# ENDOMETRIAL GASTROINTESTINAL-TYPE ADENOCARCINOMA, A RARE AND AGGRESSIVE VARIANT



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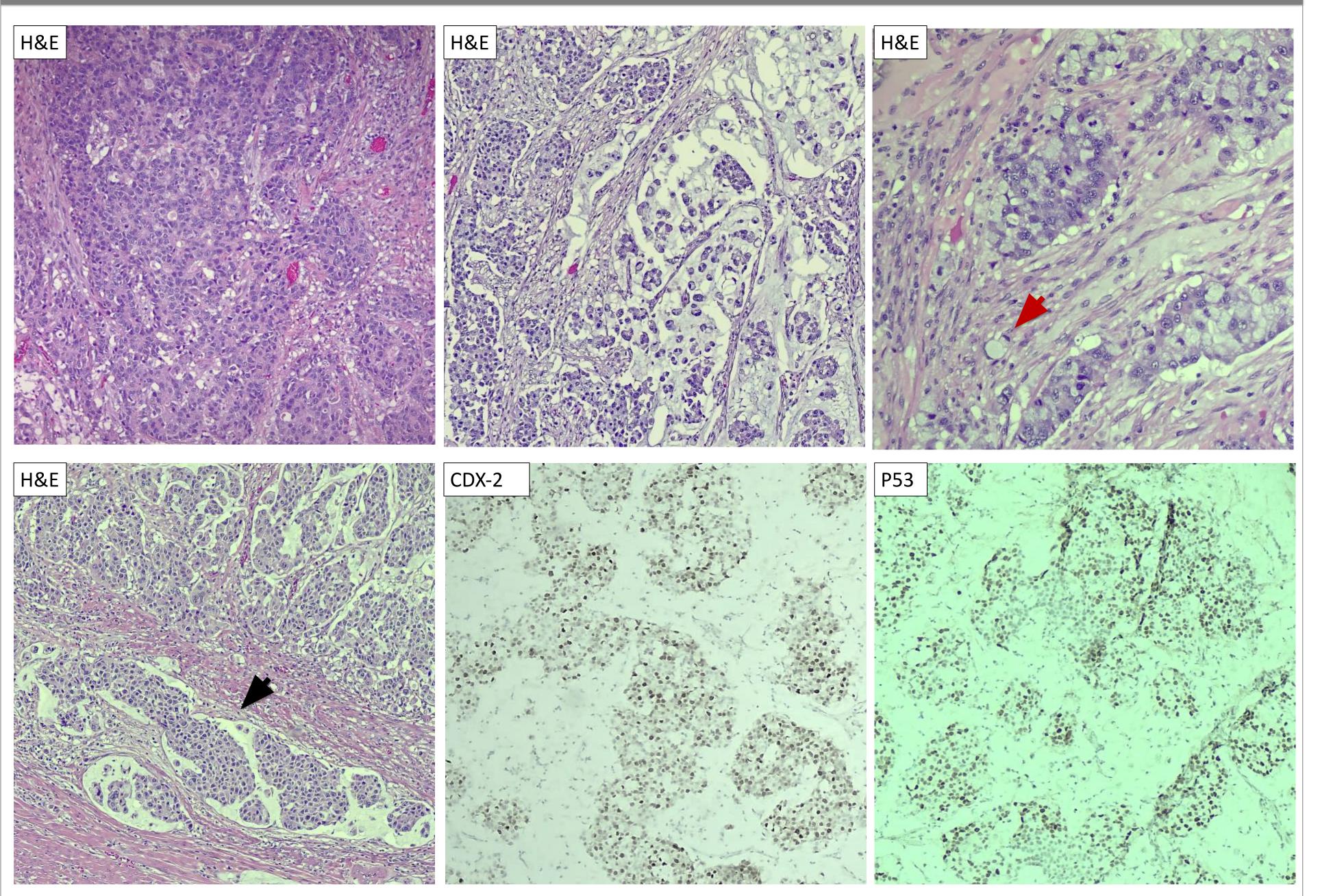
### Introduction

Endometrial carcinoma is the 6<sup>th</sup> most common type of cancer in women globally (excluding non-melanoma skin cancer) with rare histological subtypes that can cause diagnostic challenges. Endometrial gastrointestinal-type adenocarcinomas are composed of glands formed by mucin-secreting epithelium which may contain goblet cells. These tumors occur over a wide age range, but most are diagnosed in postmenopausal women with a clinical presentation of abnormal uterine bleeding and mucoid vaginal discharge. Although difficult, distinction of endometrial gastrointestinal-type adenocarcinoma from endometrioid carcinoma with mucinous differentiation is critically important because most gastrointestinal-type adenocarcinomas display aggressive clinical behavior irrespective of histologic grade.

## Case

A 65-year-old female presented with postmenopausal bleeding. Transvaginal ultrasound identified a 3.3 cm growth within the endometrial cavity and subsequent curettage showed a poorly-differentiated adenocarcinoma with signet ring cells. The patient underwent radical hysterectomy and bilateral salpingo-oophorectomy with pelvic lymph node dissection, which was diagnostic of endometrial gastrointestinal-type adenocarcinoma. There was greater than 50% myometrial invasion and substantial lymphovascular space involvement; however, all regional lymph nodes were negative for tumor cells. Immunohistochemistry showed partial CDX2 expression, aberrant p53 overexpression, and loss of PTEN expression. PAX8, ER, and PR were negative and mismatch repair proteins were retained. Esophagogastroduodenoscopy and colonoscopy were recommended to exclude the possibility of metastasis, and these studies were unremarkable.

## Case and result



**Figure 1.** Endometrial adenocarcinoma, mucinous type with gastrointestinal differentiation. The tumor composed of glands formed of mucin- secreting epithelium (red arrow). Lymphatic space invasion identified (black arow). By immunohistochemistry, the tumor cells express CDX2, P53 mutated pattern.

#### Discussion

Endometrial gastrointestinal-type adenocarcinoma is postulated to be an aggressive variant of endometrial carcinoma. Histologic criteria proposed by Wong et al include the following: 1) voluminous pale or eosinophilic cytoplasm with distinct cell borders, or the presence of goblet cells, 2) lack of a typical endometrioid component, 3) lack of cervical glandular or stromal involvement, 4) at least focal immunohistochemical expression of a gastrointestinal marker (e.g. CDX2, CK20, MUC6), and 5) less than 5% expression of ER. Importantly, there must also be no evidence of an alternative primary site. The first criterion utilizes the morphologic definition of gastric-type endocervical adenocarcinoma proposed by Kojima et al; hence absence of cervical involvement is necessary to establish endometrial origin. The significance a signet ring cell component in endometrial gastrointestinal-type adenocarcinoma, as seen in this case, is unclear. In a recent case report, Seay et al hypothesized that signet ring cells and loss of E-cadherin expression may render a poor prognosis due to deep myometrial invasion and increased metastatic potential. However, the rarity of these tumors makes it difficult power a detailed study.

#### References

- 1. Wong R, Ralte A, Grondin K, Talia K, McCluggage G. Endometrial Gastric (gastrointestinal)-type Mucinous Lesions. Report of a Series Illustrating the Spectrum of Benign and Malignant Lesions. Am J Surg Path. 2020 March; 44(3):406-419
- 2. 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 May;31(5):664-72
- 3. Seay K, Bustamante B, Truskinovsky A, Menzin A, Golberg G. Intestinal type adenocarcinoma of the endometrium with signet ring cells, a rare aggressive variant. Gynecologic Oncology Reports 42. 2022 July; 101046 (4).