Case reports

Quadruple primary neoplasms of the skin, colon, kidney and chronic lymphatic leukemia: a case report.

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ABSTRACT

Multiple primary neoplasms of different systems represent rare and clinically important entities. We present the 75-year old male patient in whom synchronous colon, renal and lymphatic malignancies (chronic lymphatic leukemia) were incidentally diagnosed 22 years after surgery for facial basal cellular skin cancer and 15 years after left lobectomy for follicular adenoma of the thyroid. Patient was admitted for the treatment of pneumonia. Incidentally, severe leukocytosis was found that persisted to treatment. Bone marrow biopsy showed chronic lymphatic leukemia. Due to microcytic anemia, colonoscopy was performed that revealed tumor in the ascending colon involving two thirds of the lumen. Subsequent abdominal imaging (ultrasound and CT) demonstrated large (7.7 cm) kidney neoplasm. Right hemicolectomy and left nephrectomy were performed. This represents the unique presentation of four primary neoplasms, underlying the need for more intensive use of screening methods in patients with previous malignancies.

KEY WORDS: colorectal neoplasms; renal neoplasms; chronic lymphatic leukemia; skin basal cell carcinoma

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INTRODUCTION

Quadruple carcinomas have been reported in about 0.007% of autopsies (1) and are more common in older patients (2). Individual grouping of neoplasms often occurs within a defined spectrum of malignancies (2). With increased survival rates, timely detection of other, synchronous or metachronous neoplasms is becoming more important, emphasizing the importance of screening protocols. We present herein a unique case of synchronous occurrence of three primary neoplasms: colon and renal cancers and chronic lymphatic leukemia, in a patient who had previous surgery for facial basal cell carcinoma. To our best knowledge, this combination of primary neoplasms has not yet been described.

CASE REPORT

A 75-year old white male was admitted to the hospital due to bronchopneumonia. Patient's medical history revealed surgery for facial basal cell skin cancer in 1980, and left lobectomy for thyroid follicular adenoma in 1987.

On admission, patient was dispnoic, with enlarged cervical lymphatic nodes (behind the sternocleidomastoid muscles on both sides).

Blood analysis showed severe leukocytosis, with white blood cell count of 45.8x109/L. Differential peripheral white cell blood count demonstrated prominent lymphocytosis with over 85% of B lymphocytes.

Bone marrow cytology demonstrated rich aspirate with particles. Microscopically, marked hypercellularity was seen, with predominant small lymphatic cells. Erythropoiesis was reduced, and

thrombocytopoiesis was mature. No foreign cells were found. The finding was consistent with the diagnosis of chronic lymphatic leukemia.

Due to microcytic anemia, gastrointestinal tract was examined. Upper endoscopy showed gastric polyp at the greater curvature, with edematous and erythematous gastric mucosa. Digital rectal examination was normal, and colonoscopy revealed an expansive neoplastic process in the ascending colon, involving two-thirds of the circumference, with two adjacent small polyps, sigmoidal diverticulosis and two polyps in the rectum (0.5 and 1 cm in diameter). Both rectal polyps were removed endoscopically (they proved to be tubulovillous adenomas with grade I/II epithelial dysplasia).

Subsequently, abdominal ultrasound and CT scan were performed, revealing renal mass in the left kidney, measuring 77 mm in diameter. No other significant pathology was found.

Simultaneous right hemicolectomy, with central lymphadenectomy and termino-terminal ileotransverse anastomosis (hand sawn, one layer running suture), and left nephrectomy was performed.

Histological examination showed an exophytic tumor of the ascending colon measuring 6 cm in diameter. Tumor was found to be well differentiated and infiltrated the muscular layer of the colonic wall, without the penetration through the serosa. Fourteen lymph nodes were harvested, the largest measuring 1 cm in diameter, with no lymphatic metastases (T2N0, Astler-Coller B1, Dukes A).

Renal cancer was a 9-cm, yellow and partially necrotic tumor, without the involvement of either renal vein or ureter. Histologically, tumor was made up of epithelial cells with light, partially eosinophilic cytoplasm. The finding was consistent with the diagnosis of renal adenocarcinoma (T2N0, G2). No cancer was diagnosed in first line relatives.

DISCUSSION

We presented a patient who developed a quadruple carcinoma, three of which were diagnosed synchronously, 22 years after the resection of the first cancer (basal cell skin cancer). Such association of primary neoplasms has not yet been described.

Familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC) are often associated with other neoplasms (3). However, the patient presented in this paper did not satisfy the Amsterdam criteria (4) for either hereditary form of colorectal cancer or FAP.

Higher incidence of other neoplasms, both colorectal and extra-colonic, was reported in patients with microsatellite instability (MSI) (5, 6). Germline mutations of the mismatch repair (MMR) system are characteristically associated with HNPCC, but they can also be found in 10-14% of patients with sporadic colorectal cancer (7).

It has been shown that in patients with non-melanoma skin cancer there is increased incidence of non-Hodgkin's lymphoma (8). Previous non-melanoma skin cancer has recently been implicated as a marker of worse prognosis for patients with non-Hodgkin's lymphoma (NHL) and chronic lymphatic leukemia (CLL), and to a certain extend for patients with colon cancer. Both basal cell and squamous cell cancer significantly increased mortality of patients with subsequent diagnosis of NHL/CLL, and the effect was most evident if skin cancer preceded lymphatic malignancy less than 1 year. For patients with colon cancer, only previous squamous cell cancer significantly affected survival (9). Mortality was significantly increased for patients with non-Hodgkin's lymphoma or chronic lymphatic leukemia who were under 80 years of age at the time the diagnosis of NHL/CLL was established (9).

According to medical history, immune incompetence is unlikely the common ground for the development of skin cancer and CLL in the presented patient, and immune incompetence is more often associated with squamous cell cancer (10). Chronic lymphatic leukemia (CLL), unlike other types of leukemia, is not associated with the exposure to environmental carcinogens (radiation, alkylating agents etc.) (11). Also, hypothetical incipient CLL is unlikely the trigger for the skin cancer, since the patient underwent left thyroid lobectomy for follicular adenoma seven years after the surgery for basal cell cancer, and no signs of CLL were apparent at that time.

Renal cancer has recently been reported to develop simultaneously with colorectal cancer in about 3.8% of patients (12, 13). Such a high incidence of these two primary neoplasms, as compared to much lower incidences reported earlier (0.05%)(14), has been attributed to the widespread use of imaging techniques (12, 14). In their study, Nishikubo et al. reported that the incidence of primary renal cell cancer and lymphoid malignancies was increased compared to the incidence that would be expected by chance alone (15), differently from findings reported in other large cohort studies (16). Possible explanations are again genetic alterations, or immunologic disorders. One possible

immunomodulatory factor may be interleukin 6, that was found to be excessively produced by renal carcinoma cell, and enhanced the proliferation of multiple myeloma in vitro (17).

To our best knowledge, there have been no previous published reports of patients with quadruple carcinoma of the skin, kidney, colon and chronic lymphatic leukemia. This is even more important since the presented patient did not satisfy the criteria for hereditary non-polyposis colorectal cancer (non-compliance with Amsterdam criteria).

With extensive use of diagnostic procedures, and the successful prolongation of life in patients with some malignancies, the incidence of synchronous multiple neoplasms is likely to increase. This may warrant prolonged follow-up and more intensive use of screening methods in patients with previous malignancies. Even simple screening methods (complete blood count and occult fecal blood test) may be of great value, as in the presented case. For this reason, it is important to observe other associations of neoplasms, beside the ones already defined which will undoubtedly aid the definition of screening protocols, including DNA microarray testing.

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