Lymphoepithelioma-like Carcinoma of Cervix: An Incidental Finding in a Case of Abnormal Uterine Bleeding

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Abstract

Introduction: Lymphoepithelioma-like carcinoma (LELC) of cervix is relatively an unusual variant of squamous cell carcinoma (SCC). LELC carries a favorable prognosis compared to conventional SCC of cervix and also differs from it on morphologic basis.

Case presentation: A 38-year-old female underwent abdominal hysterectomy in the process of receiving treatment for abnormal uterine bleeding. On gross examination, apart from thickened posterior cervix, no significant pathology could be identified. Histopathologically, the cervix was involved with LELC in its posterior part.

Conclusion: LELC is considered to be a rare subtype of SCC. On histopathological examination, it simulates many other malignant and terribly fatal neoplasms. But careful discrimination of its signature clinicopathologic identity satisfactorily demonstrates the definitive diagnosis.

Keywords: Lymphoepithelioma-like carcinoma; Cervix; Squamous cell carcinoma; Syncytial

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Consent: We confirm that family members of the patients have given their informed consents for the case report to be published.

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Introduction:

Cervical cancer is the most common malignancy among women worldwide as well as in India. Its age adjusted (AAR) incidence rates per 100,000 persons range from 5.1 - 22.8 in this subcontinent [1]. Squamous cell carcinoma (SCC) accounts for 70–80% of all malignant cervical epithelial neoplasms. Of the various subtypes of SCC, lymphoepithelioma-like carcinoma (LELC) is an extremely rare variant. Among Western population it represents 0.7% of all primary cervical malignancies and that among Asians peak is as high as 5.5% [2]. Back in 1968, Hamazaki A et al first described a case of LELC [3]. Histopathologically, it closely resembles classic nasopharyngeal carcinoma. This neoplasm should be promptly differentiated from conventional SCC since it follows an indifferent clinical course with much favorable outcome [4].

However, the rarity of LELC especially in a background of high prevalence of cervical cancer in India and its potential histologic mimickers frequently pose diagnostic uncertainty for pathologists. Herein we describe a case of LELC in uterine cervix from a 38 years aged female who was treated with abdominal hysterectomy in an attempt to alleviate her abnormal uterine bleeding.

Figure 1. Grossly, normal uterine dimensions with indifferent cut-surface except thickened posterior cervical wall and a small polyp.
Case Report

A 38-year-old multigravida female presented with recurrent irregular vaginal bleeding. She was otherwise symptom-free on routine physical examination. Her pelvic examination as well as pelvic ultrasound turned out to be non-contributory in terms of detecting any specific organic dysfunction. Cervical Pap smear also failed to pinpoint any specific pathology. Initial hormonal therapy aimed at regularizing her menstrual cycle proved to be disastrous with minimal tendency towards any symptomatic relief. Finally, abdominal hysterectomy was performed preserving bilateral ovaries in situ.

Grossly, the uterine dimensions lingered over normal reference ranges. Even the cut surface was deceptively bland except the thickened posterior cervical wall. Mucosal lining of the entire uterine canal was smooth, without any appreciable signature of neoplastic involvement (Figure 1). Sections from the thickened posterior cervix and endomyometrium were subjected to histopathological examination.

Figure 2. Microscopically, invasive well-circumscribed neoplastic mass arising from the squamo-columnar junction [H&E stain, 40x] with frequent entrapment of normal endocervical glands (upper inset) [H&E stain, 40x]. Circumscription of the tumour is obvious at macroscopic inspection of stained section (lower inset).

Histologically, the ecto-endocervical junctional distinction was abolished; rather it was replaced by a well-circumscribed but infiltrative neoplastic mass arising from mucosal epithelium. The circumscription was such a prominence that it was obvious even on naked-eye inspection of the
stained section (Figure 2). Tumour was composed of undifferentiated cells in syncytial nests, surrounded by dense lymphoplasmacytic infiltrates (Figure 3). Epithelial components were frequently masked by the infiltrates in such a manner that it intimately resembled lymphoproliferative disorders under low-power objectives. Few non-involved intact endocervical glands were seen to be entrapped within the tumor confinement (Figure 2). Cytomorphologically, the neoplastic cells featured uniform round-to-ovoid vesicular nuclei, prominent nucleoli, moderate amount of cytoplasm and indistinct cell border. Severe anaplasia or high mitotic count was absent (Figure 3). Histologically, the differential considerations to this histomorphology included LELC, nonkeratinizing SCC with marked stromal inflammation, glassy cell carcinoma, non-Hodgkin lymphoma etc. However, considering its unique histological features, the neoplasm was diagnosed as ‘Lymphoepithelioma-like carcinoma’.

![Image](attachment://image.jpg)

Figure 3. Microscopically, neoplastic undifferentiated cells in syncytial nests, surrounded by dense lymphoplasmacytic infiltrate [H&E stain, 10x]. Tumour cells consist of vesicular nuclei, prominent nucleoli, moderate amount of cytoplasm and indistinct cell border (inset) [H&E stain, 40x].

The mass was absolutely focal in localization, invading within musculo-collagenous cervical stroma up to the depth of 6 mm, corresponding to stage IB of FIGO staging. Any evidence of lymphovascular or parametrical invasion could not be substantiated. Radical hysterectomy with pelvic node dissection was executed on immediate follow-up. Her metastasis workup was negative. 12 months following the diagnosis, she was free of any complications or recurrence from the disease.
Discussion

Carcinoma cervix ranks top amongst the gynecological cancers in India, in spite of the recent trend of decreasing incidence. In the year 2010, around 68,903 cases of cervical cancer were estimated to occur which may decrease to 53,654 cases by the year 2020. Early age at first intercourse, multiple sexual partners, poor sexual hygiene, repeated child birth etc are some of the reproductive risk factors for cervical cancers [5].

LELC is a distinctive subtype of conventional SCC. It rarely arises in extranasal or extrapharyngeal sites. Similar tumours have occasionally been documented in skin, lung, thymus, salivary gland, stomach and tonsils [4]. Although it is equally uncommon at uterine cervix, a more than usual association is observed among Asian patients. In the cervix its prognosis is better than conventional SCC [6]. Most researchers employ strict morphologic criteria to diagnose LELC such as- complete absence of glandular or squamous differentiation, indistinct cell-margins, vesicular nuclei with conspicuous nucleoli and negativity for lymphoid markers within epithelial components [7].

Gross appearance of cervix has been variously described in SCC, ranging from focal induration or ulceration to exophytic papillary or polypoid excrescences. Endophytic growth ulcerates at surface or becomes nodular and gradually penetrates deeper within stroma to produce a hard, bulky cervix [2]. As in current case, grossly unsuspicious cervix in an endophytic SCC, is only incidentally encountered by researchers.

Microscopically, LELC is characterized by a sharply defined mass lesion, composed of undifferentiated neoplastic cells in syncytial aggregates. Tumour syncytia are surrounded as well as infiltrated by dense inflammatory infiltrate which is possibly representative of host immune response against the neoplasm [4]. Accordingly, the differential diagnoses of LELC encompass nonkeratinizing SCC with prominent stromal inflammation, glassy cell carcinoma, malignant lymphoma (especially lymphoepitheloid – Lennert's lymphoma) and metastatic nasopharyngeal carcinoma [8]. LELC needs prompt separation from these mimickers as it harbors a relatively favorable outcome. Careful deliberation of every minute pathological detail along with clinicoradiological and immunohistochemical corroborations for epithelial and lymphoid markers, aids in differentiating LELC from its aggressive differentials [4]. But similar to the discussed patient, Kaul R et al [9] also convincingly diagnosed a case of LELC relying solely upon the histopathological evidences.

LELC has been rarely described on exfoliative cytology. Reich O et al [8] and López-Ríos F et al [10] appreciated two rare cases of LELC on cervico-vaginal smears; as clusters of uniform, large tumor cells; often intermingled with inflammatory cells; having round-to-oval vesicular nuclei, prominent nucleoli, finely granular cytoplasm and ill-defined cell borders. On the contrary, lack of visible mucosal abnormality, localized nature of the lesion and selective sampling have often been attributed to poor diagnostic yield on cervical smears [11]. Recapitulating similar phenomenon, the pap smear in present case was interpreted as ‘negative for intraepithelial lesion or malignancy’.

Although the pathogenesis of LELC is still unclear, Epstein-Barr virus (EBV) has been suggested to have a potential role among Asians. However, its involvement is less likely in Western population. Human Papilloma virus (HPV) may also play a significant pathogenic role [2].

Cervical LELC behaves more indolently than classic SCC, with limited tendency towards nodal involvement [6]. Surgery is the best curative option. Localized, low-stage LELC is also effectively eradicated by radiotherapy [13]. The reported case was diagnosed with stage IB following abdominal hysterectomy and remained symptom-free for the next one year.

Finally to conclude, LELC is a rare variant of SCC in cervix. Histologically it mimics many other malignant and more virulent neoplasms from the same site. But its distinctive clinicopathological presentation is useful enough to clinch the diagnosis. The best ever disease-free survival is documented with surgical removal of the mass.
References