
Case report

Multiple synchronous malignant neoplasms in an elderly lady with a history of early onset breast cancer

HD Wijesinghe^{1, 2}, CS Fernando^{1, 2}, J Fernando¹

Introduction

Synchronous tumours are two or more distinct tumours occurring at the same time in the same organ, opposite sides of paired organs, or different organs (1). Cases of three or more synchronous tumours are rare and have been reported in the breast, colon, genitourinary tract, female reproductive tract, gastrointestinal tract and skin (2-6). We report an unusual case of synchronous tumours of the breast, colon and ovary occurring in a female with history of early onset breast cancer.

Case History

A 71 year old woman who had been treated for carcinoma of the right breast at the age of 29 years, presented with altered bowel habits associated with loss of appetite and loss of weight of six months duration. She had no family history of malignancy but had a history of primary subfertility.

Examination revealed an irregular left breast lump measuring 3x2x2cm in the upper outer quadrant that was highly suspicious of malignancy on mammography. A large tumour in the rectosigmoid colon was seen on colonoscopy. It was confirmed to be an adenocarcinoma on biopsy.

A Trucut biopsy of the breast lump was performed followed by an anterior resection for the colonic tumour. During surgery for the colonic tumour, she was incidentally found to have a tumour arising from the right ovary and an oophorectomy was also performed. All three samples were received at our laboratory.

Sections from the breast biopsy revealed a tumour with a cribriform architecture comprising glandular spaces lined by luminal and myoepithelial cells. The constituent cells had bland, hyperchromatic, angulated nuclei and

¹Department of Pathology, National Hospital of Sri Lanka

²Department of Pathology, Faculty of Medicine, University of Colombo

Correspondence: HD Wijesinghe, Department of Pathology, Faculty of Medicine, University of Colombo. E.mail:harshima@hotmail.com

scanty cytoplasm. Small true lumina containing PAS positive material with pseudolumina containing Alcian blue positive mucin were present. The luminal cells were positive for CK7 and negative for CK20. The myoepithelial cells were highlighted by S100. The tumour was negative for oestrogen, progesterone and HER2 receptors. The breast tumour was diagnosed as an adenoid cystic carcinoma which was confirmed by a subsequent mastectomy. The lymphnodes did not contain metastases.

The rectal tumour was a greyish white, exophytic, fungating mass located entirely in the non peritonealised area. Microscopic examination revealed a moderately differentiated adenocarcinoma of the rectum with a mucinous component that extended to the superficial part of muscularis propria. The tumour cells were CK7 negative and CK 20 positive, confirming a primary large intestinal tumour. The ovary measured 7x4.5x3.5cm and had a yellow, white variegated cut surface. Sections revealed sheets and nests of markedly pleomorphic cells with enlarged vesicular nuclei and prominent nucleoli. Numerous mitotic figures were seen. The tumour cells were positive for CK7 and negative for CK20, inhibin, synaptophysin and chromogranin. A metastatic deposit from the colorectal carcinoma was excluded and a diagnosis of an undifferentiated carcinoma of the ovary was made.

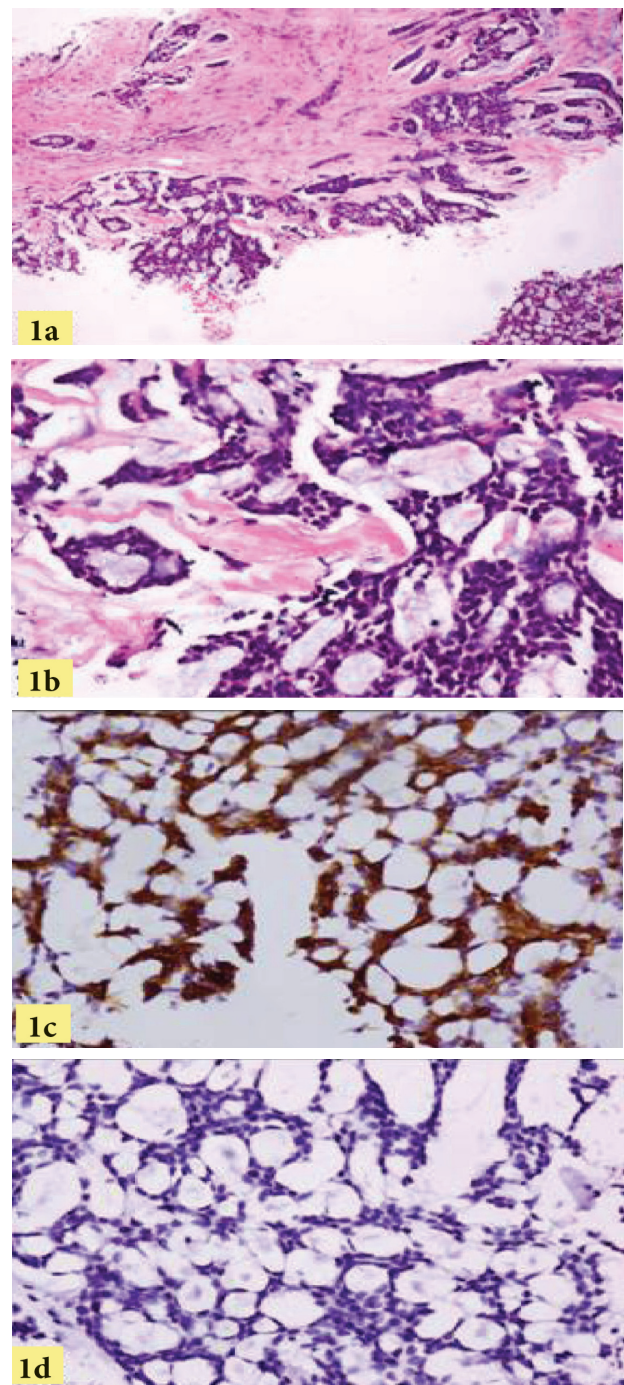


Fig. 1. 1A. Adenoid cystic carcinoma of the breast: Invasive tumour with a cribriform architecture (H&E x40); 1B. Glandular spaces lined by cells with bland, compact, angulated nuclei and scanty cytoplasm (H&E x400); 1C. Strong cytoplasmic positivity of luminal cells for CK7 (CK7 x400); 1D. Negativity for CK20 (CK20 x400)

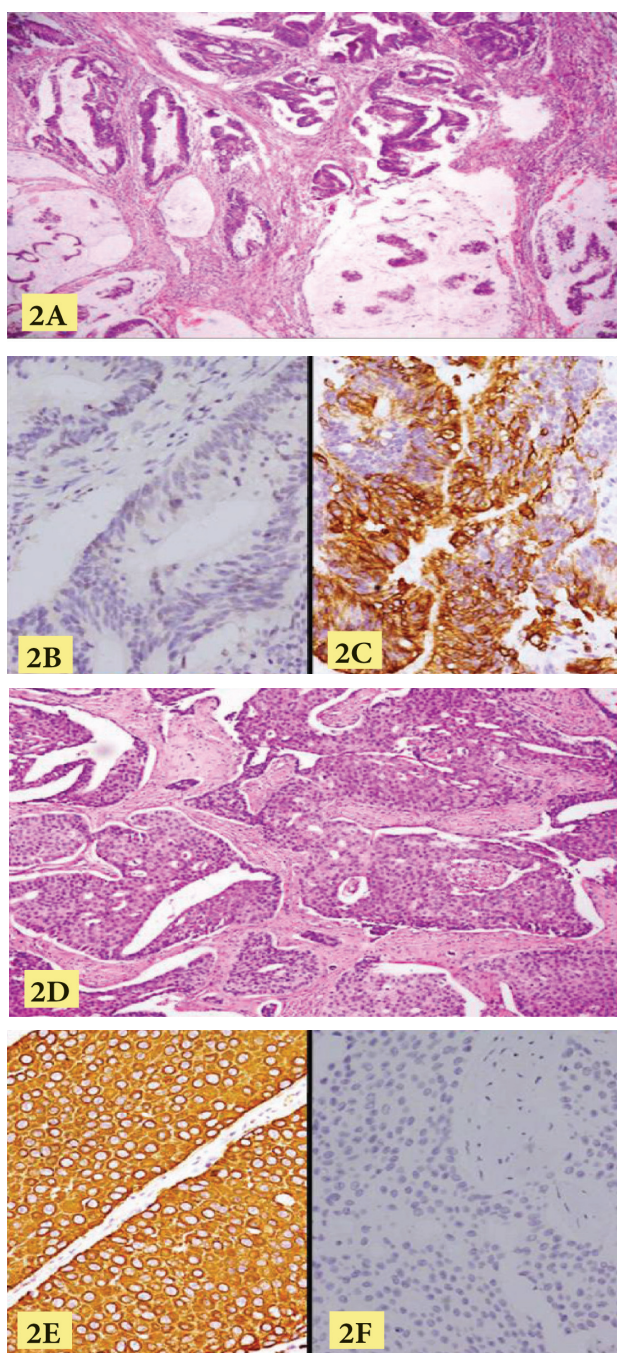


Fig.2. Microscopy of colonic and ovarian tumours: 2A. Adenocarcinoma of colon with a mucinous component (H&E x100); 2B. Negativity for CK7 (CK7 x400); 2C. Cytoplasmic positivity for CK20 (CK20 x400); 2D. Undifferentiated carcinoma of the ovary (H&E x100); 2E. Cytoplasmic positivity for CK7 (CK7 x400); 2F. Negativity for CK20 (CK20 x400)

Discussion

Adenoid cystic carcinoma is a tumour of low malignant potential that accounts for <0.1% of breast carcinomas (7). Lymph node metastases are rare and simple mastectomy is usually curative.

Undifferentiated carcinoma of the ovary is a primary ovarian carcinoma with no/only small foci of differentiation and accounts for 5% of ovarian cancers. The prognosis is worse than other serous carcinomas of the ovary.

This patient presented with three separate simultaneous malignant primary tumours. She had a history of early onset breast carcinoma at the age of 29 years for which she had received adjuvant chemotherapy and radiotherapy. She had no family history of breast carcinoma. Under these circumstances, the possibility of an inherited cancer syndrome, chemoradiotherapy induced malignancy and exposure to environmental carcinogens had to be considered.

Radiotherapy induced tumours usually involve the tumour bed edges and the radiation field and chemotherapy related tumours usually involve the aero-digestive mucosa, gastrointestinal tract, liver, kidney and lung (8). The latent time interval of over forty years seen

in this patient is unusual for a chemotherapy induced malignancy. There was no history of exposure to carcinogens.

We were unable to determine the cause of multiple synchronous tumours in our patient. However, an inherited breast cancer syndrome such as BRCA1 and BRCA2 syndromes or Li Fraumeni syndrome is a possibility.

BRCA1/2 syndromes are inherited in an autosomal dominant fashion, associated with a markedly increased risk of breast and ovarian tumours and have a high association with breast carcinoma occurring below 35 years. Confirmation of diagnosis requires genetic testing by sequencing of patient DNA samples in a clinically approved diagnostic laboratory. (7)

The lack of a positive family history and high grade “medullary like” histopathological features in the tumour such as pushing margins, lymphoid infiltrate and a high mitotic count (9) are against the diagnosis of a BRCA1 associated cancer. However, if this patient was diagnosed with a BRCA1 associated syndrome by genetic testing, counseling could have been offered to other family members. In addition since tumours carrying BRCA1/2 are sensitive to PARP (poly ADP ribosome polymerase) inhibitors it also

provides an opportunity for targeted therapy (10).

Li Fraumeni Syndrome is caused by germline mutations in TP53 gene and is associated with multiple primary neoplasms of which breast cancer is the most common. The breast cancer associated with this syndrome is usually diagnosed at an early age <30 years. The histology of breast carcinoma is similar to sporadic tumours but it is usually associated with amplification of HER2. Although guidelines are in place for testing and screening of carriers, the clinical benefit is currently limited (7).

Conclusion

Although rare, the possibility of an inherited cancer syndrome should be considered in patients presenting with breast cancer at a young age and in patients with multiple malignancies.

References

1. Howe HL (ed). A Review of the Definition for Multiple Primary Cancers in the United States. Workshop Proceedings From December 4–6, 2002, in Princeton, New Jersey. Springfield (IL): North American Association of Central Cancer Registries May 2003.

2. Deppe G, Dolan TE, Zbella EA, Heredia R. Synchronous multiple primary malignant neoplasms of the breast, colon and vulva. A case report. *The Journal of Reproductive Medicine* 1984;29(12):878-80.
3. Atasever M, Yilmaz B, Dilek G, Akcay EY, Kelekci S. Synchronous primary carcinoma in 5 different organs of a female genital tract: an unusual case and review of the literature. *International Journal of Gynecological Cancer* 2009;19(4):802-7. doi: 10.1111/IGC.0b013e3181a39b95.
4. Otrrock ZK, Mahfouz RA, Salem ZM. Four primary tumors of lung, bladder, prostate, and breast in a male patient. *Southern Medical Journal* 2005 Sep;98(9):946-9.
5. Love RR. Small bowel cancers, B-cell lymphatic leukemia and six primary cancers with metastases and prolonged survival in the cancer family syndrome of Lynch. *Cancer* 1985;55:499-502.
6. Swaroop VS, Winawer SJ, Lightdale CJ, Martin L. Six primary cancers in individuals: report of four cases. *Cancer* 1988;61 :1253-1254.
7. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, Van de Vijver MJ (Eds.):WHO Classification of Tumours of the Breast. IARC: Lyon 2012.
8. Mehdi I, Shah AH, Moona MS, Verma K, Abussa A, Elramih R, El – Hashmi H. Synchronous and metachronous malignant tumours expect the unexpected. *Journal of Pakistan Medical Association* 2010;60(11):905 -909.
9. Lakhani SR, Jacquemier J, Sloane JP, Gusterson BA, Anderson TJ, Van de Vijer M et al. Multifactorial analysis of differences between sporadic breast cancers and cancers involving BRCA1 and BRCA2 mutations. *Journal of the National Cancer Institute* 1998;90:1138-1145.
10. Tutt A, Robson M, Garber JE, Domcheck SM, Auedh MW, Weitzel JN et al Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and advanced breast cancer:a proof of concept trial. *Lancet* 2010;376:235-244.