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Uterine cervix gastric-type adenocarcinoma with finding of lymph node endosalpingiosis

Adenocarcinoma tipo gástrico do colo uterino com achado de endossalpingiose linfonodal

Caroline **LINK**[1], Ana Flávia **BOTELHO**[1], Janiceli Blanca Carlotto Hablich **SILVESTRE**[1], Mario Rodrigues **MONTEMOR-NETTO**[1]

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INTRODUCTION

It is believed that about 20 to 25% of invasive cervical neoplasms are of the endocervical adenocarcinoma type, with an increasing incidence over the years.[6] Gastric-type endocervical adenocarcinoma, a particularly aggressive subtype, was first described by Kojima15 in 2007, initially defined as a malignant neoplasm identified by the expression of gastric mucin and with a morphology analogous to the glandular epithelium of the pylorus. Due to its rarity, it was only in 2014 that this condition was recognized as a histological subtype of cervical cancer, being included in the World Health Organization Classification of Female Genital Tract Tumors (WHO 2014).[8]

Endosalpingiosis is a benign incidental finding of surgery or microscopic analysis first documented by Sampson17 in the mid-1930s. It is a rare condition, described as the finding of tubal-like glandular epithelium outside the fallopian tubes and without endometrial stroma, being analogous to endometriosis.

The present study reports the case of a 59-year-old female with gastric-type cervical adenocarcinoma and an incidental finding of endosalpingiosis, two rare conditions.

CASE REPORT

A 59-year-old patient (menopause at 45 years, six gestations, two abortions and four childbirths), with hydrorrhea and cytopathological examination of the uterine cervix with repeated finding of squamous cell atypia of undetermined significance (ASCUS), was attended. The transvaginal ultrasound (TVUS) demonstrated a large amount of homogeneous liquid content in the endometrial cavity, and an oval hyperechogenic image of well-defined limits, measuring 6X5 mm, located along the left lateral margin of the endometrial margin. This finding was difficult to differentiate from a polyp and submucosal leiomyoma. The cervix uteri showed an echogenic area containing multiple small cystic areas along the lining of the endocervical canal. She was submitted to colposcopy and a biopsy was performed, which showed moderate chronic cervicitis with squamous metaplasia. Hysteroscopy was indicated, but the patient did not return, and the diagnostic workup was discontinuous.

She returned after two years still complaining of hydrorrhea and the diagnostic investigation proceeded. On physical examination, she had increased uterine volume. The TVUS and cytopathological examination of the uterine cervix showed a small amount of homogeneous fluid inside the endometrial cavity, and cervix uteri with echogenic area containing multiple small cystic areas along the endocervical canal and atypical glandular cells of undetermined significance. She was submitted to hysteroscopy and endocervical canal resection, with results of "in situ" adenocarcinoma, endocervical pattern; endocervix with focal intestinal metaplasia and tubal metaplasia; endocervical margin coincident with the neoplasm and ectocervical margin free from neoplasm. An uneventful total hysterectomy (type A) with laparoscopic bilateral adnexectomy was performed.

Histopathological examination of the uterus and adnexa were consistent with: 1) mild and nonspecific chronic cervicitis; 2) endometrium with an atrophic pattern; 3) atrophic ovarian tissue with epithelial inclusion foci; 4) uterine horn without significant histological changes; 5) fragments of fibro-muscular tissue interspersed with congested vessels; and 6) foci of nonspecific chronic inflammation. A complementary report indicated a gastric-type endocervical adenocarcinoma with surgical stage IB123 (Figure 1).

A positron emission tomography was performed without metabolic signs of neoplasia. A complementary treatment included National Comprehensive Cancer Network, lymphadenectomy and parametrectomy. This procedure, vaginal vault resection, inframesenteric pelvic and retroperitoneal lymphadenectomy and omentectomy were performed and failed to show histopathological

metastases in resected lymph nodes (8 retroperitoneal/9 left pelvic/6 right pelvic) and in 1 left pelvic lymph node presented cystic area with epithelial lining (celomic pattern) with mucoid/eosinophilic aspect content.

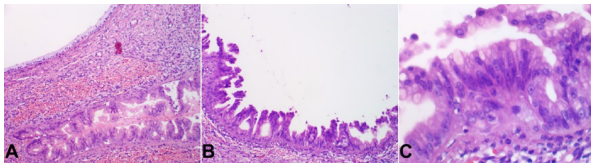

FIGURE 1 - Uterine cervix presenting gastric–type endocervical adenocarcinoma in situ with proliferated epithelium, forming cysts with papillae in the lumen, with mild to moderate atypia, sparse mitotic figures, large, eosinophilic or finely vacuolated cytoplasm. Hematoxylin stain (100x). A) 100 x B) 100 x C) 400 x.

An immunohistochemical analysis of the left pelvic lymph node was requested, with positivity for markers AE1/AE3 and WT-1, negativity for calretinin, p53 protein, monoclonal CEA and p16, compatible with glandular inclusion, endosalpingiosis or mullerianosis in the lymph node.

Quarterly follow-up in the first year, four-monthly in the second year, semester from third to fifth year and annual from the sixth year, was proposed.

DISCUSSION

Our case refers to a gastric-type endocervical adenocarcinoma, a rare subtype of endocervical adenocarcinoma which, unlike the usual endocervical adenocarcinoma, is not related to the human papilloma virus (HPV).[21]

The clinical picture of gastric-type adenocarcinoma is characterized by abundant and watery vaginal discharge, abnormal uterine bleeding, often located in the upper endocervical portion, associated with increased volume of the uterine cervix due to diffuse growth, being described as cervix-shaped barrel.[6,15] In cervical cytology samples, it shows only nonspecific changes.[22]

This neoplasm presents a differentiated pattern of metastasis to uncommon locations, such as the omentum, abdomen, ovaries, and other distant locations.[13] In addition, patients with gastric-type adenocarcinoma may present with Peutz-Jeghers syndrome, defined as an autosomal dominant disease that expresses itself due to a germline mutation of STK11.[15]

One study showed important differences between endocervical adenocarcinoma of the usual type and of the gastric type regarding the behavior of the tumor and the survival rate, with significantly worse clinical outcomes for patients with gastric type adenocarcinoma, even when pairing the stages of these diseases.[18] A common feature between these two types of neoplasms is the patients' onset age, which is between 49 and 51 years.[15]

The WHO defines endocervical tumors with gastric phenotype as "a mucinous endocervical adenocarcinoma associated with a gastric-type differentiation", subdividing them into atypical lobular endocervical glandular hyperplasia and gastric-type adenocarcinoma. However, this description does not provide sufficient criteria to diagnose the tumor morphologically, and does not provide information about the etiology, clinical or biological characteristics of these aggressive neoplasms either.[18,25] According to Kojima[7] the histological recognition of this condition is made by finding cells with clear, voluminous, and even pale eosinophilic cytoplasm with distinct borders throughout the tumor area.[6] Immunohistochemical evidence of gastric differentiation can occur by expression of MUC6 and HIK10839, but HIK1083 is not routinely used for diagnostic purposes and MUC6 is not fully specific.[15]

Glandular lesions of the gastric type can present in different ways. Examples of benign lesions are lobular endocervical glandular hyperplasia, simple gastric metaplasia, and cluster tunnel (type A). Premalignant or in situ lesions include atypical lobular endocervical glandular hyperplasia and gastric-type adenocarcinoma in situ. Among the malignant lesions, we can cite the gastric-type adenocarcinoma and the mucinous variant of minimal deviation adenocarcinoma.[20]

The differential diagnosis of well-differentiated gastric-type endocervical adenocarcinoma includes lobular endocervical glandular hyperplasia and diffuse laminar glandular hyperplasia. Lobular endocervical glandular hyperplasia may present as a well-demarcated or cystic mass composed of a laminar proliferation of closely demarcated glands of the underlying stroma and covered by a gastric-type mucinous columnar epithelium with insipid nuclei,22 and the immunohistochemistry is similar to gastric-type endocervical adenocarcinoma, with positive expression of gastric mucin and MUC6 and HIK1083 markers.[15] The use of three markers, SMA, p53 and PAX2, aid in the diagnostic differentiation, with positive SMA in gastric-type endocervical adenocarcinoma and negative around lobular endocervical glandular hyperplasia,[9] immunohistochemical staining with positive wild-type p53 mutation in lobular endocervical glandular hyperplasia and positive PAX2 in lobular endocervical glandular hyperplasia and negative in gastric-type adenocarcinoma.[15]

Regarding the differential diagnosis of moderately and poorly differentiated forms of gastric adenocarcinoma, there are endometrioid adenocarcinoma and endocervical adenocarcinoma of usual type, in which the first is HPV and p16 negative, and the second has pseudoendometrioid features.[22]

The ovarian conservation in patients with gastric-type adenocarcinoma during treatment may not be advised. Omentectomy is usually advised as part of surgical treatment. However, the gastric-type adenocarcinomas are resistant to conventional chemotherapy treatment when compared to the usual endocervical adenocarcinoma associated with HPV.[15]

Endosalpingiosis is a rare condition; however, it can affect approximately 7% of women undergoing laparoscopy.[5] This condition occurs in women of all ages, although it may preferentially occur in post-menopause, as showed in this study. It has also been described that it may be associated with other entities, with endometriosis occurring simultaneously in 35% and gynecologic malignancy in about 50% of cases.[16] In a cohort with

58161 patients who underwent gynecologic surgery, uterine cancer and ovarian cancer were more frequently in women with endosalpingiosis, without differences in the frequency of cervical cancer.[3]

It is unclear if the association between endosalpingiosis and other gynecological entities is a true association or the result of a lack of control group. Although, one study compared women who underwent surgery for sterilization with women undergoing surgery for other reasons, finding a higher prevalence of endosalpingiosis in the second group.[19]

It may be an incidental finding located in the peritoneum, bladder, intestine, vermiform appendix, skin and pelvic, para-aortic, inguinal and femoral lymph nodes, in addition to mimicking metastatic carcinoma.[1,2,11,24] Upon inspection of cell morphology, the endosalpingiosis presents as small glands lined with ciliated tubal epithelial cells, being differentiated from metastatic carcinoma because it is different from the primary tumor, and lacks cell atypia, desmoplasia and mitosis.[4] Another methods described for distinguishing between endosalpingiosis and lymph node metastasis are tissue rinse liquid-based cytology10 and immunohistochemestry markers.[12]

There are descriptions that endosalpingiosis is an asymptomatic condition, although others indicate the occurrence of dysmenorrhea, abnormal uterine bleeding, chronic pelvic or lumbar pain and infertility.[14]

From
[1]*Instituto Sul Paranaense de Oncologia (ISPON), Ponta Grossa, PR, Brazil.*

Correspondence
Caroline Link
E-mail: caroline-link@hotmail.com

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Authors' contribution
Conceptualization: Caroline Link
Methodology: Janiceli Blanca Carlotto Hablich Silvestre
Project administration: Ana Flávia Botelho
Writing (review and editing): Mario Rodrigues Montemor-Netto

REFERENCES

1. Carlson GJ, Samuelson JJ, Dehner LP. Cytologic diagnosis of florid peritoneal endosalpingiosis. A case report. Acta Cytol. 1986;30(5): 494-496.
2. Doré N, Landry M, Cadotte M, Schürch W. Cutaneous Endosalpingiosis. Arch Dermatol. 1980;116(8):909-912.
3. Esselen KM, Terry KL, Samuel A, Elias KM, Davis M, Welch WR, Berkowitz RS. Endosalpingiosis: More than just an incidental finding at the time of gynecologic surgery? Gynecologic Oncology. 2016;142(2),255–260.
4. Fisher CJ, Hill S, Millis RR. Benign lymph node inclusions mimicking metastatic carcinoma. J Clin Pathol. 1994;47(3):245-247.
5. Hesseling MH, De Wilde RL. Endosalpingiosis in laparoscopy. J Am Assoc Gynecol Laparosc. 2000;7(2):215-219.
6. Karamurzin YS, Kiyokawa T, Parkash V, Jotwani AR, Patel P, Pike MC, Park KJ. Gastric-type Endocervical Adenocarcinoma. Am J Surg Pathol. 2015;39(11):1449–1457.
7. Kojima A, Mikami Y, Sudo T, Yamaguchi S, Kusanagi Y, Ito M, Nishimura R. Gastric morphology and immunophenotype predict poor outcome in mucinous adenocarcinoma of the uterine cervix. Am J Surg Pathol. 2007;31(5):664-72.
8. Kurman R, Carcangiu ML, Herrington CS. WHO Classification of Tumours of Female Reproductive Organs. Lyon, France: WHO; 2014.
9. Lu S, Shen D, Zhao Y, Kang N, Wang X. Primary endocervical gastric-type adenocarcinoma: a clinicopathologic and immunohistochemical analysis of 23 cases. Diagn Pathol. 2019;14(1):72-76.
10. Matsumiya H, Todo Y, Yamazaki H, Yamada R, Minowa K, Tsuruta T, Yamashiro K. Diagnostic criteria of sentinel lymph node micrometastasis or macrometastasis based on tissue rinse liquid-based cytology in gynecological cancer. Int J Clin Oncol. 2020;25(12),2138–2143.
11. McCluggage WG, Clements WD. Endosalpingiosis of the colon and appendix. Histopathology. 2001;39(6):645-646.
12. White MJ, Vang R, Argani P, Cimino-Mathews A. Endosalpingiosis Is Negative for GATA3. Arch Pathol Lab Med. 2021;145(11):1448–1452.
13. Mikami Y, Kiyokawa, T, Hata S, Fujiwara K, Moriya T, Sasano H, Naganuma H. Gastrointestinal immunophenotype in adenocarcinomas of the uterine cervix and related glandular lesions: a possible link between lobular endocervical glandular hyperplasia/pyloric gland metaplasia and "adenoma malignum." Modern Pathology. 2004;17(8):962–972.
14. Ong NCS, Maher PJ, Pyman JM. et al. Endosalpingiosis, an unrecognized condition: report and literature review. Gynecol Surg. 2004;1:11–14.
15. Pirog EC, Park KJ, Kiyokawa T, Zhang X, Chen W, Jenkins D, Quint W. Gastric-type Adenocarcinoma of the Cervix: Tumor With Wide Range of Histologic Appearances. Adv Anat Pathol. 2019;26(1):1-12.
16. Prentice L, Stewart A, Mohiuddin S, Johnson NP. What is endosalpingiosis? Fertil Steril. 2012;98(4):942-947.
17. Sampson, J.A. Postsalpingectomy endometriosis (endosalpingiosis). Am J Obstet Gynecol. 1930;20:443–480.
18. Stolnicu S, Barsan I, Hoang L, Patel P, Terinte C, Pesci A, Aviel-Ronen S, Kiyokawa T, Alvarado-Cabrero I, Pike MC, Oliva E, Park KJ, Soslow RA. International Endocervical Adenocarcinoma Criteria and Classification (IECC): A New Pathogenetic Classification for Invasive Adenocarcinomas of the Endocervix. Am J Surg Pathol. 2018;42(2):214-226.
19. Sunde J, Wasickanin M, Katz TA, Wickersham EL, Steed DOE, Simper N. Prevalence of endosalpingiosis and other benign gynecologic lesions. PLoS ONE. 2020;15(5):e0232487.
20. Talia KL, McCluggage WG. The developing spectrum of gastric-type cervical glandular lesions. Pathology. 2018;50(2):122-133.
21. Tsuboyama T, Yamamoto K, Nakai G, Yamada T, Fujiwara S, Terai Y, Ohmichi M, Narumi Y. A case of gastric-type adenocarcinoma of the uterine cervix associated with lobular endocervical glandular hyperplasia: radiologic-pathologic correlation. Abdom Imaging. 2015;40(3):459-65.
22. Turashvili G, Morency EG, Kracun M, DeLair DF, Chiang S, Soslow RA, Park KJ, Murali R. Morphologic Features of Gastric-type Cervical Adenocarcinoma in Small Surgical and Cytology Specimens. Int J Gynecol Pathol. 2019;38(3):263-275.
23. Werner HM, Trovik J, Marcickiewicz J, et al. Revision of FIGO surgical staging in 2009 for endometrial cancer validates to improve risk stratification. Gynecol Oncol 2012;(125):103–108.
24. Young RH, Clement PB. Müllerianosis of the urinary bladder. Mod Pathol. 1996;9(7):731-737.
25. Yuan CT, Lin MC, Kuo KT, Wang TH, & Mao TL. Gastric-type adenocarcinoma in situ of uterine cervix: cytological and histopathological features of two cases. Virchows Archiv. 2016;469(3):351–356.