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Primary gastric squamous cell carcinoma with a bilio-gastric fistula and Krukenberg sydrome

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Abstract

Primary squamous cell carcinoma (PSCC) of the stomach is a rare type of gastric malignancies. Diagnosis crireria are well defined but diagnosis is generally late made at an advanced stage with metastases explaining it's poor diagnosis. We report a case of gastric PSCC with a bilio-gastric fistula and Krukenberg sydrome.

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Key Clinical Message :

Primary squamous cell carcinoma of the stomach is a rare type of gastric malignancies. Diagnosis crireria are well defined but diagnosis is generally late made at an advanced stage with metastases explaining it's poor diagnosis.

Keywords : Primary squamous cell carcinoma, stomach, fistula, ovarian metastases.

Introduction :

Stomach cancer is the fifth most common cancer worldwile. There are different histological types and adenocarcinoma is the most frequent one. It accounts for more than 90% of gastric malignancies. Primary gastric squamous cell carcinoma (PSCC) is rare, amounting to less than one percent of all gastric carcinomas (about 0.04% to 0.07%) [1]. It is more prevalent in the sixth decade of life with a male to female ratio of 5 to 1. [2]

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The first case of PSCC was described in 1905 [3]. Since then, less than 100 cases have been reported in the literature. The pathogenesis of this tumor is controvertial and many theories have been proposed. The treatment is also controversial and its prognosis is generally poor[4].

We report a case of gastric PSCC with a bilio-gastric fistula and Krukenberg sydrome in a women.

Case Presentation :

A 66-year-old woman, with no medical history*, consulted the emergency department for* dyspnea with a three month history of intermittent epigastric pain associated with weight loss. She also reported a prior episod of melena.

Physical examination reveals stable vital signs, pale conjonctiva and an epigastric 3 cm hard painful mass. The digital rectal examination didn't show any signs of bleeding. Cardiopulmonary examination was normal.

Laboratory findings revealed a biological inflammatory syndrome (WBC= 13 570 /mm3, CRP = 133 mg/ml), a normochromic normocytic anemia at 4,5g/dl. Carcinoembryonic antigen as well as CA19-9 levels were normal.

An upper gastrointestinal endoscopy was performed, showing a normal esophagus and fundus. In the prepyloric region, a tumor reducing the lumen was objectified. There was a pertuis which seems to correspond to a fistula. By crossing this pertuis, a large cavity with a necrotic bottom and a black brown stasis fluid, was noted. The duodenum was normal (Figure1). Biopsies of the tumor and the gastric mucosa was performed and pathological examination showed well differentiated keratinizing squamous cell carcinoma (Figure 2).

Computed tomography (CT) revealed a non-stenosing irregular circumferential thickening of the antropyloric region invading the segments IV and III of the liver by contiguity resulting on an heterogeneous mass measuring 71x60mm with visibility of the left intrahepatic bile ducts. Suspicious ganglia of the hepatic hilum, the gastrohepatic ligament and the greater omentum were identified. The CT also showed a right well limited ovarian mass measuring 37x29mm, strongly enhanced in the portal phase, suggesting an ovarian metastasis: Krukenberg sydnrome, as well as a thrombosis of the left renal vein and a subsegmental pulmonary embolism. No other metastasis were indidualized (Figure 3).

A bowel opacification was also performed showing a passage of the constat agent in the biliairy ducts, as well as a pneumobilia revealing a bilio-gastric fistula (Figure 4)

Extensive evaluation, including an ENT and gynecologic examination , revealed no other possible primary sites of involvement, confirming the primary squamous cell gastric carcinoma.

A palliative symptomatic treatment with tranfusion and analgesics was indicated since the operative risk of the patient was high (performance status=3, recidivism of anemia after transfusion and pulmonory embolism) and the late stage of the tumor.

Discussion :

Primary gastric squamous cell carcinoma amount to less than one percent of all gastric carcinomas (about 0.04% to 0.07%) [1]. It is more prevalent in the sixth decade of life with a male to female ratio of 5 to 1.

The first case of PSCC was described in 1905 [3]. Since then, less than 100 cases have been reported in the literature.

The diagnostic criteria of PSCC of the stomach were defined by Parks : 1) tumor must not be occurring in the cardia; 2) tumor must not extend into the esophagus and 3) There should be no evidence of squamous cell carcinoma in any other organ, such as lung or cervix. [5] These criteria were met in our case report. Indeed, the tumor was antro-pyloric. There was no evidence of extending into the esophagus and no other possible primary sites of involvement was found.

Boswell and Helwig described 4 histopathologic criteria for diagnosis of PSCC, of which at least 1 must be present: (1) keratinized cell masses forming keratin pearls, (2) mosaic cell arrangement, (3) intercellular

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bridges, and (4) high concentration of sulfhydryl and/or disulfide groups, indicating the presence of keratin or prekeratin [2]

The Japanese had proposed an other classification for the diagnosis of PSCC of the stomach (1) All the tumor cells are squamous cell carcinoma cells and any part does not contain gland cancer cells, and (2) there is sufficient evidence to show that squamous cell carcinoma originates in the gastric mucosa [2]

Strong staining for p63 and high-molecular-weight cytokeratin (CK5/6) were associated with PSCC with a specificity of 99% and a sensitivity of 98%. Thus Immunohistochemistry can help the diagnosis [4].

The pathogenesis of this tumor is controvertial and many theories have been proposed : totipotent stem cells, metaplastic squamous focus, heterotopic squamous epithelium in the stomach, the overgrowth of a squamous epithelium element in a primary adenocarcinoma, Ebstein-barr virus or human papilloma virus. [6,7].

The diagnosis is always late, at an advanced stage. It was the case in our patient in whom the CT scan revealed a liver infiltration, as well as in the patients of Juan Antonio González-Sánchez et al [2] and Gil R Faria et al [8].

Other organs can also be envolved including the pancreas, the spleen and the left kidney in the case of Kehua Zhou et all [9], the head of the pancreas and the transverse mesocolon in the patient of Shengqiang Gao et al [1].

Liver metastases are frequently associated as reported by Kchaou et al [10] , Michael Beattie et al [11] and Kimura et al [13].

However, no cases of PSCC of the stomach with ovarian metastases have been reported in the literature.

In fact, secondary tumors of the ovary account for 10–25% of all ovarian malignancies . The most common primary sites are the gastrointestinal tract especially the stomach followed by the colon and the appendix, the breast and less frequently the gallbladder, the biliary tract, the pancreas, the small intestine, the ampulla of Vater, the cervix, and the urinary bladder. [13,14]

Krukenberg tumor (KT) is rare, most commonly in the stomach-ovarian axis and it's often defined as a metastatic signet ring cell adenocarcinoma of the ovary [14]. So, signet ring cells that produce mucin and the sarcomatoid proliferation of the stroma are the distinguishing features for the diagnosis of KT [13]. Thus ovarian metastases are always associated with adenocarcinoma, however some cases of squamous cell carcinoma have been reported [15].

In our case, the diagnosis of KT has been suggested on the findings of the CT scan but no histopathological evidence is available to confirm the presence of signet ring cells producing mucin.

As far as treatment is concerned, there is no clear recommendations for the management of Gastric PSCC. It's steal controvertial. Certainly, surgery remains the best option, since it represents the only radical treatment. Some cases of gastric PSCC have responded well to the combination of radiotherapy and chemotherapy with 5FU and Cisplatin. [10,16]

Gastric PSCC has poor prognosis as it is usually diagnosed at an advanced stage with local infiltartion and metastases to the liver, the lymph nodes, and other organs. [4] The overall survival rates range from 7 months to 8 years [16].

In our patient, the prognosis was very poor as the tumor was associated with liver infiltration, a bilio-gastric fistula, ovaian metastases and thromboembolic complications.

Conclusion :

Primary squamous cell carcinoma of the stomach is a rare entity. Although dignosis criteria are well defined. The pathogenesis and treatment remain controvertial. Further researchs are needed to standardize the management of this tumor, whose prognosis remain very pejorative.

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References :

1. Gao S, Chen D, Huang L, Dai R, Shan Y. Primary squamous cell carcinoma of the stomach: a case report and literature review. Int J Clin Exp Pathol. 2015;8(8):9667-71.

2. González-Sánchez JA, Vitón R, Collantes E, Rodríguez-Montes JA. Primary Squamous Cell Carcinoma of the Stomach. Clin Med Insights Oncol. 2017;11:1179554916686076.

3. Boswell JT, Helwig EB. Squamous cell carcinoma and adenoacanthoma of the stomach. A clinicopathologic study. Cancer. 1965;18(2):181-92.

4. Chen Y, Zhu H, Xu F, Cao Y, Gu X, Wan Y, et al. Clinicopathological Characteristics, Treatment, and Prognosis of 21 Patients with Primary Gastric Squamous Cell Carcinoma [Internet]. Vol. 2016, Gastroenterology Research and Practice. Hindawi; 2016 [cité 4 févr 2021]. p. e3062547. Disponible sur: https://www.hindawi.com/journals/grp/2016/3062547/

5. Parks RE. SQUAMOUS NEOPLASMS OF THE STOMACH. :3.

6. Chang YS, Kim MS, Kim DH, Park S, You JY, Han JK, et al. Primary Squamous Cell Carcinoma of the Remnant Stomach after Subtotal Gastrectomy. J Gastric Cancer. 2016;16(2):120-4.

7. Wu X-D, Zhou Y, Fan R-G, Zhou B, Shi Q, Jia J. Primary squamous cell carcinoma of the stomach presenting as a huge retroperitoneal tumor: a case report. Rev Esp Enfermedades Dig. 2016;108(5):283-4.

8. Faria GR, Eloy C, Preto JR, Costa EL, Almeida T, Barbosa J, et al. Primary gastric adenosquamous carcinoma in a Caucasian woman: a case report. J Med Case Reports. 2010;4:351.

9. Zhou K, Faraz A, Magotra M, Tahir M. Exophytic primary gastric squamous cell carcinoma and H. pylori gastritis. BMJ Case Rep. 2019;12(7).

10. Kchaou A, Ben Ameur H, Rejab H, Trigui A, Frikha F, Mzali R, et al. Carcinome épidermoïde de l'estomac : une entite rare. J Afr Hepato-Gastroenterologie. 2014;8(4):223-5.

11. Beattie M, Mansour R, Thigpin D, Haus C. Metastatic Primary Gastric Squamous Cell Carcinoma: An Uncommon Presentation of a Rare Malignancy [Internet]. Vol. 2019, Case Reports in Gastrointestinal Medicine. Hindawi; 2019 [cite 4 fevr 2021]. p. e5305023. Disponible sur: https://www.hindawi.com/journals/crigm/2019/5305023/

12. Y K, H M, H S, E O, M M, K S, et al. Case of early adenosquamous carcinoma of the stomach. Fukuoka Igaku Zasshi Hukuoka Acta Medica. 2013;104(9):315-20.

13. Lionetti R. Treatments and overall survival in patients with Krukenberg tumor. Arch Gynecol Obstet. :9.

14. Al-Agha OM, Nicastri AD. An in-depth look at Krukenberg tumor: an overview. Arch Pathol Lab Med. 2006;130(11):1725-30.

15. Ge HJ, Bi R, Cheng YF, Chang B, Yu L, Tang SX, et al. [Clinicopathologic analysis of primary carcinoid of the ovary]. Zhonghua Bing Li Xue Za Zhi. 2018;47(7):517-21.

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16. Bonnheim DC, Sarac OK, Fett W. Primary squamous cell carcinoma of the stomach. Am J Gastroenterol. 1985;80(2):91-4.

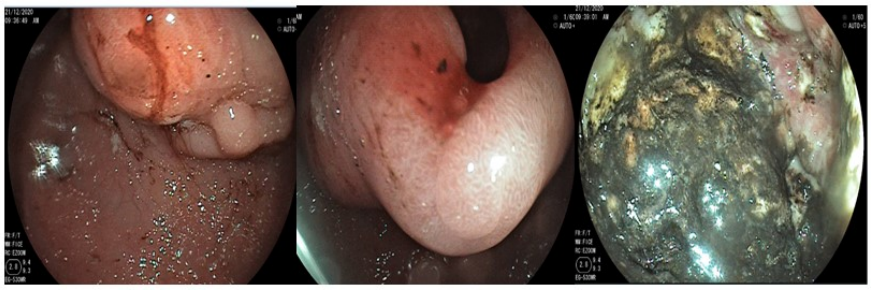
Figures

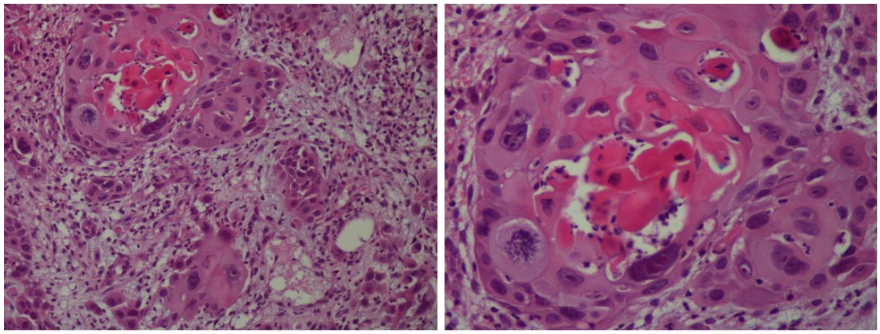
Figure 1 : Upper gastrointestinal endoscopy : A tumor reducing the lumen in the prepyloric region with a a pertuis (arrow) corresponding to a fistula conducting to a large cavity with a necrotic bottom and a black brown stasis fluid, bleeding easily (star).

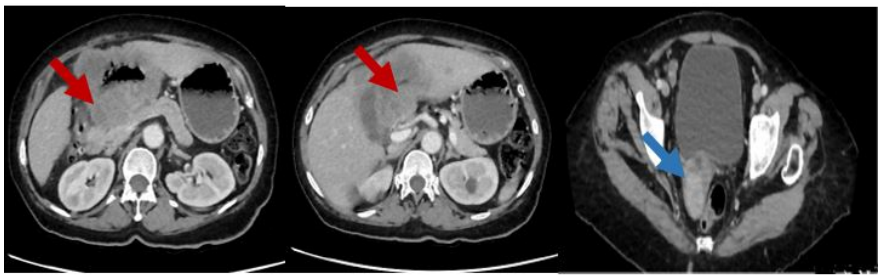
Figure 2 : Infiltrating carcinomatous proliferation made up of lobules and clusters of atypical squamous cells (Gx200) centered by keratin (black arrow) with mitoses (red arrow) (Gx400)

Figure 3 : CT images in longitudinal section showing a non-stenosing irregular circumferential thickening of the antropyloric region invading the liver (red arrows) and ovarian metastases (blue arrow)

Figure 4 : CT images in longitudinal section with opacification showing a passage of the constat agent in the biliairy ducts, as well as a pneumobilia revealing a bilio-gastric fistula (arrows)







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