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CASE REPORT

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Synchronous primary neoplasms of the bladder, skin and breast in a male patient: a case report

Antonio Luigi Pastore^{1*}, Giovanni Palleschi¹, Domenico Autieri¹, Antonino Leto¹, Andrea Ripoli¹, Cristina Maggioni¹, Davide Moschese¹, Yazan Al Salhi¹, Natale Porta², Claudio Di Cristofano², Andrea Fuschi¹, Luigi Silvestri¹, Carlo Della Rocca², Silverio Tomao³, Vincenzo Petrozza², Antonio Carbone¹ and Sapienza University of Rome, Faculty of Pharmacy and Medicine

Abstract

The incidence of multiple primary malignant neoplasms increases with age, reflecting an increase in overall cancer risk in older patients. Cases of two or more concurrent primary cancers are still rare, although its incidence is increasing. Here, we report the case of a 57-year-old man who was referred to our institution with synchronous squamous cell carcinoma of the skin on the forehead, infiltrating ductal carcinoma of the breast, and transitional cell carcinoma of the urinary bladder. To the best of our knowledge, this is the first reported case in literature of this combination of primary neoplasms.

Background

Multiple primary cancers (MPC) in a single patient was first documented by Billroth et al. in 1889 [1]. Since then, many cases of double, triple or even quintuple primary malignant neoplasms have been documented involving single or multiple organs [2]. MPCs are first classified as either synchronous or metachronous depending on their timing of diagnosis. Synchronous lesions are relatively uncommon, with most cases involving metachronous lesions [3,4].

However, there remains some confusion over the terms used to describe MPC, such as synchronous, simultaneous, and metachronous or successive neoplasms. All these definitions are based on the time that the neoplasms are discovered rather than the onset of disease. Thus, the term 'synchronous' refers to neoplasms discovered simultaneously, while 'metachronous' indicates a distinct neoplasm discovered when the same patient is already known to have a neoplasm (successive neoplasm) [5].

The generally accepted definition of MPC was introduced by Worren and Gates, who stated that each neoplasm must represent a distinct malignancy, and that a

metastatic origin must be excluded [6]. Ray et al. reported that 13.5% patients with MPC had genitourinary neoplasms [7].

In this report, we describe the case of a patient who developed synchronous primary transitional cell carcinoma (TCC) of the urinary bladder, squamous cell carcinoma (SCC) of the skin on the forehead, and infiltrating ductal breast carcinoma. This combination, to the best of our knowledge, has never previously been reported in the literature.

Case presentation

A 57-year-old man, a farmer and heavy smoker (90 to 100 cigarettes a day from the age of 15 years), was referred to our institute for gross haematuria with clots retention that required an acute catheterisation with bladder irrigation. An ultrasound examination showed papillary neoplasms arising from the posterior-lateral left wall of the bladder.

The patient had suffered lower urinary tract symptoms over the preceding 1 year and seemed cachectic, but had not previously reported weight loss or any other specific complaints. He did have a family history of malignancy though, as his father had developed rectal cancer and his sister had a kidney neoplasm.

He had no signs or symptoms until his physician noticed a hard lump with skin retraction on his left nipple.

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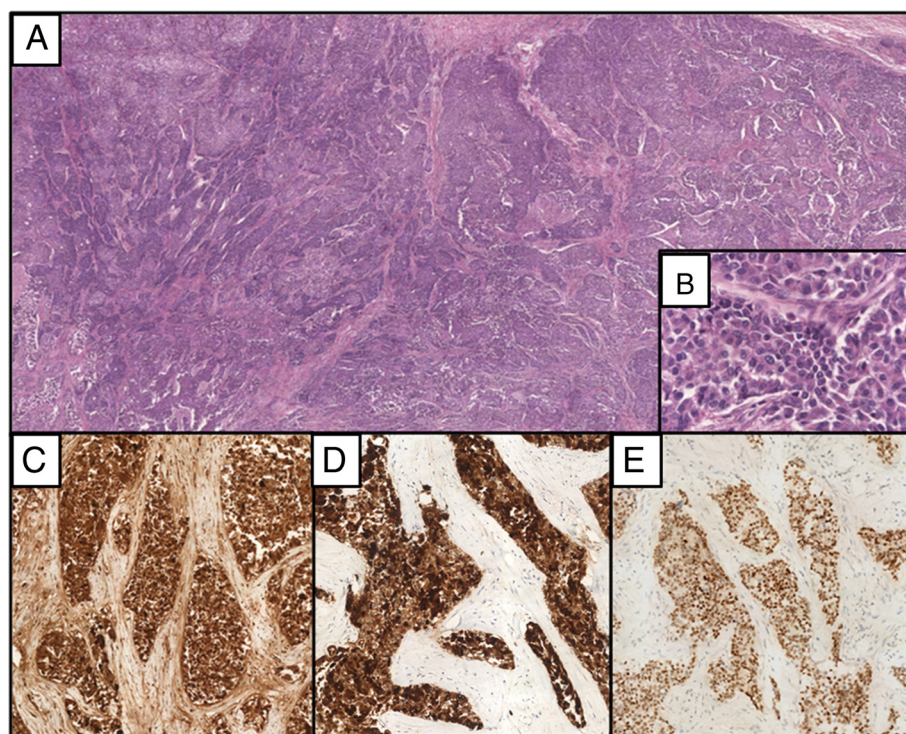


Figure 1 Malignant breast neoplasia. (A) Low-power photomicrograph breast epithelial proliferation mainly organized in solid nests and cords, with occasional pseudoglandular aspects (magnification 4x); (B) High-power photomicrograph showing epithelial cells of medium-great size, with altered nucleus-cytoplasm ratio, leptocromatinic nucleus, nucleolus often prominent and large eosinophilic cytoplasm (magnification 40x); the cell showed immunoreactivity for GCDP-15 (C), CK7 (D) and ER (E) (magnification 40x).

66 The patient also had an erythematous nodular skin lesion developing on his forehead. For these lesions, the
67 patient underwent left modified radical mastectomy (based on the Madden technique) with axillary lymph
68 node dissection. Histopathological examination revealed
69 an infiltrating ductal carcinoma (grade III, score 8
70 according to Nottingham) with metastasis to one of the
71 11 axillary lymph nodes examined. Approximately 90%
72 of the neoplastic cells stained positive with antibody to
73 the oestrogen receptor, and 20% stained positive with
74 antibody to the progesterone receptor. The proliferative
75 index using a Ki-67 monoclonal antibody was 10%.
76
77
F1 78 HER-2/neu was not over-expressed (Figure 1). The
79 nodular skin lesion was completely resected, and histo-
80 pathological examination revealed it to be a SCC (grade
F2 81 II), infiltrating the hypodermis (Figure 2). Immediately
82 after these surgical procedures, the patient was hospitalised
83 in our institution where a cystoscopy was performed con-
84 firming ultrasound findings of multiple bladder papillary le-
85 sions arising from the posterior-lateral left wall, with a large
86 base plant and active bleeding. A trans-urethral resection of
87 the bladder lesion (TURB) was performed at the same time
88 in which the neoplasm was completely excised. Subsequent
89 histopathological examination showed a grade 3 papillary

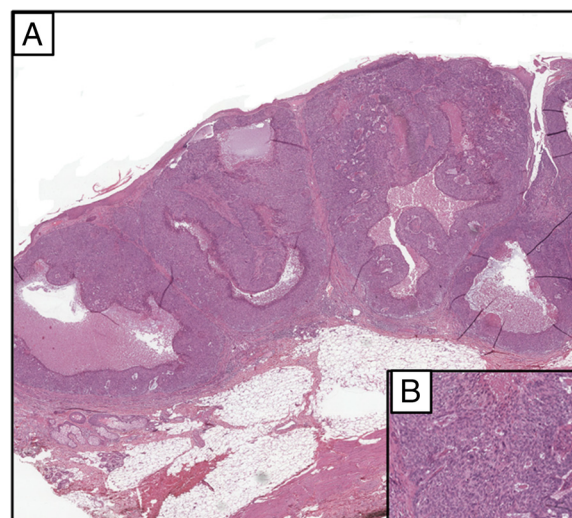


Figure 2 Skin epithelial neoplasia. (A) Low-power photomicrograph hypodermis infiltration, consisting of squamous cells arranged in solid nests and cords, with large areas of necrosis (magnification 4x); (B) High-power photomicrograph showing neoplastic cells characterized by moderately polymorphic nucleus, sometimes with evident nucleolus, large eosinophilic cytoplasm with ill-defined limits (magnification 40x).

90 TCC that was in the process of infiltrating the muscular
91 bladder wall (T2). The neoplastic cells were positive for
92 cytokeratin 7 and negative for both cytokeratin 20
93 and Gross Cystic Disease Fluid Protein 15 (GCD-
F3 94 Figure 3). Although a bone scan failed to find any skel-
95 etal metastasis, a whole body computed tomography
96 (CT) scan revealed a diffuse thickening of the left blad-
97 der wall approximately 12.2 mm in diameter. This was
98 found to be hypervascularised and in contact with the
99 left vesicoureteral junction with minimal local infiltra-
100 tion of the perivesical area. There was also adenopathy in
101 four retroperitoneal lymph nodes and concomitant left
102 moderate hydronephrosis. Therefore, the patient
103 underwent total cystoprostatectomy with pelvic lymphade-
104 nectomy and a continent ileal urinary diversion. In consid-
105 eration of the patient's age and overall physical condition,
106 an orthotopic bladder replacement (neobladder recon-
107 struction) using the Paduan technique was chosen.
108 After surgery, the patient received adjuvant therapy
109 (gemcitabine and cisplatin) for bladder and breast can-
110 cer, which were considered the most important prognos-
111 tic factors among the three neoplasms. He is currently
112 receiving adjuvant chemotherapy, including gemcitabine
113 and cisplatin.

Discussion

114 In case of synchronous MPCs, it is important to consider
115 the stages of the different neoplasms, their likely biological
116 behaviour, and the patient's age, life expectancy, and co-
117 morbidities as all of these can affect the treatment strat-
118 egies and prognosis. The case we describe here met the
119 criteria of Warren and Gates [6], namely that each neo-
120 plasm must be a distinct malignancy and not a metastasis
121 of the other. In this patient, three primary and histologi-
122 cally distinct cancers were found in three different organs,
123 that is, primary TCC of the urinary bladder, SCC of the
124 skin on the forehead, and infiltrating ductal carcinoma of
125 the breast, all within a 2-month period. All these cancers
126 were considered primary neoplasms; thus, a diagnosis of
127 synchronous triple primary cancer was made. Synchron-
128 ous neoplasms are defined as ≥ 2 primary neoplasms diag-
129 nosed within 6 months of each other, while metachronous
130 neoplasms are defined as those detected after an interval
131 of >6 months [5]. A patient with a history of cancer may
132 have an increased risk of developing another neoplasm
133 due to exposure to common carcinogenic factors, such as
134 tobacco and alcohol, or genetic predisposition (for example,
135 Li-Fraumeni or Beckwith-Wiedemann syndrome), or as a
136 side-effect of previous chemotherapy or radiotherapy [8]. In
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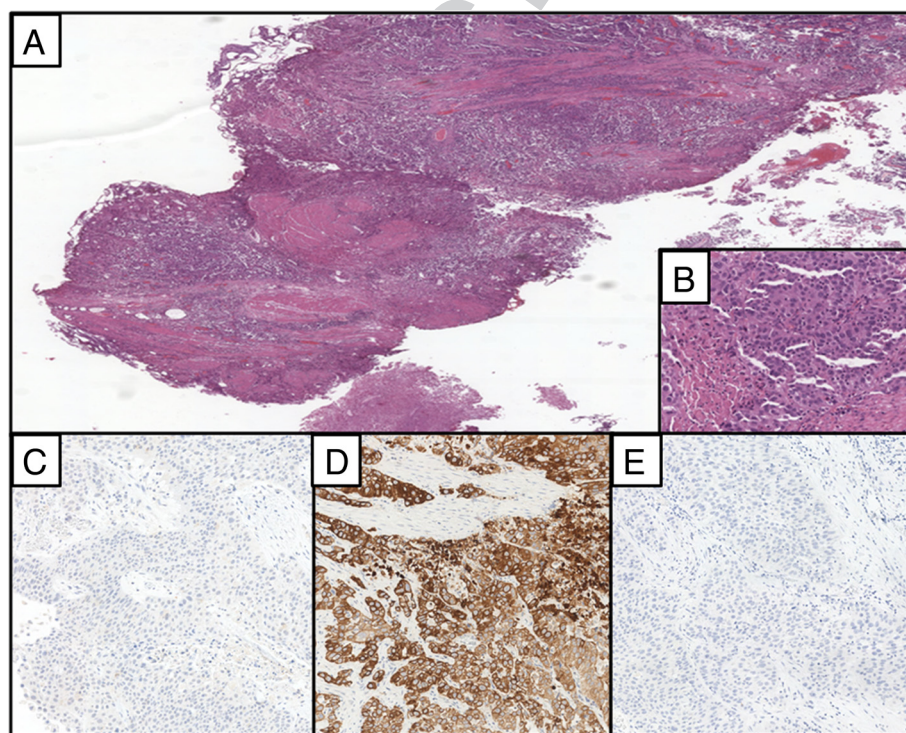


Figure 3 Bladder cancer. (A) Low-power photomicrograph showing malignant bladder epithelial proliferation organized in papillary structures, nests, sometimes with central necrosis, solid and cords that diffusely infiltrate subepithelial corium and the muscularis (magnification 4x); (B) High-power photomicrograph showing epithelial cells of medium-great size, with altered nucleus-cytoplasm ratio, leptocromatinic nucleus, nucleolus often prominent and large eosinophilic cytoplasm (magnification 40x); the cells resulted negative to immunohistochemical staining for GCD-15 (C), positive for CK7 (D) and negative per CK20 (E) (magnification 40x).

the current case, three likely causal factors were that the patient was a heavy, chronic smoker, that he had been exposed to chemicals, especially those in pesticides, and that he had experienced prolonged exposure to ultraviolet radiation from working outside. Gallagher et al. suggested that prior exposure to insecticides, herbicides, and fungicides or seed treatments are associated with an increased incidence of SCC of the skin [9]. No other predisposing factor or a family history was found that might have contributed to the development of these three neoplasms.

To our knowledge, this is the first reported case in the literature reporting this combination of primary neoplasms, although Pastore et al. previously described a case of synchronous ureteral and bladder metastases arising from infiltrating ductal breast carcinoma in an elderly woman [10]. We suggest that the onset of multiple primary neoplasms are the result of a combination of different factors, including improved cancer survival rates increasing the length of time over which additional cancers can develop [5].

Conclusions

The incidence of MPC is probably influenced by a combination of environmental and genetic factors, and the prognosis for a patient with multiple malignancies is most probably determined by whichever neoplasm is the most aggressive. To the best of our knowledge, this is the first case in the literature to report distinct bladder, breast and skin primary neoplasms in the same patient.

Consent

Written informed consent was obtained from the patient for publication of the case report and any accompanying images. A copy of written consent is available for review by the Editor-in-Chief of this journal.

Abbreviations

CT: Computed tomography; MPC: Multiple primary cancers; SCC: Squamous cell carcinoma; TCC: Transitional cell carcinoma; TURB: Transurethral resection of bladder.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

ALP, GP, AL, LS, AD, KS, AR, CM, NP, DM and AF were involved in the review of literature, acquisition of data and drafting and completing the manuscript. AC, CDR, VP and CDC conceived the study, participated in the co-ordination and the acquisition of data, and helped to draft the manuscript. All authors read and approved the final version of the manuscript.

Acknowledgements

The authors declare that this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors have no conflicts of interest to disclose.

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Received: 23 April 2013 Accepted: 30 September 2013
Published: 20 October 2013

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doi:10.1186/1477-7819-11-282

Cite this article as: Pastore et al.: Synchronous primary neoplasms of the bladder, skin and breast in a male patient: a case report. *World Journal of Surgical Oncology* 2013 **11**:282.

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