## References

[1] Moerman P, Fryns JP, Vandenberghe K, Lauweryns JM. Constrictive amniotic bands, amniotic adhesions, and limb-body wall complex: discrete disruption sequences with pathogenetic overlap. Am J Med Genet 1992;42:470–9.
[2] Torpin R. Amniochorionic mesoblastic fibrous strings and amnionic bands: associated constricting fetal malformations or fetal death. Am J Obstet Gynecol 1965;1(91)65–75 Jan.
[3] Van Allen MI, Curry C, Walden CE, Gallagher L, Patten RM. Limb-body wall complex: II. Limb and spine defects. Am J Med Genet 1987;28:549–65.
[4] Squier W, Jansen A. Polymicrogyria: pathology, fetal origins and mechanisms. Acta Neuropathol Commun 2014;2:80.
[5] Yamanouchi H, Ota T, Imataka G, Hagiwara Y, Nakagawa E, Eguchi M. Congenital bilateral perisylvian syndrome associated with congenital constriction band syndrome. J Child Neurol 2002;17:448–50.



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## A case of gastric-type mucinous endocervical adenocarcinoma in presence of nabothian cysts

Dear Editor,

A group of benign and malignant endocervical glandular lesions unrelated to human papillomavirus (HPV) and showing gastric differentiation, has been described in the last years [1]. Minimal deviation adenocarcinoma (MDA) and lobular endocervical glandular hyperplasia (LEGH) exhibit a gastric phenotype and immunophenotype [2]. Gastric-type adenocarcinoma (GAS) has been recently described as a subtype of cervical adenocarcinoma [3].These neoplasms have aggressive clinical behavior. There is a likely LEGH-GAS sequence, and an absence of HPV in cases of LEGH, and MDA suggested that this sequence represents an HPV-independent pathway of carcinogenesis [1]. Morphologically defined GAS exhibits immunoreactivity for MUC6 and/or HIK1083, representative markers for pyloric gland differentiation. Notably, GAS is negative for p16INK4a, a marker for high-risk HPV-driven neoplasm [4]. Clinical manifestations include watery vaginal discharge, although women can be asymptomatic [5]. Surgery remains the main treatment for patients with early-stage lesions. Radiotherapy and/or chemotherapy are recommended for women with advanced disease.We described a case of gastric-type mucinous endocervical adenocarcinoma in a woman with positive Pap smear tests for atypical glandular cells of undetermined significance (AGUS) but negative HPV-DNA test. A 46 years old nulliparous woman gave a medical examination for hydrorrhea. The gynecological examination showed plentiful mucinous secretions from vagina with vaginal fornix preserved. The specular examination showed an eroded and enlarged cervix. The transvaginal ultrasound (US) scan showed multiple Naboth cysts, as well as an uneven appearance and a plentiful vascularization of the uterus, but regular ovaries. The last two Pap smear tests, performed six months and one year before respectively, showed the presence of atypical glandular cells of undetermined significance (AGUS), so patient underwent colposcopy that confirmed the eroded and enlarged aspect of cervix but turned out to be negative for HPV-related lesions. After 3 months, the patient redid Pap smear test which showed the persistence of AGUS, whereas HPV-DNA test was negative. For this reason, the woman underwent a cervical conization: the histologic examination of cervical sample, measuring $4 \times 4 \times 2.5$ cm, showed a mucinous adenocarcinoma (NOS) moderately differentiated (G2) infiltrating endocervical margin and part of squamous cervical epithelium tissue, with vascular infiltration. Her cancer markers (α-FP, CEA, CA 19-9, CA 15-3, CA 125) turned out to be all negative. Abdomen and Pelvic MRI showed a tumor that invaded the cervix for all its thickness without involvement of nearby lymph nodes. The patient was referred to our institution and underwent a laparotomy procedure. Uterus and both annexes appeared macroscopically regular. She underwent a total hysterectomy, with bilateral salpingo-oophorectomy and pelvic and obturator lymphadenectomy. Definitive pathologic examination showed a mucinous adenocarcinoma gastric-type, moderately differentiated (G2), infiltrating cervical canal for all its thickness, with a microscopic metastasis in a lymph node isolated in the right parametrium and in two of pelvic and obturator lymph nodes (pT1B1N1) (Fig. 1A–B). Immunohistochemical analysis turned out to be negative for estrogen receptor (ER) and progesterone receptor (PR) (Fig. 1C) and positive for MUC6 (Fig. 1D). The patient is currently being treated with pelvic EBRT (external beam radiation therapy) and concurrent chemotherapy with cisplatin. The diagnosis of GAS is established primarily based on morphology: tumor cells with abundant eosinophilic cytoplasm, distinct cell borders, and a greater degree of cytological atypia characterize it [2,4]. However, immunohistochemistry may contribute to the diagnosis. GAS shows the gastric phenotype, as demonstrated by HIK1083, MUC6, or carbonic anhydrase type IX staining, negativity for p16, as well as a frequent mutant pattern of p53 staining [2]. Unlike MDA and LEGH, the MRI findings of GAS have not been clearly described yet, although image analysis based on T2-WI have recently showed a tumor shape classified as type II, infiltrative [5]. GAS is associated with aggressive behavior and a poor prognosis, including a possible propensity for peritoneal and adnexal dissemination [5]. Indeed, since the first description of GAS in 2007, it has been reported its poorer outcomes than those of usual-type adenocarcinomas (UEA), tipically associated to high-risk HPV in over 90% of cases. GAS is rather common in Japan, accounting for up to 20%–25% of all endocervical adenocarcinomas while it is considered rare in Western countries [2]. Kojima et al. showed that GAS had a 5-year disease-specific survival of 30% compared to 77% for UEA [5]. The mean age of presentation ranges between 45–48 years. It's related to high rate of lymphovascular invasion (LVI) and regional lymph node metastases [2].Here, we discussed the diagnostic difficulties for endocervical glandular lesions with gastric differentiation and the possible relationship with the

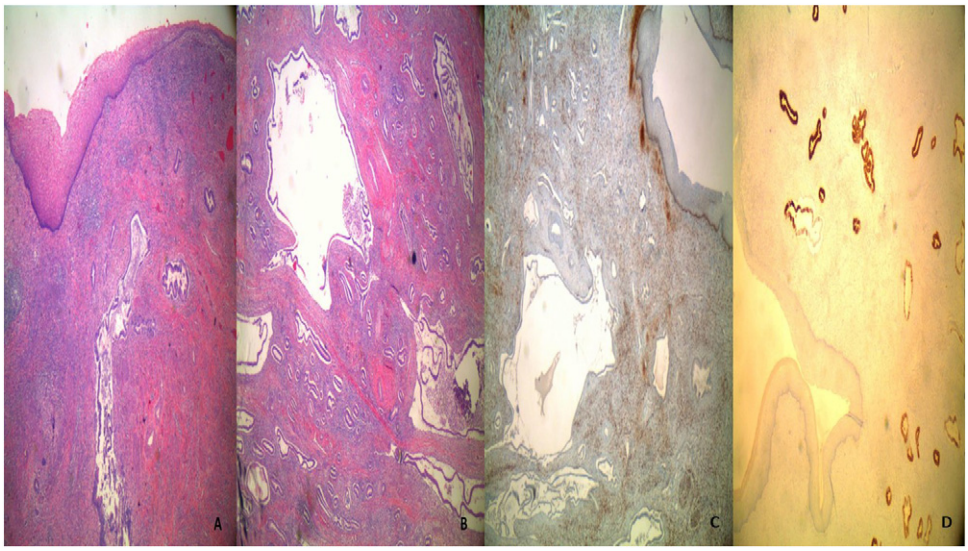


**Fig. 1.** A–D: A. High view of the adenocarcinoma that resemble the gastric adenocarcinoma, this particular field highlight a lymphovascular invasion; B. It is possibile to notice the infiltrative pattern of the adenocarcinoma gastric-type. The glands are composed by cells with high clear cytoplasm and distinct borders; C. Immunohistochemical analysis: negativity for the estrogen and progesterone receptors that are commonly negative in this type of cervix adenocarcinoma; positive controls stated by the fibroblasts in the stroma; D. Immunohistochemical analysis: positivity for MUC6.

nabothian cysts. This uncommon entity needs a particular attention for its aggressive behavior and because it is not HPV related. Screening methods for cancer control for the usual endocervical type like HPV DNA testing are ineffective and this may result in a probable delay in diagnosis and a worse prognosis. It would be really interesting to evaluate the role of nabothian cysts in the pathogenesis of this particular tumor.

## Declaration of interest statement

The authors declare that they have no conflicts of interest and nothing to disclose.

## References

[1] Park CM, Koh HM, Park S, Kang HS, Shim SS, Kim SY. Gastric type mucinous endocervical adenocarcinoma of the uterine cervix: very rare and interesting case. Obstet Gynecol Sci 2018;61(January (1)):165–9.
[2] Asaka S, Nakajima T, Momose M, Miyamoto T, Uehara T, Ota H. Trefoil factor family 2 protein: a potential immunohistochemical marker for aiding diagnosis of lobular endocervical glandular hyperplasia and gastric-type adenocarcinoma of the uterine cervix. Virchows Arch 2019;474(January (1)):79–86.
[3] Chung T, DO SI, Na K, Kim G, Jeong YI, Kim YW, et al. Stromal p16 overexpression in gastric-type mucinous carcinoma of the uterine cervix. Anticancer Res 2018;38(January (6)):3551–8.
[4] Yamanoi K, Ishii K, Tsukamoto M, Asaka S, Nakayama J. Gastric gland mucin-specific O-glycan expression decreases as tumor cells progress from lobular endocervical gland hyperplasia to cervical mucinous carcinoma, gastric type. Virchows Arch 2018;473(September (3)):305–11.
[5] Park KJ, Kim MH, Kim JK, Cho KS. Gastric-type adenocarcinoma of the uterine cervix: magnetic resonance imaging features, clinical outcomes, and prognostic factors. Int J Gynecol Cancer 2018;28(July (6)):1203–10.

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## Apparent germline mosaicism for a 15q11-q13 deletion causing recurrent Angelman syndrome in a Chinese family

Dear Editors,

Angelman syndrome (AS) is a genetic and neurological disorder characterized by severe developmental delay and learning disabilities, speech impairment, ataxia, tremulousness with jerky movements of limbs and a happy, sociable disposition. This disorder affects males and females in equal numbers with a prevalence of approximately 1 in 12,000–20,000 live births. The etiology is the loss of function of the imprinted UBE3A gene in 15q11-q13. The four known mechanisms include chromosome deletions, genetic imprinting errors, mutations in the UBE3A gene, and paternal uniparental disomy (UPD) [1]. By far, the most common cause of AS is the interstitial 15q11-q13 deletion, which occurs in about 80 percent of cases. Almost all of 15q11-q13 deletions arise de novo, being present in affected patients, but not in their parents nor in healthy siblings. Here, we report a family