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內文：

Abstract

1. Cancer survivors have a higher risk of new primary cancer, in the same or in another organ, than the general population.
2. We report a 78-year-old woman who has metachronous quadruple adenocarcinoma, includes bilateral breast cancer, ovarian cancer and retroperitoneal neuroendocrine carcinoma.

Introduction

1. Cancer survivors are a growing group owing to improvements in widely scanning and treatment
2. Two reasons occurrence of multiple primary cancers are likely to increase
 - (1) The diagnosis of a new second cancer
 - (2) Older people population increases
3. Cancer patients have a 20% higher risk of new primary cancer compared with the general population
4. Second cancers have become a leading cause of death among long-term cancer survivors
5. Individual susceptibility factors remain largely unknown but, it may not necessarily be attributable solely to prior cancer treatment but may also reflect the effect of shared etiologic factors, environmental exposures and inherited predisposition
6. Multiple cancers (two or more primary cancers), each of the tumors must present a definite pattern of malignant disease, each must be distinct, and the possibility that one tumor is a metastasis of the other must be excluded.
7. In cancer survivors, the number of second or higher order cancers is burgeoning and accounted for about 16% of incident cancers in 2003
8. The development of second cancer in cancer survivor is expected but third, or higher order malignancies are rare
9. This is the first detected case with this combination of primary adenocarcinomas

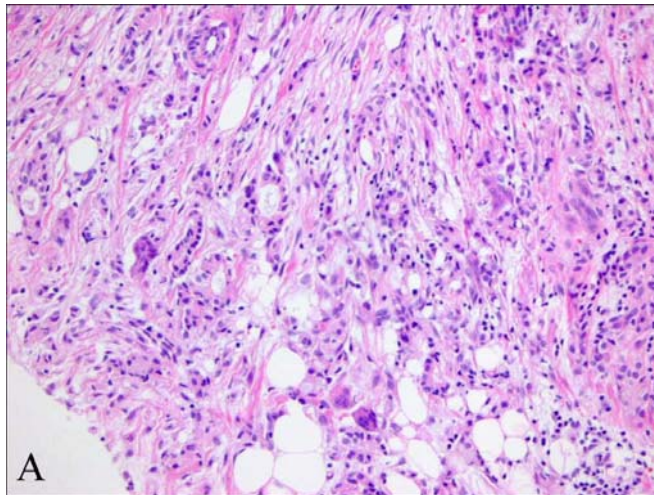
Case

A 78-year-old patient who had metachronous quadruple cancer was admitted to our clinic.

Family history: her grandmother had lung cancer

1996

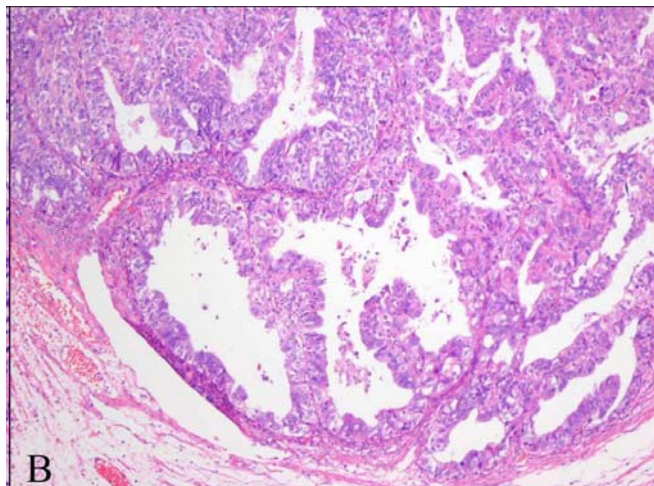
1. **invasive breast cancer (A)**
2. right modified radical mastectomy +C/T + R/T + hormone therapy as tamoxifen



Invasive ductal carcinoma :
Glandular differentiation is apparent as tubular structures with central lumina.
A proportion of tumor cells are arranged in cords, clusters and trabeculae

1998

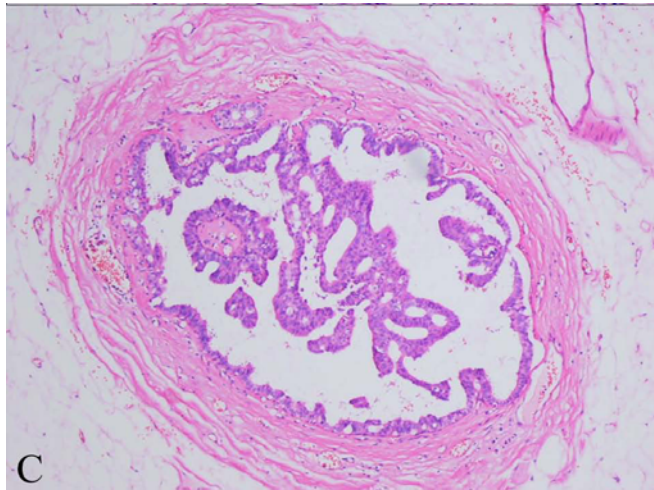
1. right ovarian mass
2. total abdominal hysterectomy(開腹子宮切除術) +bilateral salphingoopherectomy (輸卵管卵巢切除術) + partial omentectomy (網膜切除術)
3. Pathologic examination showed **poorly differentiated serous carcinoma(B)**
4. No metastatic lesion was detected
5. Treated with combined paclitaxel and cisplatin regimen for 6 cycles(第一線治療晚期卵巢癌的標準) and followed-up without any sign of recurrence



Poorly differentiated serous carcinoma :
Glandular and papillary architecture of tumor.
The glands are typically irregular and slit-like

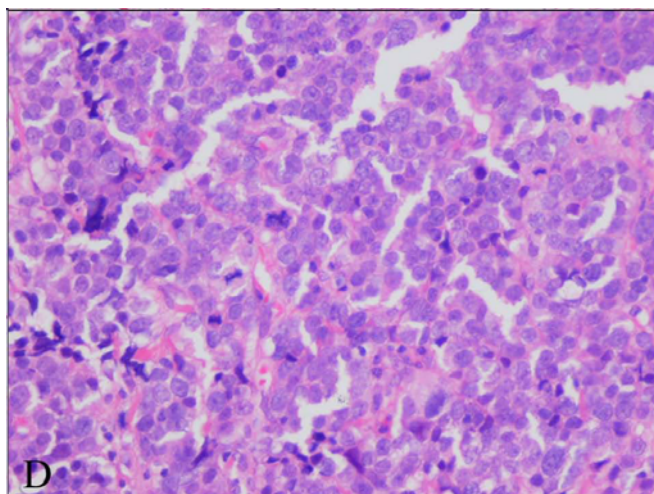
2006

1. accidentally a lump of the left breast
2. **intraductal carcinoma(C)** in left breast mass was primary breast cancer
3. right modified radical mastectomy was carried out and pathologic examination showed intraductal carcinoma
4. Hormone receptor status was negative
5. She did not have any adjuvant treatment



Intraductal carcinoma :
cribriform and micropapillary
pattern

1. Lobular border solid mass in left renal hilus was detected by abdominal CT
2. Trucut biopsy (粗針活組織切片檢查) was done and pathologic examination showed **undifferentiate neuroendocrine carcinoma(D)**
3. In the surgery abdominal aorta was surrounded by tumor in pancreas tails
4. She was treated with combined cisplatin and etoposid C/T regimen
5. After 3 cycles response was evaluated as partial response and stable disease after 5 cycles of chemotherapy



Undifferentiate neuroendocrine
carcinoma :
Sheets of polygonal, round cells
with salt and pepper nuclei and
numerous mitotic figures

In August 2008, her clinical status was deteriorated and detected as progressive disease and combination carboplatin and etoposide regimen was administered

Discussion

1. Multiple primary malignancies are common, in a study encountered in 3~5% of malignant tumors which are most often secondary, triple tumors occur in only 0.5%, quadruple tumors in 0.3% of malignant tumors
Németh Z et al
2. Our patient has a quadruple cancer accordingly International Agency for Research on Cancer (IARC) 國際癌症研究署, but not according to Surveillance Epidemiology and End Results(SEER) rules 美國國家癌症研究院之「流行病監測及最終結果」資料庫為目前美國最完整的癌症病人長期追蹤資料，包含癌症病人存活狀況、多重癌症史、居住地區及其他分析所需之個人資料
Contralateral malignant lesions of the breast are considered as subsequent primary tumors according to SEER rules
3. The increased risk of subsequent malignancies among cancer ages 30 to49
4. Second primary cancers can be examined into three categories
 - (1) therapy related
 - (2) syndromic
 - (3) resulting from shared etiologic influencesTravis et al
5. SEER program data were diagnosed with a second cancer by 25 years F/U for patient who have already developed a second malignancies, recognition of the types of possible additional malignancies, the associated latency periods, and underlying risk factors such as treatment, genetic predisposition, environmental cofactors will have important implications for F/U and screening
6. Second malignancies are a result of success and are not observed unless a patient survives and initial cancer diagnosis
7. 67(5.4%)cases of multiple primary malignancies of the genital organs and breast in their different combinations in 1235 multiple primary malignancies
Deligdisch et al
8. A higher incidence of multiple primary cancers were found in embryologically related organs such as endometrium and ovary. Similar result were reported as the most frequent organ involved in multiple tumors was breast, the largest amount of data exist for contralateral breast cancer, probably due to embryology or common etiologic factors
9. Breast and ovarian cancers are likely due to genetic factors and hormonal influence. Cancer treatment(C/T or R/T) and insufficient hormone therapy may cause contralateral breast cancer in our case

10. Familial cancer syndrome should be thought because of combination of ovarian and breast cancer, although our case had no evident family history of cancer

11.

consecutive autopsy case	double	triple or more
5456	285(5.2%)	58(1.1%)

Watanabe et al.

12.

cancer p't	multiple malignancies		
719	53(7.4%)	second	49
		third	4

Colorectal(直腸結腸) and gynecological(婦科) malignancies appeared with breast cancer in 5 cases

Antal et al.

13.

Hodgkin lymphoma p't 1319	second malignancies	181	34 M
	third malignancy	18 breast cancers lung cancers genitourinary cancers	

Ng et al

14.

childhood cancer survivors	Subsequent malignancies	
1380	1	141
	2	26
	3	5
	4	1

The third neoplasm included 28 solid malignancies, 1 hematologic malignancy

The estimated 10 year cumulative incidence of developing a third malignancy was 21% from the time of diagnosis of the second malignancy

Latent period between second and third malignancies was 8 years

Bhatia et al.

15. In our patient, neuroendocrine tumors(NET) was the forth developed cancer and they are they are frequently associated with synchronous or metachronous secondary malignancies

p't with neuroendocrine tumors (NET)	NET and secondary malignancies		
96 69 yrs(56~86 yrs)	14	synchronous	5
		metachronous	9

Progemmer et al.

16. Our case has metachronous quadruple adenocarcinomas and she may develop fifth or more malignancy in the following times
17. We need an improvement for our knowledge of the risk and patterns of high-order malignancies

題號	題目
1	關於 Merkel cell carcinoma (neuroendocrine carcinoma of skin) 以下何者錯誤 (A) 出現在老年人身上較多 (B) 在組織切片上，可看到'tennis bracket' (C) 復發率達 55%，且經常跟 draining lymph nodes 有關 (D) 最常出現的地方是臉部的皮膚
答案(B)	出處：Oral and Maxillofacial PATHOLOGY third edition p432,433
題號	題目
2	關於 salivary gland malignancies 以下何者正確 (A) Adenoid cystic carcinoma 組織切片可看到三個主要的型，分別為(1)cribriform (2)tubular (3)follicular (B) Mucuepidermoid carcinoma 是很少見的 salivary gland malignancies (C) Minor salivary gland malignancies 最好發在頰側黏膜上 (D) Polymorphous low-grade adenocarcinoma 最好的治療方法是進行 wide surgical excision
答案(D)	出處：Oral and Maxillofacial PATHOLOGY third edition p474,487,496,497