Case Report

Russell Body Cervicitis in a Human Immunodeficiency Virus-positive Female: An Unusual Presentation of Prolonged Cervical Inflammation

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Abstract

Individuals living with HIV face an elevated susceptibility to various plasma cell disorders, encompassing a spectrum that spans from benign conditions like plasma cell chronic inflammation to more severe conditions such as aggressive multiple myeloma. The present case is one of the few cases of plasma cell rich inflammation of the cervix, and is probably the first being reported in an HIV positive female. A 34-year-old female, P2L2 with last child birth 8 years back visited gynecology OPD with complaints of copious vaginal discharge from last 1 year. The discharge was yellowish in color, non-foul smelling, watery in consistency and present all through the menstrual cycle. On per speculum examination, the cervix looked unhealthy and bleeding on contact was present. The Pap Smear was suggestive of a high grade squamous intra-epithelial lesion (HSIL). Biopsy revealed intense plasma cell-rich inflammation in the subepithelial stroma with Russel bodies. A summary of all reported cases of Russel cell cervicitis, reported till date and key points to differentiate it from other plasma cell rich cervical lesions like malakoplakia and plasmacytoma are also presented.

Keywords: *Human immunodeficiency virus, plasma cell-rich cervicitis, people living with human immunodeficiency virus, rare forms of cervicitis, Russell body cervicitis*

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Introduction

Individuals living with human immunodeficiency virus (HIV) face an elevated susceptibility to various plasma cell disorders, encompassing a spectrum that spans from benign conditions such as plasma cell chronic inflammation and polyclonal hypergammaglobulinemia to more severe conditions such as aggressive multiple myeloma (MM), monoclonal gammopathy of unknown significance (MGUS), solitary plasmacytoma, and, less frequently encountered, plasmablastic myelomas and lymphomas.[1,2] In individuals with HIV, plasma cell-rich inflammation can manifest as an immune system response to any form of viral infection. HIV infection can lead to persistent immune activation and inflammation, which can affect various components of the immune system, including plasma cells. In the context of HIV, chronic immune activation can lead to dysregulation and abnormal functioning of plasma cells.[3] This dysregulation may contribute to the development of conditions such as polyclonal hypergammaglobulinemia, where there is an increase in the production of multiple types of antibodies. In addition, HIV-associated inflammation may play a role in the development of certain plasma cell disorders such as MM, MGUS, and other related conditions. The intricate interplay between HIV, the immune system, and plasma cells underscores the complexity of the relationship between HIV infection and plasma cell inflammation.

Although a few cases of Russell body gastritis have been reported to occur in people living with HIV,[4,5] this is the first case of Russell body cervicitis, being reported in an HIV-infected female. A comprehensive analysis of all the cases of Russell body/plasma cell-rich

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cervicitis documented in English literature has also been conducted to investigate the clinicopathological characteristics of this rarely encountered condition.

Case Report

A 34-year-old female, P2 L2 with last childbirth 8 years back visited the gynecology outpatient department with complaints of copious vaginal discharge from the last 1 year. The discharge was yellowish in color, nonfoul smelling, watery in consistency, and present all through the menstrual cycle. There was no history of itching in the perineal region, menstrual irregularity, dysuria, or dyspareunia. There was no history of pain lower abdomen or any bladder or bowel complaints. Her past history was significant in that she was HIV positive, acquired through a blood transfusion, and she had been on a combination of zidovudine, lamivudine, and nevirapine for the last 5 years. Her last CD-4 cell count was cell 534/μL. She was in chronic stage of HIV and has severe anemia (hemoglobin – 6.5 g/dl) with reactive thrombocytosis (platelet count: 6.64 lakh/ml). The patient also had multinodular goiter with Hashimoto thyroiditis. Antithyroid peroxidase antibody titer was 135 IU/ml and anti-thyroglobulin antibody was 62.6 IU/ml. There was no history of hypertension, diabetes mellitus, tuberculosis, or any other chronic medical disease.

On examination, her general condition was unremarkable, except for mild pallor. On local examination, the external genitalia were normal. On per speculum examination, the cervix looked hypertrophied with perioral erosion, and nabothian cyst, about 1 cm × 1 cm at 11 o' clock position. Bleeding on contact was present. On application of acetic acid, there was thin acetowhite epithelium with irregular and geographical borders, with fine punctations (Grade 1 changes, as per 2011 IFCPC Nomenclature). The squamous–columnar junction was fully visible and located on the ectocervix (Type I TZ) [Figure 1]. On bimanual examination, the uterus was noted to be of normal size, with no abnormality palpable in either adnexa. The Pap smear was suggestive of a high-grade squamous intraepithelial lesion. Human papillomavirus DNA was negative. Ultrasound examination was suggestive of a bulky uterus (10.3 cm × 5.4 cm) with ill-defined endometrial echoes. Cervical and endometrial biopsy was done. Histological examination showed a polypoidal configuration of the surface epithelium with intense plasma cell-rich inflammation in the subepithelial stroma. Many of the plasma cells show intense eosinophilic intracytoplasmic inclusion, causing peripheral displacement of the nucleus, termed Russell bodies. There is no evidence of dysplasia in the cervical lining epithelium, and could not detect any causative organism on hematoxylin sections and special stains [Figure 2].

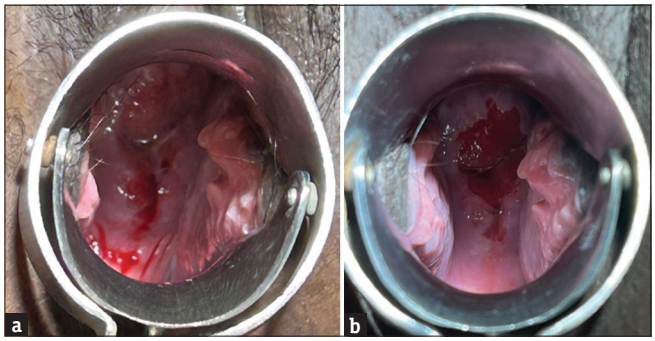

Figure 1: Per-speculum examination of the cervix showing hypertrophied cervix which bleeds on touch (a) and on the application of acetic acid, the thin acetowhite epithelium with irregular and geographical border (b)

Discussion

Russell bodies are eosinophilic, globular inclusions that can be found within the cytoplasm of certain cells, particularly plasma cells. These structures are named after the British pathologist William L. Russell, who first described them in 1890. Russell bodies are composed of immunoglobulins (antibodies) that have been produced by the plasma cells. When plasma cells actively produce antibodies as part of the immune response, they generate a large number of immunoglobulins. In some cases, these immunoglobulins may accumulate within the endoplasmic reticulum due to various reasons, such as an overwhelming production of antibodies or impaired secretion mechanisms. The accumulation of immunoglobulins forms the distinctive Russell bodies, which are often seen in conditions characterized by chronic stimulation of the immune system, such as certain infections, autoimmune diseases, or plasma cell disorders, and are not specific to any particular disease.

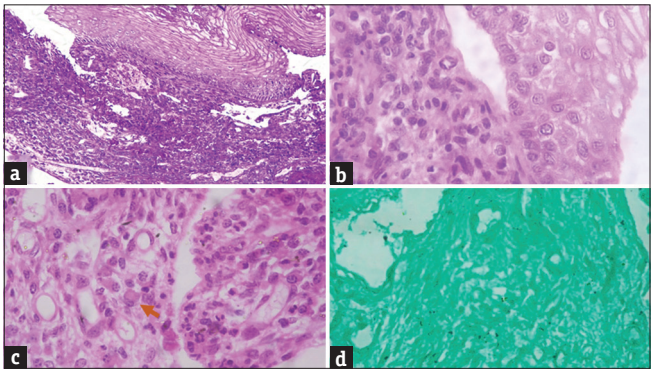

Figure 2: Ectocervix with dense plasmocytic infiltrate in the subepithelial stroma (a) (H and E, ×40), Ectocervix does not show any dysplastic changes (b) (H and E, ×400), plasma cell with eccentrically placed nuclei with homogenous eosinophilic cytoplasmic inclusion called Russell bodies (c) (H and E, ×400). Grocott methenamine silver (GMS) stain for identification of fungi is negative (d) (GMS, ×400). Russel bodies (Red arrow)

Russell body cervicitis is a variant of plasma cell-rich cervicitis, where a variable number of Russell bodies can be visualized microscopically.[6] The presence of multiple Russell bodies in a plasma cell gives rise to Mott cell, which again does not signify any specific pathogenetic process. While it typically follows a slow and less aggressive clinical progression, the significance of chronic plasma cell cervicitis lies in its potential to create diagnostic challenges. It can masquerade as a malignant entity, both macro-and microscopically.[6-8] Distinguishing it from cervical cancer is crucial, given the markedly distinct clinical and prognostic outcomes associated with these two conditions. The authors, even after their extensive literature search, could find only 11 cases of Russell body cervicitis, in the literature, which are summarized in Table 1.

This is the first case of Russell body cervicitis, being reported in an HIV-infected female. The authors considered it important to report because this can serve as an important guide for clinicians, coming across such cases in the future. Although benign, it can definitely cause diagnostic confusion with

Table 1: A summary of all cases of Russell body cervicitis reported in literature till date

Author, year of publication	Age of the patient	Presenting complaints	Gross examination of the cervix	HPV DNA status	Management done	Follow-up if available
Altun *et al*., 2017[9]	40	HPV DNA positive on routine screening	Cervix looked suspicious	HPV-66	-	Symptom-free at 1-year follow-up period
Enow-Orock *et al*., 2016[10]	45, multiparous	Menorrhagia, lower abdominal pain, persistent vaginal discharge, and abdominal fullness. History of repeated STIs including chlamydia, candidiasis, and other nonspecific infections. Sero negative to HIV	Pap smear - severe chronic nonspecific cervicitis marked by a massive dense infiltrate of mature plasma cells Koilocytes present	HPV-18	Hysterectomy due to associated multiple fibroids	Healthy at 3-year follow-up
Foda *et al*., 2014[11]	35	Contact bleeding	Cervical polyp - 1 cm×0.5 cm×0.5 cm	Not mentioned	-	Healthy at 6-month follow-up
Doherty *et al*., 1993[12]	67	Large cervical tumor		HPV-16 positive	Hysterectomy	-
Joseph and Singuluri, 2020[13]	44	Repeated development of endocervical polyp	-	Not mentioned	Polypectomy	Asymptomatic at 14-month follow-up
Stewart and Leake, 2006[14]	35	Pap smear - LSIL	Colposcopy - consistent of HPV effect	Not mentioned	-	-
Salmo and Farroha, 2007[15]	29	Contact bleeding	Small cervical polyp	Not mentioned	Polypectomy	Not mentioned
Mitchell *et al*., 2020[16]	65, postmenopausal	6-year history of copious, yellow vaginal discharge	Erythematous papules on the cervix	Not mentioned	Vaginal application of estradiol with hydrocortisone and clindamycin	Normal and healthy at 3 months
Mitchell *et al*., 2020[16]	35 years	Copious, yellow vaginal discharge for the past 15 years	Multiple erythematous papules on the urethral meatus, vagina, and cervix	-	Vaginal application of estradiol with hydrocortisone and clindamycin	Healthy and symptom-free at follow-up
Shabeer and Gopinath, 2021[17]	41	Contact bleeding for 2 weeks	A small polyp measuring 1.5 cm×1 cm×0.5 cm was seen protruding through the cervix	-	Polypectomy	Symptom-free at 2 months
Sharma *et al*., 2023[6]	42	Postcoital bleeding for 1 month	A small cervical polyp measuring 0.9 cm×0.5 cm×0.4 cm	Not mentioned	Polypectomy	Symptom-free at 2 months

HPV: Human papillomavirus, LSIL: Low-grade squamous intraepithelial lesion, STIs: Sexually transmitted infections

other pathologic conditions. Plasma cell-rich chronic cervicitis, including Russell body cervicitis, not only needs to be distinguished from other inflammatory and neoplastic plasma cell-rich lesions but also needs to be investigated thoroughly to rule out any underlying or coexisting epithelial neoplastic process. If there is epithelial dysplasia, either squamous or glandular, in the cervical biopsy showing dense inflammation in the subepithelial region, a diligent microscopic evaluation along with immunohistochemistry should be carried out, for ruling out single-cell infiltration of neoplastic cells, for appropriate tumor staging. A remote possibility is that the Russell bodies, if present in large numbers, can raise a suspicion of primary or metastatic signet ring cell adenocarcinoma, which can be confirmed by performing a pan-cytokeratin immunostaining.[18] Furthermore, any infective etiology, such as fungal etiology, has to be ruled out, especially in cases with HIV-positive status. In the present case, periodic acid–Schiff (PAS) and Grocott methenamine silver stain did not reveal any fungal element and neither did the ectocervix display any cytologic atypia. Malakoplakia, a chronic inflammatory

Table 2: Comparison of plasma cell-rich inflammations of the cervix

	Russell body cervicitis	Malakoplakia of cervix[19,20]	Extramedullary plasmacytoma of cervix[21,22]
Incidence	Not known, less than 15 cases reported in the literature	Not known, <15 cases reported in the literature	Not known, <10 cases reported in the literature
Clinical presentation	Contact bleeding, endocervical polyp, copious yellow vaginal discharge, erythematous papules on cervix, rarely as LSIL/HSIL on Pap smear	vaginal discharge, bleeding, or discomfort, sometimes soft, yellow-brown plaques or nodules	Abnormal bleeding, pelvic pain, or other gynecological symptoms
Most common site (for similar presentation, outside the FGT)	Gastrointestinal tract, most commonly the stomach	Urinary bladder. In the female genital tract-vagina	Upper respiratory tract (80% of cases)
Associated disease	HIV, HPV-positive status	Acquired immunosuppression such as HIV, corticosteroid therapy	MM
Etio-pathology	Often associated with conditions characterized by chronic stimulation of the immune system, such as certain infections, autoimmune diseases, or plasma cell disorders	Often linked to chronic bacterial infections, especially those caused by certain bacteria such as *Escherichia coli*	Often associated with plasma cell disorders such as MM. However, plasmacytomas can occur as solitary lesions without evidence of widespread disease
Histopathology	Predominantly plasma cell-rich inflammation in the subepithelial stroma, with intense eosinophilic intracytoplasmic inclusion, causing peripheral displacement of the nucleus, termed Russell bodies	Accumulation of large histiocytes (immune cells) with distinctive intracytoplasmic basophilic (blue) inclusions known as Michaelis–Gutmann bodies	Diffuse sheets of atypical plasma cells with lambda light chain restriction
Treatment	No evidence-based guidelines available at present Polypectomy if polyp is present Usually, no treatment is required. Some authors have tried local application of estrogen in combination with antibiotics and steroids	No evidence-based guidelines available at present Addressing the underlying infection, if present, and may include antibiotics such as ciprofloxacin or trimethoprim–sulfamethoxazole. In some cases, surgical excision of the affected tissue may be necessary	Local therapies such as surgery or radiation therapy In cases where there is evidence of systemic involvement or progression to MM, systemic treatments such as chemotherapy
Need for follow-up	Usually not required	Usually not required	Extramedullary plasmacytomas carry a risk of progressing to systemic disease, so need surveillance to achieve the most optimal long-term survival outcome

HSIL: High-grade squamous intraepithelial lesion, LSIL: Low-grade squamous intra-epithelial lesion, HPV: Human papillomavirus, MM: Multiple myeloma, FGT: Female genital tract

lesion, can rarely present as a plasma cell-rich lesion of the cervix. It is characterized by the presence of diagnostic PAS-positive Michaelis–Gutmann bodies, which was absent in this case. A summary of the plasma cell-rich chronic cervical inflammations such as Russell body cervicitis and malakoplakia and plasmacytoma is presented in Table 2. Our case showed an admixture of mature lymphocytes with the plasma cells, which suggests a reactive or nonneoplastic phenomenon. In cases of plasma cell dyscrasia, there would be sheets of mature and immature plasma cells that will either show either kappa or lambda light chain restriction.[22]

Conclusion

Russell's body cervicitis is an extremely uncommon condition with only a handful of cases documented in literature. Histopathology is the gold standard toll for its diagnosis. Immunohistochemistry of special stains is not imperative for diagnosis but can act as a supplementary ancillary tool to clear any diagnostic dilemma. Its association with HIV-positive status needs to be further evaluated to find possible associations and labeling it as an "AIDS-defining illness." Increased awareness and further studies on these lesions will aid in understanding the possible etiologies and identifying specific causative agents that would help in establishing specific nonsurgical treatment protocols.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and that due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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