A case of Multiple primary malignancies including Peritoneal Mesothelioma surviving over 11 years

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Abstract

We present a patient with 3 separate primary cancers over the course of 11 years: Follicular Lymphoma, Abdominal mesothelioma and Rectal Adenocarcinoma respectively.

Multiple primary malignancies are exceedingly rare but they may occur sequentially in a patient.

Key words

Multiple Malignancies, Lymphoma, Peritoneal Mesothelioma, Rectal Adenocarcinoma

Key Clinical Message

Multiple primary malignancies are exceedingly rare but they may occur sequentially in a patient, so in the follow-up of patients with a history of malignancy, always pay attention to second and third primary malignancies as well.

Introduction

Follicular lymphoma (FL) is the second most common non-Hodgkin lymphoma (NHL) in the United States and constitutes more than 70% of all indolent NHL histologies. FL has a heterogeneous clinical course characterized by a relapsing and remitting pattern [1].

Mesothelioma is a rare malignancy, accounting for fewer than 1% of all malignancies [2].

In both sexes combined, colorectal cancer is the fourth most common cancer and second cause of cancer death worldwide [3] .

The development of multiple primary malignancies in an individual is rare and unfortunate, and the care of such a patient presents specific challenges. We present a case report describing a patient with 3 separate primary cancers

over the course of 11 years: Follicular Lymphoma, Abdominal mesothelioma and Rectal Adenocarcinoma respectively (Figure 1).

Case presentation

In March 2009, a 55years old woman presented to physician with Multiple cervical Nodules. The patient reported that the nodules had been present for several weeks. The patient's medical history also included hyperlipidemia and hypertension. She was a housewife and had no discrete occupational exposure to chemicals and etc. Family history included no known instance of cancer. During physical examination, multiple bilateral lymphadenopathies of Anterior cervical chain and supraclavicular were detected on palpation , which were not tender and were neither erythematous nor warm to the touch. Findings of the remainder of the physical examination were normal. The patient's medical history revealed no fever, weight loss and night sweats. Cervical excisional Biopsy was done and pathologist reported "*Folicullar Lymphoma grade III"*. Further evaluations including chest/abdomen CT and cervical sonography and Bone marrow aspiration/biopsy detected no more findings (Stage I Folicullar lymphoma). Patient received 4 courses of R-CHOP regimen (Cyclophosphamide, Doxorubicin, Vincristine and Prednisone plus the monoclonal antibody Rituximab) followed by Involved Site Radiation Therapy (ISRT). Cervical lymph nodes were completely resolved in Neck CT after completion of chemotherapy. Routine, annual visit and physical examination was recommended and continued up to April 2016.

In April 2016 an approximately 4 centimeters mass of right inguinal region was detected in physical examination which was not tender and was neither erythematous nor warm on palpation. Abdominopelvic CT showed multiple lymphadenopathies of para-aorta and iliac chains with maximum SAD of 14 milimeters in favour of metastasis. Chest CT had no abnormal findings. Excisional biopsy of inguinal/Lower Abdomen mass and Pathology/IHC study (positive for Pan-CK, CK7, Calretinin, WT-1, and negative for CD20, P63, TTF1, & CEA) made the diagnosis of "*Mesothelioma "* which was confirmed by two pathologists (Figure 2).

Patient received cisplatin+ pemtrexed regimen. Abdominopelvic CT after completion of chemotherapy showed that inguinal mass and lymhadenopathies are completely resolved. Routine, periodic visit and physical examination was recommended and continued up to May 2019.

In May 2019 an incidental finding of pelvic CT reported a mass like lesion of rectum and fat stranding of around. Colonoscopic study revealed a large ulcerative tumor of rectum. Complementery studies confirmed "*Adenocarcinoma of Lower Rectum* T_3 N_2 M_0*"*. Patient received neoadjuvant radiotherapy then underwent Abdomino Pritoneal Resection (APR) surgery.

Now our patient is a 66 years old woman and is alive 11 years after the diagnosis of Folicullar Lymphoma and 4 years after diagnosis of Mesothelioma and 1 year after diagnosis of rectal adenocarcinoma.

Discussion

To best of our knowledge, the present report is the first to discuss a rare case of 3 primary cancers that includes an equally rare mesothelioma of the peritoneum without any known predisposig factor (e.g Radiation or asbestos exposure). Multiple primary neoplasms are uncommon clinical entities that often require intensive medical care. The prevalence of this phenomenon has been increasing in recent years because of the increased survival rate associated with cancers previously considered to be fatal (ie, allowing the patient time to develop a second or third malignancy). It is difficult to determine the prevalence of multiple primary neoplasms accurately because the only available data come from studies based on case report. Koutsopoulos et al. tabulated the results of an extensive literature search for multiple primary cancers and found 42 cases of 3 or more cancers reported between 1949 and 2003, proving that the entity is rare. Important epidemiologic parameters, such as incidence, prevalence, and prognosis, would almost certainly depend on the particular combination of cancers (5).

malignant mesothelioma is a rare malignancy mainly caused by occupational or environmental asbestos exposure and arise mostly from pleura although it rarely originate from other mesothelial structures such as peritoneum and pericardium as well. Other possible risk factors are radiation exposure and genetic predisposition [4]. Interestingly, 50% of patients with peritoneal malignant mesothelioma have no documented asbestos exposure. Although overall mesothelioma is more common in men, higher proportions of women develop peritoneal mesothelioma [5, 6].

The particular combination of cancers should be examined in an attempt to explain the occurrence through elucidation of a common risk factor or perhaps genetic predisposition; Regarding relationship between asbestos exposure and tumors of the hematopoietic system we sould know that development of non-Hodgkin lymphoma and asbestos-related mesothelioma in the same patient has repeatedly been observed [7-9]. In addition a small study has supported an association between occupational exposure to asbestos and colon cancer incidence in men[10]. Our patient had neither prior history of asbestos expoure (as a probable common risk factor of Mesothelioma, Lymphoma and rectal adenocarcinoma) nor abdominal radiation but the Genetic study was not acomplished.

A study conducted in 2018 by Hung et al. on 88 patients of peritoneal mesothelioma showed that 13% of patients are Anaplastic lymphoma kinase (ALK) positive by immunohistochemistry and in three out of eleven patients, ALK rearrangement was detected by Fluorescence in situ hybridization (FISH) as well [11]. In addition Some genetic studies of colorectal cancer have showed that ALK, ROS1, and NTRK fusions occur in 0.2% to 2.4% of patients [12]; Altough genetic study was not available for our patient but hypothetically Alk-rearrangement or other unknown Genetic disorders may be a common findig of peritoneal mesothelioma and rectal adenocarcinoma in our patient.

The lessons we learn from this patient are

1. In the follow-up of patients with a history of malignancy, always pay attention to second and third primary malignancies as well.
2. Although mesothelioma occurs mainly in the pleura and in contact with asbestos or radiation, it can rarely occur in peritoneum without a history of contact with asbestos or radiation. Peritoneal mesothelioma is highly lethal and has a poor prognosis, but sometimes the patient recovers with systemic chemotherapy such as pemetrexad/cisplatin and can live for several years thereafter.

3. In patients with multiple primary malignancies (synchronous or methachronous) and a malignancy in absence of a well known risk factor (e.g Mesothelioma in absence of Asbestos or radiation exposure), Genetic study may help to better understand the cause.

In conclusion, a review of literature showed that Multiple primary malignancies are exceedingly rare but they may occur sequentially in a patient same to our's (ie None Hodgkin Lymphoma then Peritoneal Mesothelioma and finally Rectal Adenocarcinoma) and Peritoneal mesothelioma known as a fatal malignancy may completely regress with chemotherapy and cause a survival for many yeas.

Conflict of Interests

The authors declare no conflict of interests regarding this paper.

Author Contributions

Author 1 : involved in revising the manuscript for important intellectual content
Author 2: made contributions to design the manuscript and analysis and interpretation of data

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Figure 1. Timeline of patient

Figure 2. Peritoneal Mesothelioma