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CASE REPORT

Multiple metachronous rare primary malignant tumors: A case report

Xiaozhen Ying[1†], Heying Zhang[2†], Bizheng Chen[1], He Wu[1], Liming Bao[1], Shi Qian[3] & Xihui Ying[3]

1 Department of Radiotherapy, Lishui Central Hospital, Lishui, China
2 Department of Emergency, Zhuji People's Hospital of Zhejiang Province, Zhuji, China
3 Key Laboratory of Imaging Diagnosis and Minimally Invasive Interventional Research of Zhejiang Province, Lishui Central Hospital, Lishui, China

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Correspondence
Xihui Ying, Department of Radiotherapy, Lishui Central Hospital, No.289 Kuocang Road Lishui City Zhejiang Province 323000, China.
Tel: +86 0578 2285228
Fax: +86 0578 2285228
Email: yingxihui@163.com

†These authors contributed equally to this work.

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Abstract

Multiple primary malignant tumors (MPMTs) are rarely seen among the patients with malignant neoplasms. Moreover, the existence of five MPMTs in the same patient is an extremely rare phenomenon. In this case, a 42-year-old male patient developed five metachronous MPMTs within 16 years and the duration between each malignant tumor shortened with the progression of the disease. Multidisciplinary treatments were used on this patient and he fought against the cancers until the end of his life. Our report provides us with a new awareness of MPMTs, which should be considered when we come across with cancer patients who develop various unexplainable symptoms after the diagnosis of the first neoplasm.

Introduction

The term "multiple primary malignant tumors" (MPMTs) was first used by Billroth in 1889,[1] and the first report describing MPMTs was published by Warren and Gates in 1932[2] which has provided us with the current diagnostic criteria of MPMTs. The definition of MPMTs is: (i) Each neoplasm should be histologically confirmed as malignant; (ii) each neoplasm should have unique pathomorphological features; (iii) the neoplasms develop in different places and are disconnected and (iv) the suspicion of metastasis must be excluded. MPMTs may be synchronous or metachronous. The term "synchronous" is used when the second primary cancer is diagnosed within six months of the primary cancer; "metachronous" is used when the second primary cancer is diagnosed more than six months after the diagnosis of the primary cancer. In this study,we present a rare case of a patient with five metachronous multiple primary malignant tumors.

Case report

A man who was 42-years-old in 1997, was admitted with a chief complaint of abdominal pain, and was later diagnosed with colon cancer. He was treated with sigmoid colon cancer radical surgery on 23 June 1997. Postoperative histopathological analysis revealed sigmoid colon cancer graded as Dukes C1 (Fig 1a). The patient did not receive any chemotherapy or radiotherapy after the surgery.

In October 2003, the patient again presented with abdominal pain and colonscopy revealed colon cancer. He underwent radial ascending colon carcinoma sugery in 08 October 2003. Histopathological analysis demonstrated moderately and poorly differentiated adenocarcinoma of the ascending colon invading to the outer membrane (Fig 1b). Following surgery, the patient was then treated with oral Carmofur 150 mg t.i.d.

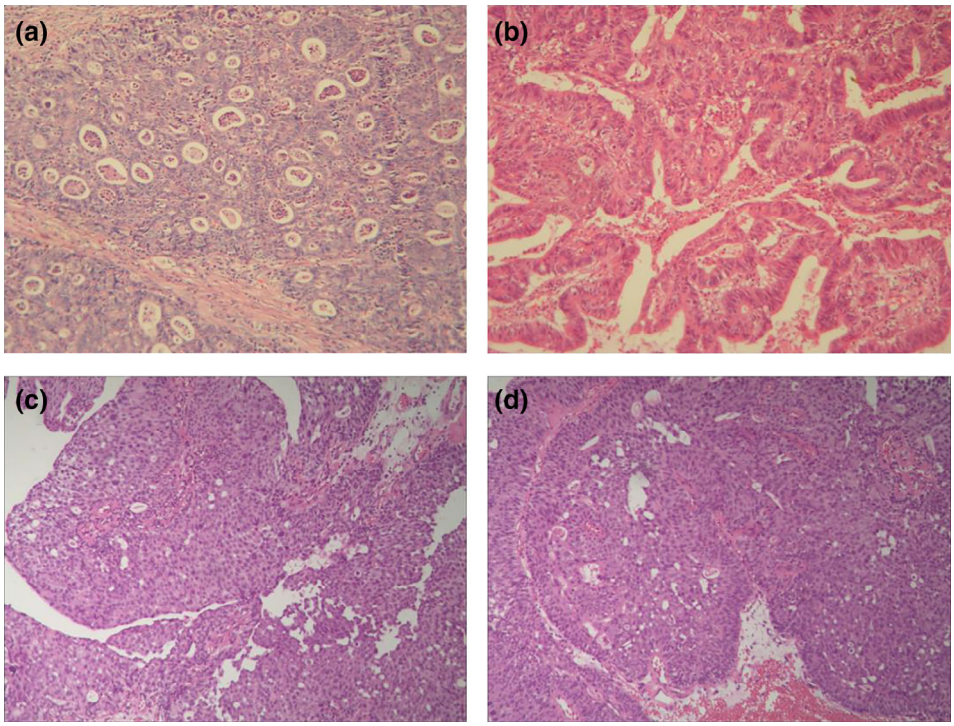

Figure 1 (a) Sigmoid colon cancer was diagnosed in June 1997. (b) Ascending colon carcinoma was diagnosed in October 2003. (c) Urinary tract cancer was diagnosed in April 2009. (d) Bladder cancer was diagnosed in October 2010, (HE staining, 100x).

In April 2009, the patient was admitted to the First Affiliated Hospital of Zhejiang University School of Medicine with gross hematuria, which was later diagnosed as bladder cancer. The patient underwent right pelviolithotomy combined with excision of the remaining right ureter and the bladder cuff. Postoperative histopathological analysis revealed (bladder, right ureter and right renal pelvis) multiple invasive stage II urothelial papillary carcinoma (Fig 1c). The patient was treated with infusion chemotherapy (Doxorubicin) following surgery.

In July 2010, the patient again complained of gross hematuria and was subsequently admitted to People's Hospital of Jinyun Town. He received a partial bladder resection and postoperative pathology subsequently indicated invasive high-level papillary urothelial carcinoma of the right wall of the bladder (Fig 1d).

In September 2011, a mass (2 × 2 cm) which was stiff and fixed in the left neck was discovered. With no treatment, biopsy of the mass was taken one month later (23 October 2011) at the Cancer Hospital of Fudan University. Pathological study showed metastatic carcinoma with necrosis (Fig 2d). Chest CT scan showed a mass (5.9 × 5.0 cm) in the right upper lobe, which was suspicious of a malignant tumor (Fig 2a–c). Radiation therapy was commenced after 27 December 2012. On 25 November 2013, the patient died of multiple organ dysfunctional syndrome (MODS).

Discussion

In the case reported here, the middle-age male patient developed five distinct primary malignant tumors within three organ systems (digestive, urinary and respiratory), thus meeting the criteria of a diagnosis of MPMTs. The survival time of this patient was 16 years. The interval from the onset of sigmoid colon cancer to ascending colon cancer was six years, and from ascending colon cancer to multiple infiltrating urinary papillary epithelial carcinoma was five years. The duration between the onset of multiple infiltrating urinary papillary epithelial carcinoma and bladder infiltrating high-grade papillary epithelial carcinoma was 15 months. It took 12 months for the new onset of pulmonary squamous cell carcinoma from bladder infiltrating high-grade papillary epithelial carcinoma (Fig 3). The progression of the patient's disease is consistent with the definition of metachronous MPMTs. The patient had received multidisciplinary treatments, including four surgical operations, multiple cycles of chemotherapy and radiation therapy. The interval between each type of tumor decreased with time. The patient's good quality of life in the first few years was mostly due to active participation in the anti-cancer treatments and an optimistic attitude. The cause of MPMTs has yet to be elucidated. Abnormal activation of oncogenes, silencing of tumor suppressor genes, epigenetic alterations, chromosome instability, excessive toxicant exposure and immune deficiency are all potential

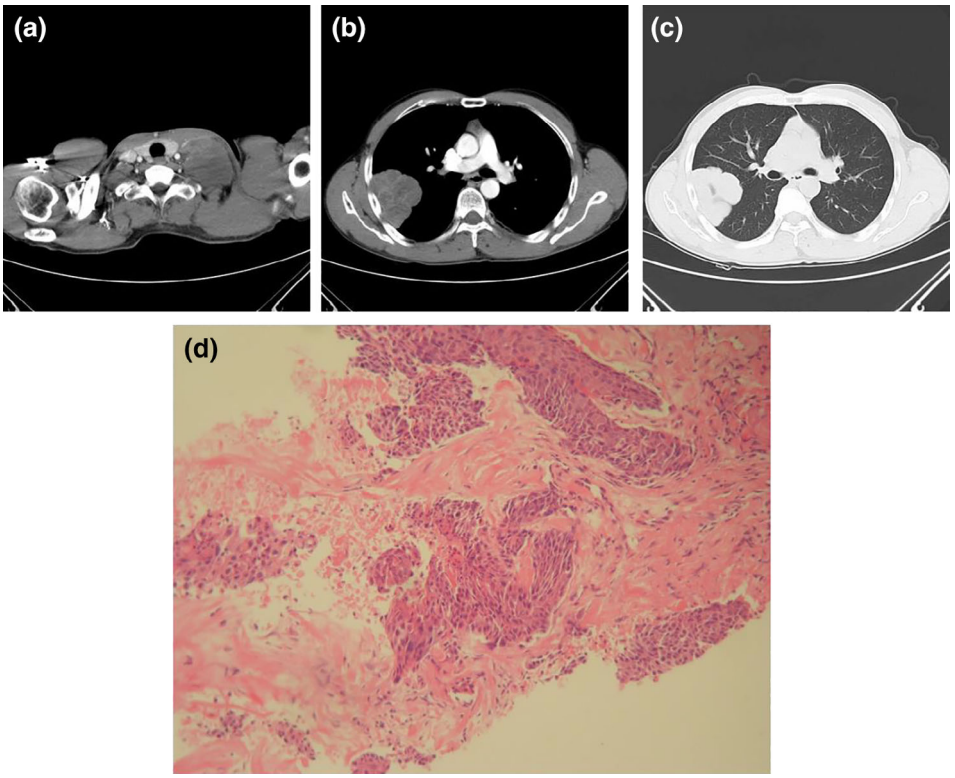

Figure 2 In September 2011, two new masses were evident. (a) A 5.2 x 5.8 cm mass at the supraclavicular edge. (b,c) A mass in the right upper lobe of the lung. (d) A pathological diagnosis of squamous cell carcinoma was made (HE staining, 100x).

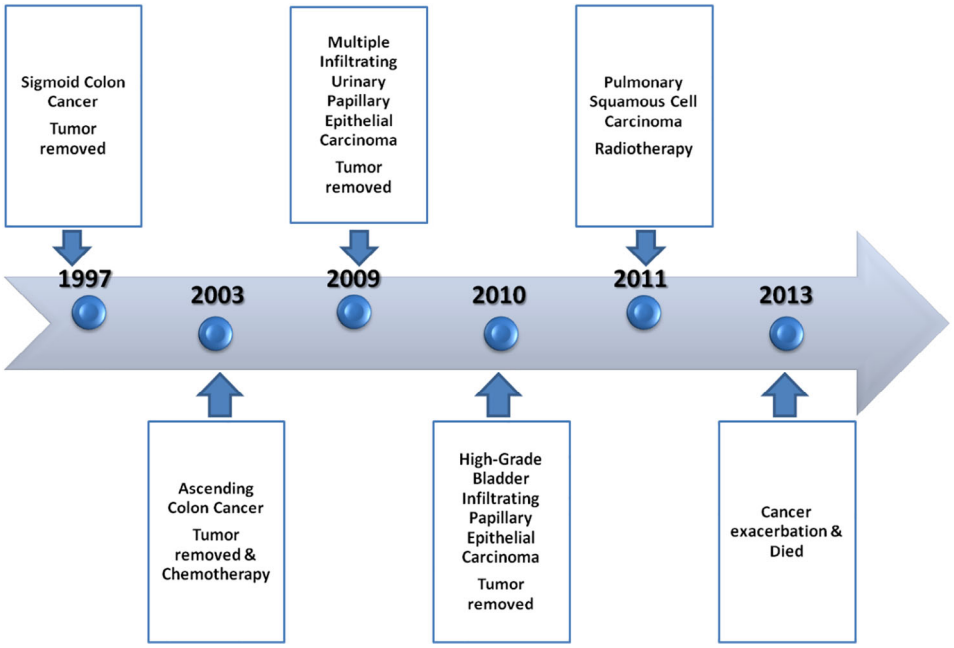

Figure 3 This illustrates the progression of the malignancies.

causes of MPMTs.[3–6] The patient's daughter had died of colon cancer at the age of 22, which strongly indicated that there must be some genetic defect in the whole family, and whole genome sequencing is necessary for further investigation of the genetic aspect.

This rare case of five metachronous multiple primary malignant tumors has provided us with a new understanding of MPMTs. In future clinical work, we should investigate the clinical symptoms that cannot be explained by one type of cancer. No matter how rarely it occurs, the

possibility of MPMTs deserves our attention. Thorough examination and pathological analysis is important to prevent misdiagnosis and missed diagnosis. In terms of the treatment, the nature of each type of tumor must be taken into consideration.

Disclosure

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