. The histologic result on the bladder tumor was transitiocellular carcinoma, while the latter ones were squamous cell carcinomas. Three of the tumors were treated effectively (no local recurrence or metastasis developed), but the fourth led to the death of the patient.

The literature on multiple tumors of the head and neck is reviewed, and possible etiologic factors are discussed. It is pointed out that, besides primary and secondary prevention, close observation of these patients is required, repeated panendoscopy of the upper aerodigestive tract and genetic examinations are recommended.

*Key words: Multiple primary malignant tumors, head and neck, quadruple cancer.*

Since the first report by Billroth in the 1860s of several primary neoplasms occurring in the same patient, many articles have addressed that topic, and second, or multiple, primary lesions have become wellrecognized in the speciality of head and neck oncology [7, 19]. Multiple primary tumors in a single patient and familial cancers [5, 12] were described more than 100 years ago.

The criteria for diagnosing multiple primary tumors are: (a) each of the tumors must present a definite picture of malignancy; (b) each must be distinct and (c) the probability that one was a metastatic lesion from the other must be excluded [1, 18, 21]. The expression “multiple tumor” correctly refers to more than two malignant tumors, the tumor observed first is always termed the “index tumor”.

The sequence of appearance of multiple tumors is defined as simultaneous (if the malignant tumors are first observed at the same time), as synchronous (if the second tumor appears within 6 months after the first), or metachro-

nous (if the multiple tumor is diagnosed more than 6 months after the recognition of the previous one) [4, 6].

Multiple primary cancers seem to be increasing in frequency [13, 15]. This may have come about with improved clinical awareness, the possible effect of new environmental carcinogenic forces, the increased use of chemotherapeutic agents or irradiation which are themselves carcinogens, and, to some extent, the increased longevity of cancer patients which enables them to live long enough to develop a second primary cancer [8].

It has been shown that certain environmental and lifestyle factors are important for the induction of cancers of specific sites. Tobacco usage, in particular, has been identified as causative for cancers of the lung, larynx, oral cavity, esophagus, and urinary bladder. Several investigators have observed that patients with cancers on these sites developed a second primary cancer within a same anatomic region [22].

In up to 20% of the of the patients affected by head and