**Primary combined carcinoid and adenocarcinoma of the ileum associated with transitional carcinoma of the bladder.**

Single case report


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RESUMEN

Las neoplasias compuestas, el carcinoide y el adenocarcinoma se ha observado que aparecen en varias partes del organismo, como el estómago, la ampolla de Vater, el intestino grueso, el pulmón y la vejiga urinaria.

Publicamos aquí el caso de un varón de 74 años con un tumor compuesto de tipo carcinoide-adenocarcinoma del íleon asociado a un carcinoma vesical de células transicionales. El examen macroscópico del tumor compuesto mostró una mezcla de tumor carcinoide típico y adenocarcinoma moderadamente diferenciado. Desde el punto de vista inmunohistoquímico, los dos componentes estaban claramente diferenciados.

Una revisión de la bibliografía reveló que este es el primer caso que se publica de un tumor compuesto de tipo carcinoide-adenocarcinoma del íleon asociado a un carcinoma de células transicionales de la vejiga urinaria.

Palabras clave: Carcinoide compuesto. Íleon. Véjiga urinaria.

INTRODUCTION

Lubarsch in 1888 first described the histology of carcinoid tumors (1) and the term carcinoid was proposed in 1907 by Oberndorfer (2) when described a submucosal tumor of the small intestine. Since then, carcinoid has been reported to develop in various organs, including gastrointestinal tract, liver, lung, breast, gall bladder, skin, trachea, parotid gland, and thymus (3).

It is well known that sometimes carcinoid tumor is sometimes associated with other tumors. Approximately 15% of carcinoid tumors of the small intestine are associated with non-carcinoid neoplasms, most frequently adenocarcinomas of the gastrointestinal tract (4). The concurrent occurrence of carcinoid and other tumors in various organs is extremely rare. Two morphological patterns for such a combination have been described: one showing an admixture of the two components (composite tumor), and the other showing independent tumors with-
out histologic transition or admixtures (collision tumor) (5). An association between a composite carcinoid and other carcinoids in the same organ has been reported once (6).

We describe a case of a composite carcinoid-adenocarcinoma of the ileum associated with a carcinoma of the urinary bladder. This is the first report of such an association.

CASE REPORT

A 74-year-old male was admitted to our hospital with a 3-month history of hematuria. Physical examination on admission revealed no particular abnormalities. No peripheral lymphadenopathy or hepatosplenomegaly was found. Hematological analysis were normal. There were no clinical features suggestive of a carcinoid syndrome, and as there was no clinical suspicion, biochemical tests for carcinoid syndrome were not performed. Because of the macroscopic haematuria an urine cytology examination was proposed, and findings were suggestive of high-grade transitional cell carcinoma (Fig. 1). Subsequently a cystoscopy was performed, and a huge tumor occupying the posterior wall of the bladder was found. Computed tomography of the abdomen revealed a large tumor of the bladder but no other abnormalities. A total cystectomy was performed. During the operation, while exploring the abdomen, a tumor with a maximum diameter of 2 cm was incidentally found in the terminal ileum, from which a biopsy sample was taken. The patient refused to have a second operation in order to remove the tumor of the ileum. At 28 months after the operation there is no radiographically-demonstrated metastasis, and the patient is in good condition.

Pathological findings

The specimens consisted of an indurated bladder with the perivesical fat, and the biopsy material from the ileum. Upon opening the bladder there was a protuberant tumor occupying the posterior wall. On the cut sections the tumor was soft, gray-white, and measured 11 x 7 x 3.8 cm. A microscopic examination of the tumor showed a papillary transitional cell carcinoma, grade II. There was no infiltration of the lamina propria and the muscularis propria.

The biopsy material taken from the tumor at the terminal ileum had a maximum diameter of 1.4 cm. It consisted of two intimately intermingled components, i.e., carcinoid and adenocarcinoma. The carcinoid component was prominent and represented by typical mixed insular-acinar structures. Nuclei were round to oval, and the cytoplasm was moderate, eosinophilic, and finely granular. Mitoses were scanty. The adenocarcinoma component was represented by glands, which were diffusely scattered among the endocrine cell structures (Fig. 2). Immunohistochemical studies were carried out for EMA (Fig. 3), chromogranin (Fig. 4), CEA, CA19-9, and NSE. The carcinoid component was positive for chromogranin and NSE, and negative for EMA, CEA and CA19-9. The adenocarcinoma component was positive for EMA, CEA and CA19-9, and negative for chromogranin and NSE. Accordingly, a diagnosis of composite carcinoid-adenocarcinoma of the ileum associated with transitional cell carcinoma of the bladder was made.

DISCUSSION

The association of endocrine and nonendocrine cells in tumors of the gastrointestinal tract is well known (7,8). This association may be expressed by different patterns, including: a) dispersed endocrine cells in an ordinary car-
cinoma (9); b) well-defined mixed-cell carcinomas such as the goblet cell carcinoid or adenocarcinoid (10); c) independent tumors each with pure endocrine or carcinomatous components (collision tumors) (11-13); and d) composite tumors with an admixture of both carcinoid and adenocarcinoma (14-18). The latter group includes the composite tumor in our case.

An immunohistochemical examination highlighted the differences between the endocrine and adenocarcinomatous structures of the tumor. Neuroendocrine markers such as chromogranin and NSE were diffusely and heavily restricted to carcinoid cells, whereas nonendocrine markers such as EMA, CEA, and CA19-9 were expressed exclusively in nonendocrine glands.

Although the exact histogenesis of mixed tumors is unknown, it is believed that these arise from undifferentiated basal stem cells (19) or common totipotential precursor cells (20). Some case reports support the view that there is a simultaneous proliferation of different cell lines (5). Ali et al. (21) reported a composite gastric carcinoid and adenocarcinoma, and provided strong evidence for the common, endodermal derivation of mucus-secreting and endocrine cells in a gastric neoplasm. A common histogenesis for both adenocarcinoma and carcinoid structures has also been suggested from metaplastic intestinal epithelium, which would render the designation of composite tumor appropriate (6).

The question of whether composite carcinoid-adenocarcinoma tumors are more aggressive than common adenocarcinoma is currently debated. In general, carcinoids have a relatively benign clinical course. In a few reported cases carcinoid tumors become less favorable when they are admixed with adenocarcinomas (17, 22). In our case the clinical behavior of the tumor was not so aggressive. Although no total resection was made, the patient is in a good condition at 18 months after the operation, without evidence of metastasis both clinically and radiologically.

Due to the small number of tumors reported as composite carcinoid-carcinoma there is a need for a larger number of similar cases, as well as for long-term follow-up, to determine their natural history and prognostic significance. To our knowledge, our case constitutes the first report of a composite carcinoid-adenocarcinoma of the ileum associated with a carcinoma of the urinary bladder.

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