Pattern of occurrence and treatment outcome of second primary malignancies: A single center experience

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Abstract

Background: The incidence of cancer survivors is increasing, but these individuals, unfortunately, face the risk of second primary malignancies (SPMs). This increasing incidence can be credited to increased survival rates of cancer patients, environmental factors, host factors, and genetic predispositions. Hence, vigilance on the part of the patient as well as clinician for the development of new signs and symptoms is mandatory. **Aims:** Retrospective analysis of the pattern of incidence and clinical outcome of patients diagnosed with SPM and to review the literature. **Settings and Design:** A hospital-based retrospective collection of prospective data of patients diagnosed with SPM. **Materials and Methods:** Thirty-six patients with histopathologically proven SPM from January 2009 to July 2015 were included in this study. Factors such as age, sex, site, stage, histology, treatment received, and outcome were recorded. **Statistical Analysis Used:** Basic statistical tools have been used for analyzing the data. **Results and Conclusions:** The likelihood of occurrence of second malignancy, either synchronous or metachronous, should always be kept in mind while evaluating a cancer patient. Appearance of new signs and symptoms during the initial evaluation as well as during follow-up should raise a suspicion, and both patient and oncologist should have a low threshold for further assessment. Early diagnosis and treatment will reduce morbidity and mortality and lead to better survival outcome.

Key words: Cancer survivors, second primary malignancy, synchronous and metachronous dual malignancy

Introduction

The occurrence of second primary malignancy (SPM) can be explained by increased cancer survival. Moreover, it can be attributed to tobacco and excessive alcohol intake, environmental determinants, host factors, genetic predisposition, gene–environment interactions, and late sequelae of cytotoxic treatment for previous malignancy including radiotherapy and chemotherapy.[1,2] SPM can be either synchronous or metachronous. Synchronous cancers are second tumors occurring simultaneously or within 6 months after the first malignancy, whereas metachronous multiple malignancies are secondary cancers that developed after more than 6 months of the primary malignancy.[3] We have done a retrospective compilation of the pattern of occurrence of SPMs after an index primary and discussed available pertinent literature.

Materials and Methods

This retrospective study analyzed data from the hospital database of patients either presenting with histologically proven synchronous or metachronous double primaries over a period of 7 years from January 2009 to July 2015. Warren and Gate's criteria have been used to designate a case as multiple primary tumors, and the prerequisites are as follows: (1) Each of the tumors must be histopathologically confirmed, (2) each must be geographically separated and distinct, and the lesions should be separated by normal mucosa, (3) probability of one being the metastasis of the other must be excluded.[4] The inclusion criteria of patients in the study were the presence of at least two malignant lesions, confirmed by histopathological examination. We excluded patients without histopathological confirmation of each tumor and also the patients in whom the second tumor was suspected to be a metastasis of the primary tumor. Various details such as age at diagnosis of primary index tumor, sex, whether synchronous or metachronous, site of origin, stage at diagnosis, histology, treatment received, site of second primary, and treatment outcome were recorded.

Results

Over a period of 7 years, a total of 36 cases with multiple primary malignancies were observed. The median age at the diagnosis of primary malignancy was 60 years (range 26–83). The most common age group was between 51–60 and 61–70 years with ten patients in each decade [Figure 1].

Thirteen cases (36.1%) of double malignancies were observed in females. Only two were synchronous malignancy, and 34 (94.4%) were metachronous. The most common site of primary tumor was head and neck with most common subsite being oral cavity (ten) followed by oropharynx (eight) and larynx (four). Second most common site was breast (five) followed by gastrointestinal tract, gynecological cancer, trachea, and genitourinary (two) each [Figure 2].

Among the SPM, most common site was again head and neck (22) with oral cavity being the most common subsite (15), followed by gynecological cancers (four) and gastrointestinal tract (two). Skin malignancy, lymphoma, external auditory canal carcinoma, and leukemia were encountered in one patient each [Figure 3].

The time to occurrence of second primary varied from 2 months to 17 years. The treatment modality in all the patients was determined primarily on the basis of performance status. About 15 patients underwent surgery. Re-irradiation was done in 21 patients in head and neck malignancies. A high rate of toxicity was noted in patients receiving concurrent chemoradiation, patients with lesser time interval between primary irradiation and re-irradiation and with greater planning target volumes. At the time of analysis, 17 (47.2%) patients are disease free, nine (25%) patients have expired due to disease progression, three patients are undergoing chemotherapy, and seven patients are lost to follow-up [Figure 4].

Discussion

In our study, 43.3% of patients were older than 60 years of age and only 8% were younger than 40 years. Most common site for primary as well as secondary malignancy was head and neck, accounting for 61 and 50% of cases, respectively. Etiology of occurrence of SMP is multifactorial. Various familial cancer syndromes are linked to SPM, including Lynch

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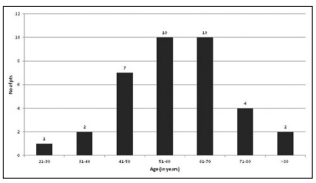

Figure 1: Age distribution in primary malignancy

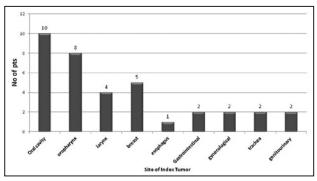

Figure 2: Site distribution of the primary malignancy

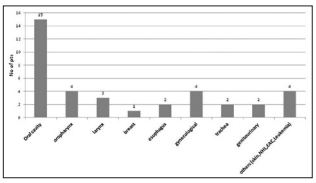

Figure 3: Site distribution of the second malignancy

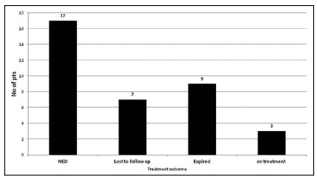

Figure 4: Treatment outcome of patients of second primary malignancy

I and II syndromes, Li–Fraumeni syndrome, Fanconi anemia, xeroderma pigmentosum, and Von Hippel–Lindau. Mutations in tumor suppressor genes and activation of proto-oncogenes are also associated with increased risk. Cancer treatment such as radiation and chemotherapy has also been implicated in the causation of second primaries.[5] Children with primary retinoblastoma, lymphoma, soft tissue, and bone sarcoma have a long-term overall survival and have a higher risk of developing a second malignancy attributable to genetic predisposition or long-term effects of treatment of primary malignancy. However, in our study, we encountered no patient in pediatric age group.

The treatment of SPM is as per the standard guidelines, and it is not different from primary tumor. Treatment of the primary tumor should be kept in mind while planning the management of second malignancy. In a patient previously treated with radiation therapy, prior radiation fields, doses, radiation techniques, concurrent chemotherapy should be taken into account, in case if re-irradiation is being considered. Appropriate dose constraints have to be assigned to the previously irradiated organs.

A SPM developing in close vicinity of the previous one poses challenges in the management, especially if it develops in a previously irradiated volume. Surgical resection is the mainstay of treatment in such cases. Previously, re-irradiation was associated with high rates of treatment-related toxicity, but emerging data support the safety and feasibility of conformal delivery techniques in cases of re-irradiation.

Conclusions

As the number of long-term cancer survivors continue to increase, oncologists and clinicians must have a basic understanding of their biologic, psychological, and socioeconomic needs. It is important on the part of clinician to inform the patient regarding the risk of development of second tumors after the successful management of primary neoplasm. Modifiable risk factors should be addressed with preventive strategies such as smoking cessation and avoidance of ultraviolet light. A regular follow-up with careful monitoring and early detection of the disease leads to appropriate management.

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Conflicts of interest

There are no conflicts of interest.

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