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Multiple Primary Malignant Tumour: Case Report and Review of the Literature

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Abstract

Two or more histologically distinct malignancies in one individual are termed as multiple primary malignant tumours (MPMT). There are currently no universal protocols based on evidence; instead, management is empirical and dependent on the judgments made by interdisciplinary teams. The authors' aim was to report one case of MPMT seen in Madagascar and discuss according to the literature review. This case concerns a 63-year-old menaopausal Malagasy woman, followed in 2009 for an unprecised stage of adenocarcinoma of the colon, treated by a surgery followed by an adjuvant chemotherapy. Follow-up was fine with complete remission. Fourteen years later, another cancer localised in the endometrium was diagnosed as a high grade adenocarcinoma treated by surgery followed by a radiotherapy, which was combined with an invasive breast carcinoma treated by neoadjuvant chemotherapy, mastectomy and lymph node dissection, local radiotherapy and hormonotherapy. Management of MPMT is multidisciplinary and tailored to the stage of each tumor, prioritizing tumors with a poor prognosis.

Keywords

Cancer, Endometrial, Colon, Breast, Multiple Primary Malignant Tumour

1. Background

Multiple primaries Malignant Tumour are defined as more than one synchronous or metachronous cancer in the same individual. For epidemiological studies, tumours are considered multiple primary malignancies if arising in different sites and/or are of a different histology or morphology group. This avoids misclassification of multifocal/multicentric tumours or metastases as multiple primaries. A cancer is classified as index cancer if there has been no prior record of invasive

cancer [1]. Warren and Gates first described this condition in detail in 1932, and they established the diagnostic criteria for it. A cancer must meet three requirements in order to be classified as an MPMT: it must be 1) distinct histologically, 2) definitively malignant, and 3) the possibility of metastasis must be ruled out [2]. The terms "synchronous" or "contemporaneous" refer to a second primary cancer diagnosed within six months of the index cancer, and "metachronous" refers to a second primary cancer identified six months or more subsequently. Only in the absence of any past records of invasive malignancy is a cancer considered index cancer [2].

The definitions and understanding of a multiple primary have changed over the time and may differ from one study to another. The two most common definitions currently used are provided by the Surveillance Epidemiology and End Results (SEER) project and the International Association of Cancer Registries and International Agency for Research on Cancer (IACR/IARC) [3]. The incidence of multiple primaries in a cancer population varies between 2.4% and 8%, up to 17% within 20 years of follow-up [4].

Genetic factors, behavioural influences, lifestyle and comorbidities generally influence patient's outcomes. In general, black patients have a lower incidence of multiple primaries and also a lower relative survival independent of cancer site or stage at diagnosis (2.37% in black vs 3.41% white women age-adjusted prevalence for cancer survivors in the US population) [5].

To our knowledge, this study represent the first case of MPMT seen in Madagascar. The authors' aim was to report one case of MPMT seen in Madagascar and discuss about the epidemiological, therapeutic and prognosis profile of MPMT according to the literature review.

2. Case Presentation

This case concerns a 63-year-old menaopausal Malagasy woman G5P4A1 (Gravida 5, Parity 4, Abortion 1), no history of birth control, no history of alcohol and tobacco use. This patient has a family history of breast cancer in her mother. Presented a metachronous colon cancer associated by a synchronous endometrial and breast cancer.

This patient was followed in 2009 for an unprecised stage of colon cancer, there was no precise description about the TNM stage and the histologic grade, documented as an adenocarcinoma, treated by a surgery without protocol, followed by an adjuvant chemotherapy with a combination of Fluoro u racile and oxaliplatine drugs. Follow-up was fine with complete remission for this colon cancer.

Fourteen years after the history of colon cancer, this patient presented a vaginal bleeding. Investigation found a thick endometrium diagnosed as a high grade endometrioid adenocarcinoma. This patient was treated by a total laparoscopic hysterectomy with bilateral adnexectomy without lymph node dissection, negative surgical margin, stage IB, referred in Oncology unit for an adjuvant treatment. A breast tumor was discovered during the physical examination. The right breast

was with a 5cm swelling in the upper outer breast with retracted nipple and thickening skin, a non-inflammatory 2 cm ipsilateral axillary lymph node. The pathological diagnosis was a grade II invasive carcinoma.

On immunohistochemical analysis, breast tumor specimen was revealed to be positive for estrogen receptor (ER) 60% and progesterone receptor (PR) 80%, but negative for Human Epidermal growth factor 2 HER2, and Ki 67 20%.

A chest and abdominal computed tomography (CT) scanner performed to assess the extent of the disease revealed a mass in the right breast measuring 47 × 40 mm, infiltrating the overlying skin. This was associated with ipsilateral axillary lymphadenopathy (23 mm) and three right pulmonary micronodules suspect of metastases according to the radiologist description without anatomopathological exploration , classified as T3N2aM1 oligometastatic.

A multidisciplinary concertation meeting conducted to two different types of cancer according to the anatomopatological result for a primary breast tumor and a primary endometrium tumor and indicated an adjuvant concomitant chemotherapy and radiotherapy for the endometriod carcinoma starting after the breast carcinoma treatment.

The breast was treated by a 4 cycles of neoadjuvant chemotherapy (Doxorubicin and Cyclophosphamid), a radical mastectomy with axillary lymph node dissection, 4 cycles adjuvant chemotherapy (Paclitaxel), local radiotherapy and hormonotherapy.

The anatomopathological result revealed a grade II invasive carcinoma, axillary nodes were affected in 6 among 12 nodes, negative margin.

Oncogenetic examination and investigation was not done for this case which cannot precise the hereditary predisposition.

3. Discussion

In the literature, the average age of patients with multiple primary malignant tumors is 63 years [6]. The pathogenesis of this disease is complex and not fully understood. Nevertheless, it is clear that early diagnosis, tumor treatment, and improved survival rates for cancer patients lead to an increasing incidence of multiple cancers [7].

However, risk factors have been identified, such as an unhealthy lifestyle: smoking, obesity, side effects of treatment for the first primary cancer during chemotherapy or radiotherapy, viruses like HPV (Human Papillomavirus) which can cause both gynecological and oral cancers, or cancers associated with tumor syndromes (Lynch syndrome: digestive and urogenital cancers). Furthermore, advanced age is a risk factor: it has been noted that older people are more likely to develop multiple primary malignant tumors. Patients with a history of cancer also have a 20 times higher risk of developing cancer with multiple primary tumors [7]. Hence the importance of regular follow-up of cancer patients to detect early tumor recurrence, or to remain vigilant for a possible second metachronous tumor.

In the literature, multiple metachronous primary cancers are more frequent than

multiple synchronous primary cancers [8]. And in most cases, the diagnostic interval between two metachronous tumors is approximately 60 months [9]. In multiple primary malignant tumors, the most frequent histological types are adenocarcinoma and squamous cell carcinoma; and the most frequent associations seen are: gastrointestinal cancers (esophagus-stomach), gynecological cancers (endometrium and ovary), gastrointestinal (stomach)-lung cancer, gastrointestinal (esophagus)-head and neck cancer, and gynecological and breast cancer [10].

Multiple primary cancers are considered as a complex disease, there is no single treatment plan [10]. Their management must be multidisciplinary, decided during Multidisciplinary Tumor Board meetings. Indeed, each tumor must be evaluated and staged independently. Treatment of tumors with the worst prognosis should be prioritized first [11]. It is important to emphasize that the treatment plan must be personalized and reasonable, taking into account the severity of each patient's disease. In our case, treatment of the breast carcinoma was initiated before adjuvant treatment of the endometrial adenocarcinoma. The management of multiple primary malignant tumors varies considerably depending on the location and prognosis of each tumor type. Nevertheless, some authors believe that surgical treatment should be performed as soon as possible [8]. Consequently, radical treatment is primarily used for various primary cancers, followed by a relevant treatment strategy depending on the specific primary cancer. Thus, in their study, Chongya Zha *et al*. observed that surgery, alone or combined with chemotherapy, was the most frequently used treatment for multiple primary malignant tumors. For the first cancer, surgery was performed in 32.93% of cases and in 28.14% of cases in combination with chemotherapy. For the second cancer, it was used alone in 52.17% of cases and in combination with chemotherapy in 17.96% of cases [8]. This explains why, in patients with multiple primary malignant tumors, if surgery is indicated, resection should be a priority for both tumors and may be combined with chemoradiotherapy, endocrine therapy, or other treatment methods if necessary. In our case, the patient underwent a total hysterectomy followed by radiotherapy for the treatment of endometrial adenocarcinoma. For the treatment of breast carcinoma, she underwent tumor reduction with polychemotherapy initially, followed by a radical mastectomy and lymph node dissection, and then adjuvant therapy. High-intermediate-risk endometrial adenocarcinoma is an indication for total hysterectomy with bilateral salpingo-oophorectomy and lymph node dissection followed by concurrent chemoradiotherapy if Nx or brachytherapy if N0. In our case, the patient had not undergone lymph node dissection leading to the decision for concurrent chemoradiotherapy [12]. For the management of invasive breast carcinoma with a luminal B-cell immunohistochemical profile > 3N+ and oligometastatic status, the literature recommends polychemotherapy based on anthracyclines (3 or 4 cycles) and/or taxanes (9 to 12 weeks). The subsequent therapeutic strategy will depend on the tumor response [13]. In our case, there was no tumor response but stability of the lesions indicates for a radical surgery with lymph node dissection and a second line of chemotherapy

based on TAXOL followed by closure radiotherapy and long-term hormone therapy. Regarding the prognosis of multiple primary malignancies, patients over 65 years of age at the time of their second cancer diagnosis have shorter survival than patients ≤ 65 years of age; and patients with distant metastases have lower survival than patients without metastases [10]. Synchronous multiple primary malignancies have a poorer prognosis than metachronous multiple primary malignancies: better survival for patients with metachronous primary malignancies than for patients with synchronous primary malignancies [14]. A number of tumors less than or equal to 2 are in a good prognosis. But the prognosis of multiple primary malignant tumors is not primarily determined by the number of primary cancers, but by factors such as the patient's age, the stage of the cancer, the pathological type and the degree of malignancy of the tumor [15].

4. Limitations

The limits of this case report are those of a report with missing or incomplete data and, at times, insufficient detail of recorded data for treatment and follow up.

5. Conclusion

Multiple primary malignant tumors remain a rare condition. The prognosis depends on the stage of each tumor. The importance of regular follow-up for cancer patients, not only to detect early recurrences of a malignant tumor but also to look for a second synchronous or metachronous tumor. Management is multidisciplinary and tailored to the stage of each tumor, prioritizing tumors with a poor prognosis. It is essential to remember that effective management of cancer requires accurate diagnosis and timely, appropriate treatment.

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Conflicts of Interest

The authors declare no conflicts of interest.

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