Int J Colorectal Dis (2016) 31:1561–1563
DOI 10.1007/s00384-016-2566-x

LETTER TO THE EDITOR

Carcinoid syndrome produced by an isolated metastase in femoral nerve from a midgut carcinoid tumor

AC. Rahy-Martín[1,2] · S. González-García[1] · V. Medina-Arana[1] · H. Álvarez-Argüelles[3] · H. Roldán-Delgado[4] · A. Martínez-Riera[5] · JL. Carrasco-Juan[6] · M. E. Castro-Peraza[7] · A. Bravo-Gutiérrez[1] · A. Alarcó-Hernández[1]

Accepted: 21 March 2016 / Published online: 30 March 2016

Dear Editor:

Carcinoid tumors are slow-growing neoplasms derived from enterochromaffin cells or Kulchintsky cells being thus neuroendocrine in nature. They may arise anywhere in the gastrointestinal tract, in the bronchi, and occasionally elsewhere (ovary, central nervous system). Within the gastrointestinal tract, most carcinoid tumors arise in the small intestine (45 %, most commonly in the ileum), followed by rectum (20 %), appendix (16 %), colon (11 %), and stomach (7 %).

Carcinoid syndrome is the term applied to a set of symptoms mediated by different humoral factors elaborated by some carcinoid tumors (diarrhea, cutaneous flushing, cardiac valvular lesions, bronchospasm, and intermittent abdominal pain). These tumors synthesize, store, and release a variety of polypeptides, biogenic amines, and prostaglandins. Some of these tumor products are responsible for the carcinoid syndrome. The relative contribution and the specificity of each of the particular components of the syndrome are uncertain. It seems that among patients with intestinal carcinoid tumors, the carcinoid syndrome does not occur in the absence of liver metastases. In contrast, bronchial and other extraintestinal carcinoids, whose bioactive products are not immediately cleared by the liver, can rarely cause the syndrome in the absence of metastatic disease.

Metastases of carcinoid tumors in peripheral nerve are extremely rare. All of them come from supradiaphragmatic

✉ AC. Rahy-Martín
aidarahy@hotmail.com

S. González-García
saragg_2000@hotmail.com

V. Medina-Arana
dnamedina@hotmail.com

H. Álvarez-Argüelles
hargue@ull.es

H. Roldán-Delgado
hecroldan@hotmail.com

A. Martínez-Riera
tonimriera@gmail.com

JL. Carrasco-Juan
jcarraju@ull.es

M. E. Castro-Peraza
mcperaza@terra.es

A. Bravo-Gutiérrez
afbravo2000@hotmail.com

A. Alarcó-Hernández
cirgediges-a@huc.canarias.org

[1] General Surgery Department, Complejo Hospitalario Universitario de Canarias and University of La Laguna, Santa Cruz de Tenerife, Spain

[2] General Surgery Department, Hospital Universitario de Gran Canaria Dr Negrín, Las Palmas de Gran Canaria, Spain

[3] Pathological Department, Complejo Hospitalario Universitario de Canarias and University of La Laguna, Santa Cruz de Tenerife, Spain

[4] Neurosurgery Department, Complejo Hospitalario Universitario de Canarias and University of La Laguna, Santa Cruz de Tenerife, Spain

[5] Internal Medicine Department, Complejo Hospitalario Universitario de Canarias and University of La Laguna, Santa Cruz de Tenerife, Spain

[6] Histological Department, Complejo Hospitalario Universitario de Canarias and University of La Laguna, Santa Cruz de Tenerife, Spain

[7] Operating Room Department, Complejo Hospitalario Universitario de Canarias and University of La Laguna, Santa Cruz de Tenerife, Spain

tumors (mediastinal and bronchogenic). We report the first case of metastase in peripheral nerve from a midgut carcinoid tumor, associated with carcinoid syndrome but in the absence of liver metastases.

Case report

A 71-year-old female was referred to our hospital with dyspnea, leg edema, left hypochondrium pain, liquid diarrhea, and constitutional syndrome 6 weeks long. Physical examination revelead severe malnutrition, bilateral pleural effusion, hepatomegaly, and leg and sacral edema (anasarca). She had normal temperature and blood pressure of 90/60 mmHg. Subsequent blood serum evaluation revealed a severe hypoproteinemia and hypoalbuminemia.

Thoracic radiography showed bilateral pleural effusion and echocardiography revealed a pericardium effusion. Abdominal computed tomography (CT) determined a swelled end-ileum and a homogeneus right retroperitoneal mass, measuring 50 × 22 mm, causing displacement of the right psoas. There were no visible hepatic metastases. Colonoscopy revealed a solid ileal tumor, and its histological examination showed a carcinoid tumor.

She underwent a segmental resection of right colon and end-ileum, along with the retroperitoneal mass described on CT. Intraoperative electrophysiological studies showed that the mass depended on femoral nerve. This lesion was resected and a termino-terminal nerve anastomosis was performed.

Macroscopically, in the ileum, there was a yellow nodular lesion of 1.9 × 1.8 cm next to the ileo-caecal valve and affecting all intestinal parietal layers. Microscopy study revealed a large ileal carcinoid tumor with metastasis to regional lymph nodes. The tumor was presented as infiltrating nests and cords of atypical monotonous cells with eosinophilic cytoplasm and rounded nuclei, while mitosis were scant. The metastasis in the femoral nerve was a firm browny-yellowish nodule of 3.4 × 2.6 cm with necrotic areas and whose surgical margins were negative for tumor. Histological examination of the metastasis revealed a tumoral proliferation composed of infiltrating cords and nests of cells that were morphologically similar to the primary carcinoid tumor. There was intraneural invasion (including the perineurium and endoneurium) as well as extensive epineural involvement. The immunohistochemical study performed with the peroxidase-antiperoxidase (PAP) technique on embedded sections of intestinal tumor in paraffin and dyaminobenzidine (DMB) chromogen as counter-stain showed positive immunostaining for epithelial (cytokeratin) and neuroendocrine (neuronspecific enolase, chromogranine A, and synaptophysin) markers, and the metastasis exhibited similar microscopic and immunohistochemical features to the ileal tumor. The positivity for neurofilaments and protein S-100 markers confirmed the tumoral intraneural involvement of femoral nerve.

She developed liver metastases 3 years after the initial diagnosis, which were treated with right hepatectomy.

Currently, the patient has a left psoas recurrence, diagnosed 4 years after the initial diagnosis and treated with somatostatin analogs. She has a stable disease 9 years after the first resection. She is still undergoing rehabilitation treatment, with great improvements in her functional capability, maintaining a slight paralysis in her right leg.

Discussion

At least, there have been identified 40 vasoactive substances as products of carcinoid tumors. These include serotonin, histamine, tachykinins, kallikrein, and prostaglandins. The biologically active substance most commonly found is serotonin, which releasing into the systemic circulation causes symptoms called carcinoid syndrome, characterized primarily by diarrhea, flushing, pulmonary hypertension, bronchoconstriction, and wheezing, as well as intermittent abdominal pain. These symptoms lead us to believe that the mediator in this case is the serotonin.

The presence of carcinoid syndrome occurs in only 10 % of patients with small bowel disease. This is because the liver inactivates the bioactive substances produced by carcinoid tumors, so that patients with tumors of the gastrointestinal tract develop carcinoid syndrome only if hepatic metastases exists, result of the secretion of tumor products in suprahepatic veins and therefore to the systemic circulation, escaping hepatic inactivation.

Exceptionally, in the case of previous liver disease, cirrhosis, for example, or in those cases in which the tumor production of vasoactive substances is so high that the liver is unable to fully metabolize them, carcinoid syndrome may occur in the absence of liver metastases. It also can be found in cases of primary carcinoid tumors of extraintestinal origin, mainly bronchial, which secrete their products directly to the systemic circulation. Our case had the appearance of a carcinoid syndrome secondary to an ileal primary tumor in the absence of liver metastases confirmed by CT scan and hepatic scintigraphy octeotride. The origin of vasoactive substances was necessarily a metastasis in peripheral nerve (femoral nerve) whose vessels drain into the systemic circulation via the femoral vein whose anatomical situation follows the nerve.

It is not often the appearance of nervous system metastases from carcinoid tumors, where central nervous system is the main organ affected. There are very few cases of metastatic carcinoid tumors in peripheral nerve. Furthermore, there have been referred only six cases in the literature. All of those six cases are supradiaphragmatic tumors (mediastinal and bronchogenic), none of them originated from a carcinoid tumor of

small bowel. A comprehensive review of the literature has allowed us to identify no one of intestinal origin. Therefore, we believe that the case described here is the first of an ileal carcinoid tumor presented metastases at diagnosis in peripheral nerve.

Conclusions

In the present case, we report a double singularity: firstly, the presentation of a metastasis in the right femoral nerve of an ileal carcinoid, fact that is not described in previous studies, and secondly, the appearance of a carcinoid tumor syndrome in an ileal tumor in absence of liver metastases. Although midgut carcinoid tumors, including ileal tumors, most often lead to liver, lung, and bone metastases, which can cause carcinoid syndrome, our case shows that there are other rare possibilities in the spread of tumor (contiguity, perineural spread, or rarely, by direct infiltration). This can lead to metastases that escape hepatic inactivation and therefore may produce a clinically apparent carcinoid syndrome.