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Case Report

Primary clear cell adenocarcinoma of vagina - not associated with diethylstilbestrol exposure

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ABSTRACT

The primary clear cell adenocarcinoma (PCCA) of the vagina and the cervix are commonly associated with in utero exposure to diethylstilbestrol (DES). However, it can occur without DES exposure in utero. Due to rare occurrence, there is paucity of data on the literature on non-DES associated PCCA of the vagina. Here we describe a case of 45 years old woman presented with irregular vaginal bleeding with small nodule in the vagina. The growth was excised and sent for histopathological examination, after which the diagnosis turned out to be a case of PCCA of the vagina. After the diagnosis, definite treatment was planned in the form of hysterectomy and pelvic lymphadenectomy and all structures were free of tumour on histopathological examination. The patient remained disease free on short term follow up. The rarity of the occurrence of such a case of PCCA of vagina in Indian scenario and the uniqueness of it in terms of non-association with DES exposure prompted us to report this case.

Keywords: Cervix, DES, PCCA, Vagina

INTRODUCTION

The primary clear cell adenocarcinoma (PCCA) most commonly involves cervix, vagina, endometrium ovaries and urinary tract including kidneys. It accounts for 5-10% of all vaginal malignancies.¹ Ultra structurally and immunologically, vaginal and cervical clear-cell adenocarcinomas are identical to clear-cell adenocarcinomas that arise in the ovary or endometrium.² The association of vaginal and cervical clear-cell adenocarcinoma with in utero exposure to diethylstilbestrol (DES) is well known, but up to one-third of patients lack exposure.³ From 1938 until 1971, DES was used to prevent miscarriages. But, it was withdrawn worldwide by FDA due to its proven role in carcinogenesis.⁴ More than 700 cases of vaginal and cervical clear-cell adenocarcinoma have been accessioned in the Registry for Research on Hormonal Transplacental Carcinogenesis.⁵ Literature lacks information regarding

clinical behavior, pathology and prognosis of non-DES-associated primary clear cell carcinoma of the vagina (PCCAV) as they are rare. The purpose of the study was to report a case of non-DES-associated PCCAV in our effort to further improve the biological characteristic of these rare tumours in terms of prognosis.

CASE REPORT

A 45 years old woman presented with irregular vaginal bleeding and discharge. She had history of two vaginal deliveries; last one is 20 years back. There is no history suggestive of DES exposure to patient or her mother. Per abdominal examination was unremarkable. The ultrasound report of whole abdomen was inconclusive and kidney, urinary bladder and urethra region was within normal limit. There was a small nodular growth on vagina involving anterior wall, measuring 0.5 cm in maximum diameter. On the basis of history and

examination the following differential diagnosis were made: 1) infected fibroepithelial polyps, 2) leiomyosarcoma of vagina, 3) Metastasis from unknown primary.

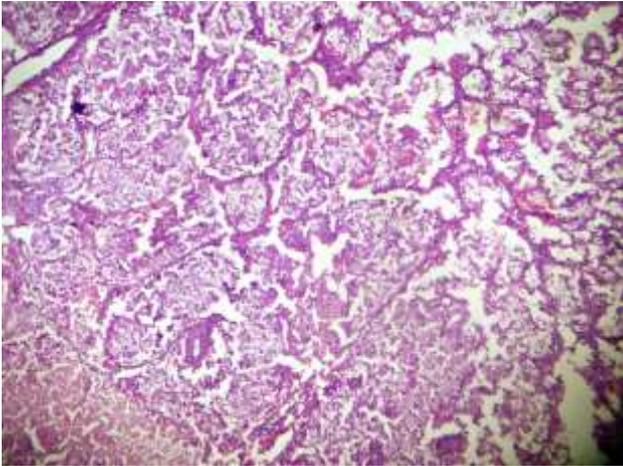


Figure 1: Routine section shows sheets of tumor cells having clear cytoplasm with vesicular nuclei, separated by fibrovascular stroma (H/E, x40).

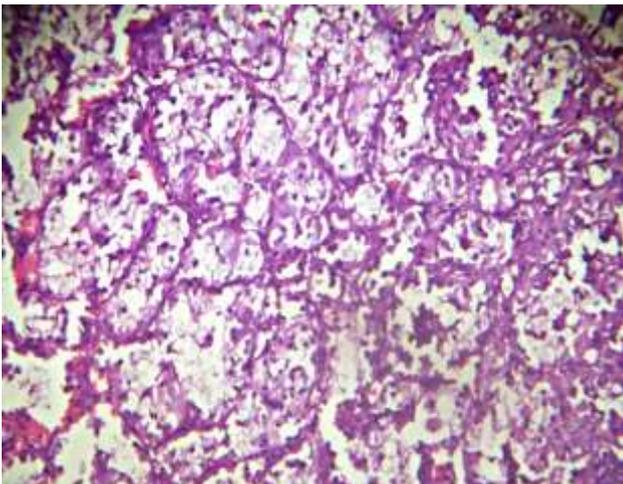


Figure 2: Routine section shows sheets of tumor cells having clear cytoplasm with vesicular nuclei, separated by fibrovascular stroma (H/E, x100).

Patient underwent polypectomy. Grossly it was sent to laboratory as multiple bits of friable tissue. On microscopic examination and Hemotoxylin/Eosin staining, a polypoidal tissue showed a tumor mass composed of confluent nests and sheets of cells having abundant clear to eosinophilic cytoplasm, separated by fibrovascular stroma (Figure 1). The cells had vesicular nuclei with prominent nucleoli, at places with nuclear inclusion and hobnailing (Figure 2). Large areas of necrosis were also seen. The cells showed positive reaction of cytoplasm on staining with Periodic-Acid Schiff stain. Based on these features a diagnosis of Primary clear cell adenocarcinoma of vagina was made.

Following the diagnosis hysterectomy was done along with removal of pelvic lymph nodes. On histopathological examination, all of these structures were within normal limits and no residual tumor or metastasis was detected. On follow up after two months the patient is doing well and the bleeding disorder has not recurred so far.

DISCUSSION

The patients range in age from 7 to 37 years, and the median age is 19 years at diagnosis. These tumours had a bimodal age distribution, the first peak occurring at a mean age of 26 years and second peak of median age of 31 years.⁶ Genetic instability, identified by somatic mutation of microsatellite repeats, has been found in these neoplasms, whereas mutations in p53, K-ras, the Wilms tumor (WT1) tumor suppressor gene, and the estrogen receptor gene have been absent.⁷ Abnormal vaginal bleeding, discharge, dyspareunia and vaginal mass are the most common presentations. Grossly, the neoplasm appears as a polypoid, nodular, flat, or ulcerated mass, usually in the anterior or lateral wall of the upper vagina. Rarely, it is confined to the lamina propria with overlying normal squamous epithelium. Clear-cell adenocarcinoma varies in size from microscopic to more than 10 cm in diameter.⁸ Microscopically, about 60% of cervical and vaginal tumors show a predominantly tubulocystic growth pattern; 20% have a predominantly solid pattern of growth, and 12% are papillary. A mixture of growth patterns is usual. Solid sheets of tumor are composed of cells with abundant clear cytoplasm. Tubules, cysts, and papillae are lined chiefly by cells that are cuboid, hobnail, or flat. Cords of cells having eosinophilic cytoplasm also may be observed. Nuclear pleomorphism is variable. Flat cells that line dilated cysts often have a bland cytologic appearance. Approximately three-fourths of all neoplasms have no more than 1 mitotic figure per 10 hpf. Foci of atypical adenosis usually are observed adjacent to the tumor, though this was absent in our case.⁸ The cells of the tumor show positivity for periodic acid-Schiff (PAS) stain due to presence of glycogen in their cytoplasm. This glycogen content is responsible for clearing of the cytoplasm.⁹ The characteristic immune profile of PCCA of the genitourinary tract for all sites is CK7, CAM5.2, 34 beta E12, CEA, CA-125, Leu-M1 and vimentin positive.¹⁰

Non-DES-associated PCCA of the vagina and cervix may also be related to adenosis and other congenital malformations such as didelphys uterus with a double vagina, renal agenesis and situs inversus.¹¹

Non-DES-associated PCCAV has a poor prognosis and significantly worse outcomes than those seen in patients with other primary carcinomas of the vagina. Local and distant recurrence rates are also more common among these patients than patients with squamous cell carcinoma who have received similar treatment.¹² Nordqvist et al

reviewed twenty one cases of vaginal and cervical clear cell adenocarcinomas, out of which thirteen had no prior exposure to DES.¹³

We take this opportunity to report this unique and relatively rare case of Primary clear cell adenocarcinoma of vagina-not associated with DES therapy in Indian scenario.

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