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Non-Hodgkin lymphoma involving stomach and ovary: extending the Krukenberg tumor concept

Constantinos Christopoulos · Marina Skopeliti ·
Evangelos Rotas · Anastasios Mavridis · Sotiria Savva ·
Efsthios Papavassiliou

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Dear Editor,

Krukenberg tumors are carcinomas metastatic to the ovaries with the primary site located in the gastrointestinal tract, usually the stomach. We present the first case of extranodal lymphoma involving exclusively the stomach and right ovary, thus mimicking a Krukenberg tumor.

A 61-year-old woman was admitted following a fainting episode associated with passing dark red blood per rectum. There was no relevant past medical or family history and she denied B symptoms. She was only taking atorvastatin for hyperlipidemia. On physical examination, a firm, painless mass was palpated in the hypogastrium. Laboratory investigations were remarkable for iron deficiency anemia (Hb 9.5 g/dl) and a raised serum lactic dehydrogenase level of 745 IU/l (reference range 230–450 IU/l). Upper gastrointestinal tract endoscopy revealed a gastric tumor with a large central ulceration (Fig. 1, top left) near the lowermost part of the greater curvature. Colonoscopy showed diverticula in the sigmoid and small adenomatous polyps in the transverse colon. Computerized tomographic (Fig. 1, top right) and ultrasound scans of the abdomen

confirmed the presence of a pelvic tumor measuring 9.5 × 11 cm. At exploratory laparotomy, the tumor was shown to arise from the right ovary. There was no associated pelvic lymphadenopathy. Histological examination of endoscopic and open biopsy samples from the gastric and pelvic tumors, respectively, showed diffuse infiltration by large-cell non-Hodgkin lymphoma (Fig. 1, bottom left). On immunocytochemistry, the neoplastic cells were positive for CD20 (Fig. 1, bottom right) and BCL-2, frequently positive for MUM1, occasionally positive for BCL-6, negative for CD1, CD3, CD5, CD10, and CD23, and showed lambda light chain monoclonality. Proliferation index was high, with 80% MKI67 positivity. No lymphoepithelial lesions could be seen on staining with the anticytokeratin antibody CAM5.2. Search for *Helicobacter pylori* in the gastric biopsies (Giemsa stain) was negative. Staging investigations did not detect any lymphadenopathy, and there was no bone marrow or other organ involvement. The diagnosis of diffuse large B cell lymphoma (WHO classification) stage IV_E (Ann Arbor classification) was made.

To our knowledge, there are no previous reports of lymphoma presenting with synchronous involvement of stomach and ovary, in the absence of other sites of disease. The gastro-ovarian axis is a well-known route of selective tumor spread in cases of gastric adenocarcinoma. Frederick Krukenberg, in 1896, described what he believed to be a peculiar primary ovarian tumor consisting of signet-ring carcinoma cells, mixed with elements resembling fibrosarcoma [1]. In the years following Krukenberg's original report, it became clear that these tumors are in fact adenocarcinomas involving one or both ovaries, and are almost invariably secondary to carcinomas of the stomach or intestines [2]. The ovarian tumor may become clinically manifest before the gastric primary, which often escapes diagnosis due to its small size [3, 4]. The mode of tumor

C. Christopoulos (✉) · M. Skopeliti · E. Rotas · A. Mavridis
First Department of Internal Medicine,
“Amalia Fleming” General Hospital,
Melissia,
Athens 15127, Greece
e-mail: cgchrist@otenet.gr

S. Savva
Department of Pathology,
“Amalia Fleming” General Hospital,
Athens, Greece

E. Papavassiliou
Department of Gastroenterology,
“Amalia Fleming” General Hospital,
Athens, Greece

Fig. 1 Lymphoma involving stomach and ovary. *Top left:* Gastroscopic aspect of ulcerated tumor. *Top right:* CT appearance of heterogeneous soft-tissue density mass within the pelvis. *Bottom left:* diffuse infiltration of gastric mucosa by large-cell lymphoma (Giemsa stain). *Bottom right:* the neoplastic cell population is uniformly positive for CD20 (immunohistochemical stain employing the peroxidase–anti-peroxidase technique)



spread from stomach to ovaries without involvement of other tissues has intrigued pathologists for a long time. Although the exact mechanism remains unknown, several lines of evidence support the concept of retrograde lymphatic spread of neoplastic cells that invade the rich lymphatic plexus of the gastric mucosa and submucosa [5].

In view of the relative rarity of extranodal lymphomas, it is statistically improbable that the morphologically and immunophenotypically identical stomach and ovarian tumors of our patient developed synchronously and independently of each other. Given the fact that primary gastric lymphomas are much more common than ovarian ones, it is plausible to assume that the pelvic mass resulted from retrograde lymphatic spread of tumor from stomach to ovary, as is the case in classical Krukenberg tumors.

The case presented here suggests that the mechanism of Krukenberg tumor formation is not exclusive to adenocarcinoma. We therefore propose the use of the term “Krukenberg syndrome” to describe any metastatic ovarian neoplasm with the primary tumor located in the gastrointestinal tract. One can hypothesize that some of the “primary” ovarian lymphomas reported in the literature might in fact represent “Krukenberg” tumors, with an

occult true primary lymphoma located in the stomach or some other extranodal site. From a practical viewpoint, the finding of an apparently isolated ovarian lymphoma should prompt a thorough search for the presence of disease in the gastrointestinal tract, especially the stomach, which would lead to review of tumor stage, with obvious prognostic and therapeutic implications.

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