A Case Report of Double Malignancy—Recurrent Nasopharyngeal Carcinoma and Adenocarcinoma of the Uterus

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Abstract
Multiple primary malignancies (MPMs) is a rare clinical condition where a patient is diagnosed with two or more cancers around the same time. Published literature reported the incidence of multiple primaries is in the range of 2% - 17%. The risk factors for MPMs are smoking, chronic alcoholism, genetic factors and previous treatment of cancer using radiotherapy that may lead to the development of other cancer. This case report describes a rare and unfortunate case of middle-aged Malaysian Chinese lady diagnosed with adenocarcinoma of the uterus and around the same time she had a recurrent nasopharyngeal carcinoma which was first diagnosed and treated 11 years ago. There were no clear risk factors identified in her and she defaulted follow up which eventually led to a fatal complication in which the nasopharyngeal cancer caused massive bleeding in her and she finally succumbed to the complication despite emergency resuscitations.

Keywords
Multiple, Primary, Malignancies

1. Introduction
Multiple primary malignancies (MPMs) are diagnosed when more than one primary malignancy arising in different sites and/or they are of a different histology or morphology group. This clinical entity is not that common, the worldwide reported frequency of multiple primaries ranges from 2% - 17% [1].

According to International Agency for Research on Cancer, when more than one tumor is confirmed in a patient at the same time or within six-month period
is known as synchronous tumor and if another tumor is diagnosed after a period of 6 months is known as metachronous [2].

The actual etiology of MPMs remain unknown but many epidemiological studies have documented MPMs are highly associated with chronic smoking, family history of malignancies, genetic susceptibility, previous exposure to radiation or chemicals and some clinical syndromes such multiple endocrine neoplasm (MEN) 1 and MEN 2 [3] [4]. However, in individuals confirmed with MPMs, very often no significant risk factors are identified.

The following case described a rare and unfortunate case of middle-aged Malaysian Chinese lady who was diagnosed with adenocarcinoma of uterus and around the same time diagnosed with a recurrent nasopharyngeal carcinoma (synchronous tumor) eleven years after the first diagnosis.

2. History

A 51-year-old Malaysian Chinese housewife who was diagnosed with nasopharyngeal carcinoma 11 years ago (in 2007) at the age of 40 years old, She completed radiotherapy treatment; however, she developed the complication of bilateral osteoradionecrosis. Few months into the follow up, she defaulted treatment and her clinical status and progress were unknown since then. There was no history of smoking, alcohol or any known family members diagnosed with cancer.

In early July 2018, which was 11 years after the initial diagnosis of nasopharyngeal carcinoma, she presented to the community clinic with the problem of heavy menses which lasted longer than her usual normal period for almost 6-month duration. She was then referred to gynecologist for further evaluation. Ultrasonography showed intruterine mass and an endometrial tissue sampling confirmed adenocarcinoma of the uterus. Stage 1A, she underwent laparoscopic hysterectomy and bilateral salphingo-oophorectomy, which was also followed by four cycles of chemotherapy. The surgery was successful, and the recovery was uneventful.

About 8 weeks following the diagnosis of endometrial cancer she presented again to the community clinic with a new complaint of right facial swelling and intermittent epistaxis for two weeks duration. Subsequently she was referred to the Department of Otorhinolaryngology in a tertiary hospital for further evaluation. Examination of the nasal cavity revealed presence of a soft tissue mass in the right nasal cavity. Facial computer tomography (CT) was requested and it showed a heterogeneous enhancing mass measuring about 5 × 5 cm at the right nasopharynx with local infiltration involving the sinonasal (Figure 1 and Figure 2), oral region and intraorbital region (Figure 3 and Figure 4). There were also intramuscular infiltrate and surrounding bony erosion. There was no intracranial involvement and no lung or liver metastasis. A tissue biopsy was obtained, and subsequent histopathological report confirmed squamous cell carcinoma arising from the nasopharynx.
Figure 1. Sagittal CT showed nasopharyngeal tumor infiltrated into the right sinonasal, intraorbital region with bony erosion.

Figure 2. Coronal view of the nasopharyngeal tumor occupying the entire right nasal cavity.

Figure 3. Inferiorly the tumor infiltrate to oral cavity.
3. Progress and Outcome

The patient was referred to oncology unit for further management and was under the multidisciplinary care comprises the otorhinolaryngologist, gynecologist and oncologist. She was planned for chemotherapy for the recurrent of nasopharyngeal carcinoma. However, due to some personal factors, she defaulted the follow up and treatment appointment. Four weeks later, on one evening she was brought by the daughter to the hospital emergency department in an unconscious state. The daughter described the mother had a sudden massive bleeding two hours prior coming to hospital. On examination, blood was actively oozing from her nose. She was pale and hemoglobin detected was 6 grams per deciliter. Her blood pressure was 70/40 mmHg, pulse 120 beats/minutes. Despite of active transfusion and resuscitation, patient succumb to her illness two hours later. The cause of death reported as hypovolemic shock secondary to massive intranasal hemorrhage due to underlying recurrent nasopharyngeal carcinoma.

4. Discussion

Multiple primary malignancies are a rare clinical condition. It is even rarer to have malignancies involving both the nasopharyngeal region and the uterus diagnosed around the same time. Within the region of South East Asia, it was reported by Singapore Cancer Registry that multiple primary cancers account for only 0.38% of all cases in their registry. It also documented there were few cases of nasopharyngeal carcinoma occurring together with uterine cervical cancer. Epstein-Barr virus could be the possible etiological agent and further study need to be conducted to look at its association especially among the Chinese lady in this region [5] [6]. Many pathological studies showed cervical epithelium is known to contain receptors for Epstein-Barr virus (EBV) and is a recognized site of viral shedding. More recent cases of nasopharyngeal carcinoma have been associated with cervical carcinoma, thus the hypothesis that EBV and cervical carcinoma...
are both related [6] [7].

As with many other multiple primary malignancies reported elsewhere, the patient presented in this case did not have any significant risk factors such as smoking or drinking alcohol. None of her family members was diagnosed with cancer. The only significant past history was she had radiotherapy 11 years ago for her first diagnosed nasopharyngeal carcinoma. However, there was no strong evidence to suggest this led to her uterine cancer after 11 years. No laboratory test performed in her to indicate any association with exposure to Epstein-Barr virus. The occurrence of multiple primary malignancies in this patient could be multi-factorial.

The prognosis and survival of multiple primary malignancies depends very much on the cancer type and also the stage at the time of diagnosis. Among other factors affecting the prognosis include genetic factors, behavioral influences, lifestyle and comorbid illnesses [8].

The most important poor prognostic factor in this particular patient which we highlighted was non-compliant to treatment. Despite of appointment for treatment and follow-up was given, she defaulted. No specific reason was given by patient or her family members as why she failed to turn up for the treatment. Following defaulting treatment, the tumour most likely had infiltrated nearby blood vessels, therefore she presented with massive uncontrollable bleed. Adequate health education remains an important factor in this region. The treating physician should be encouraged to spend more time to explain and advice the patient especially in a case of multiple primary malignancies which required close follow-up and multidisciplinary approach in the management.

5. Conclusion

Multiple primary malignancies (MPMs) is a rare clinical condition, nevertheless any patient diagnosed and treated for malignancy if presents with new clinical symptoms, the treating physician must look for the evidence of recurrence and possibility of multiple malignancies. In such circumstances, the patient usually needs multidisciplinary approach and proper advice and counseling to patient and family is necessary to ensure good response to treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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