International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2023: 1.843

HPV Independent, Gastric Type Adenocarcinoma of Cervix - Case Report of a Rare Aggressive Subtype

Dr. Shanmuga Priya S[1], Dr. Laila Raji N[2]

[1]Junior Resident, Department of Pathology, Government Medical College, Thiruvananthapuram, Kerala, India
Email: *priya.shanmuga89[at]gmail.com*

[2]Professor and Head of The Department, Department of Pathology, Government Medical College, Thiruvananthapuram, Kerala, India

Abstract: ***Adenocarcinoma of cervix, HPV independent, gastric type is an invasive adenocarcinoma showing gastric (pyloric) differentiation, unrelated to HPV infection. The patients present with highly atypical clinical features and exhibits aggressive biological behaviour, making timely diagnosis particularly challenging. In the present study, we report a case of a 46 year old female who presented with increased vaginal discharge. Vaginal vault mass excision was done. Histopathology and IHC favoured a diagnosis of Adenocarcinoma of cervix, HPV independent, Gastric type.***

Keywords: Adenocarcinoma cervix, HPV independent, Gastric type

1. Introduction

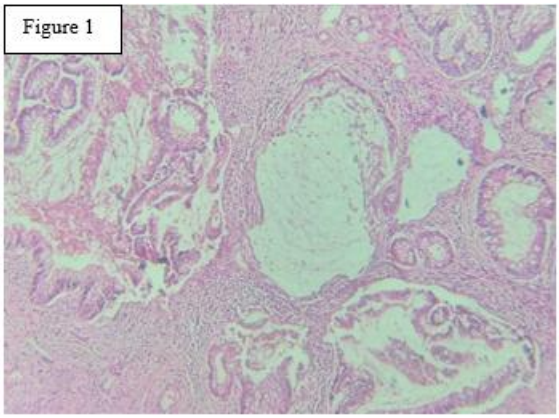
Gastric - type adenocarcinoma of the uterine cervix is a type of endocervical adenocarcinoma that is not associated with human papillomavirus (HPV) infection. This subtype is known to have a poorer prognosis compared to the more common HPV - associated endocervical adenocarcinoma. It is estimated to account for about 10% of cervical adenocarcinomas worldwide.

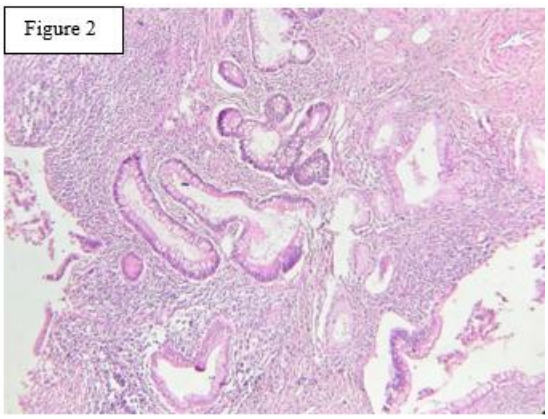
2. Case Report

46 year old female presented with increased vaginal discharge for 6 months. The patient underwent Subtotal abdominal hysterectomy in 2008 with complaints of menorrhagia and dysmenorrhoea. USG abdomen showed dilated endocervical canal with heteroechoic lesion showing mild vascularity – malignancy to be excluded. Right adnexa showed hydrosalpinx. CT abdomen showed a heterogeneously enhancing mass lesion with cystic component involving the vaginal vault, abutting the posterior wall of urinary bladder and anterior wall of upper rectum. A blind ending tubular structure arising from the lesion, extending towards the right pelvic side wall – Possibility of neoplastic lesion of vaginal vault or cervical stump with associated hydrosalpinx. MRI abdomen showed cervical canal is dilated and shows an intraluminal heterogeneously enhancing lesion. There is mild extension of the lesion into upper vaginal canal. Mild fluid in cervical canal and vaginal canal – Possibly neoplastic etiology.

Patient underwent vaginal vault mass excision and bilateral salpingo - oophorectomy. We received a grey brown nodular mass, bilateral tubes and ovaries. Grey brown nodular mass measures 7x3x2.5 cm. Cut section of the mass – grey white with cystic spaces and trabeculations. Microscopy showed widened stroma and proliferated glandular structures lined by columnar cells with distinct cell borders. Tumour cells have pale eosinophilic and voluminous cytoplasm, ovoid basally located vesicular nuclei. The glands were irregular with focal clumping. Immunohistochemistry done showed ER and PR positive in normal endocervical glands and negative in dysplastic glands. p16 was negative. Final diagnosis was Adenocarcinoma, HPV independent, gastric type of the uterine cervix.

The patient underwent radiotherapy and brachytherapy and is under follow - up.





Figures 1 and 2: Shows a neoplasm composed of proliferated irregular glandular structures

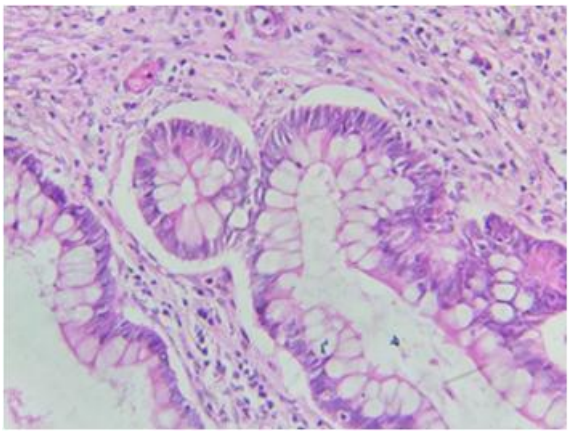


Figure 3: High power view showing glands lined by columnar cells with distinct cell borders, abundant pale eosinophilic cytoplasm and basally located nuclei

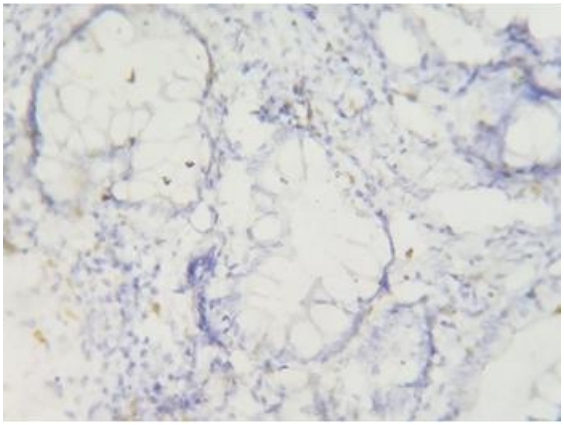


Figure 4: p16 shows negative staining

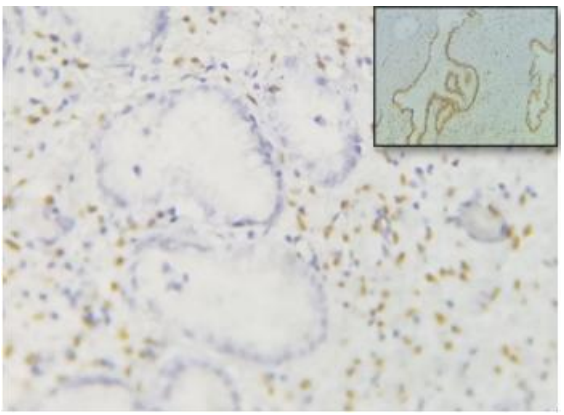


Figure 5: ER – negative in the neoplastic glands; Inset shows positive internal control in the normal endocervical glands

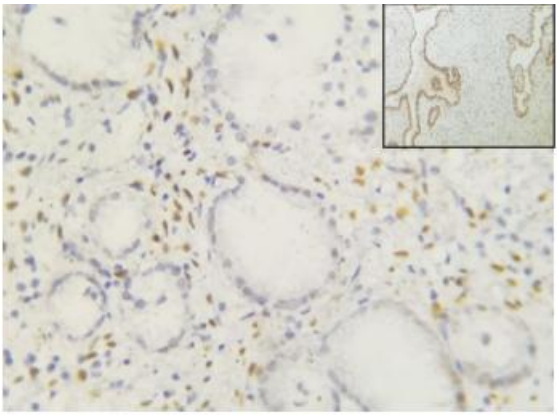


Figure 6: PR – negative in the neoplastic glands; Inset shows positive internal control in the normal endocervical glands

3. Discussion

Gastric - type adenocarcinoma of the cervix, first described by Kojima et al., is classified as a subtype of the HPV - independent group in the 2020 WHO classification of female genital tumours. This aggressive form of endocervical adenocarcinoma is characterized by mucinous morphology with gastric - type mucin, absence of association with HPV, and resistance to chemotherapy and radiotherapy.

Gastric - type adenocarcinoma of the cervix typically occurs in middle - aged women and presents with symptoms such as watery vaginal discharge, abnormal uterine bleeding and in some cases, a pelvic or abdominal mass. However, typical symptoms of cervical cancer are rare. Clinical examination is nonspecific and may reveal a smooth cervix or a thickened, hardened cervix, sometimes described as a “barrel - shaped” cervix.

Since this tumour is not associated with HPV infection, routine cervical cancer screening methods, including cytological screening and HPV testing, have limited utility. Even when colposcopy is performed, the chances of detection are low due to the lesion’s typical location deep within the cervical canal. Due to its diagnostic challenges, it is common for more than 50% of patients to present with stage II or more advanced disease at the time of diagnosis.

The precursor lesions of gastric - type endocervical adenocarcinoma include lobular endocervical glandular hyperplasia (LEGH), atypical LEGH, and gastric - type adenocarcinoma in situ of the uterine cervix. The latter two precursors share genetic alterations, such as 1p deletion and 3q acquisition.

Gastric - type adenocarcinoma of the cervix is also strongly associated with Peutz - Jeghers syndrome (PJS) often linked to mutations in the STK11 gene. It is a hereditary condition characterized by benign hamartomatous polyps in the gastrointestinal tract, hyperpigmented macules in the oral mucosa, and a markedly increased risk (10 - to 18 - fold) of developing tumours in the gastrointestinal tract and breast.

Gastric - type adenocarcinoma of the cervix is characterized by tumour cells with gastric differentiation, featuring abundant clear or pale eosinophilic cytoplasm, distinct

cytoplasmic borders, a low nuclear - to - cytoplasmic ratio, and basally located nuclei. Minimal deviation adenocarcinoma (previously called Adenoma malignum), is a subtype within the Gastric type adenocarcinoma spectrum and exhibits low - grade morphology with well - differentiated glands. These glands may show a distinctive "claw - like" proliferation pattern and are lined by cells containing abundant intracytoplasmic mucin with minimally atypical nuclei. The glands are irregularly distributed within the stroma, often with little to no desmoplasia.

Gastric - type adenocarcinoma of the cervix produces pyloric - type mucin, which stains pink or red with Alcian blue histochemical staining. In contrast, normal endocervical mucins are acidic and stain dark blue, helping to differentiate Gastric - type adenocarcinoma from other types of cervical mucinous lesions. These tumours are positive for pyloric markers like HIK1083 and MUC6. ER and PR are negative. p16 is usually negative or patchy positive. Lymphovascular invasion is frequently seen with a higher tendency to metastasize to extrapelvic organs and is associated with a poorer prognosis compared to HPV associated adenocarcinoma. These tumours are resistant to chemotherapy and radiotherapy.

The clinical management of gastric - type adenocarcinoma of the cervix is challenging due to its rarity, diagnostic complexities, limited awareness, and aggressive nature. Currently, there are no specific treatment guidelines. Surgical intervention is often considered, involving the removal of the uterus, adnexa, pelvic and/or paraaortic lymph nodes, omentum, appendix, and any visible tumour.

4. Conclusion

Adenocarcinoma of cervix can be HPV associated or HPV independent. The widespread adoption of HPV vaccinations has led to a global decline in HPV - associated carcinomas. However, patients remain at risk of developing gastric - type adenocarcinoma, a subtype unrelated to HPV infection. As the incidence of HPV - related endocervical adenocarcinomas decreases, it becomes increasingly important for clinicians to maintain a high index of suspicion for Gastric type adenocarcinoma. Additionally, reliance on p16 as a diagnostic marker may result in missed diagnoses of Gastric type adenocarcinoma, as this malignancy often shows negative or patchy p16 staining. The objective of this case report is to raise awareness of this rare and aggressive malignancy, particularly given its diagnostic challenges.

References

[1] Zhang S, Jin G, Ding F, Zhang J, Li Q, Wang G, et al. A case of endocervical adenocarcinoma of the gastric type that was repeatedly misdiagnosed: A case report and literature review. Medicine (Baltimore).2023 May 26; 102 (21): e33682.
[2] Wang J, Yang Q, Wang D, Li M, Zhang N. Case Report: Gastric - Type Endocervical Adenocarcinoma Mimicking Submucosal Myoma Under Hysteroscopy. Front Med [Internet].2022 Mar 8 [cited 2024 Dec 7]; 9. Available from: https: //www.frontiersin. org/journals/medicine/articles/10.3389/fmed.2022.845445/full
[3] Jung H, Bae GE, Kim HM, Kim HS. Clinicopathological and Molecular Differences Between Gastric - type Mucinous Carcinoma and Usual - type Endocervical Adenocarcinoma of the Uterine Cervix. Cancer Genomics Proteomics.2020 Sep 1; 17 (5): 627–41.
[4] Karamurzin YS, Kiyokawa T, Parkash V, Jotwani AR, Patel P, Pike MC, et al. Gastric type endocervical adenocarcinoma: an aggressive tumor with unusual metastatic patterns and poor prognosis. Am J Surg Pathol.2015 Nov; 39 (11): 1449.
[5] Tremblay E, Samouëlian V, Carmant L, Auclair MH, Undurraga M, Barkati M, et al. Gastric - type adenocarcinoma of the endocervix: Potentially overcoming resistant behavior with surgery. Gynecol Oncol Rep.2023 Dec 1; 50: 101282.
[6] Gastric - type adenocarcinoma of the uterine cervix: clinical features and future directions | Japanese Journal of Clinical Oncology | Oxford Academic [Internet]. [cited 2024 Dec 8]. Available from: https: //academic. oup. com/jjco/article/54/5/516/7608643
[7] Wen X, Yu L, Liu X, He X, Zhao Y, Li G. Gastric - type endocervical adenocarcinoma: a case report and literature review. Front Oncol [Internet].2024 Apr 23 [cited 2024 Dec 7]; 14. Available from: https: //www.frontiersin. org/journals/oncology/articles/10.3389/fonc.2024.1341068/full