Otorhinolaryngological manifestations account for almost 80% of the various manifestations of Human Immunodeficiency Virus (HIV) infection, of which Human Papilloma Virus (HPV) associated laryngeal papilloma and laryngeal malignancy are the most common pertaining to larynx.

Case Report
A 55 year old male patient on Antiretroviral treatment since 10 years who was a chronic smoker, presented with difficulty in breathing and hoarseness of voice. Flexible laryngoscopy revealed a white, horny, wide based keratotic lesion completely covering rima glottidis resulting in obstruction of airway and stridor. Tracheostomy was done followed by endoscopic excision of the lesion. Histopathologic examination showed features of hyperkeratotic papilloma and lesion was tested negative for HPV.

Discussion
We report this case to emphasize on the differential diagnosis of laryngeal papillomatous lesion. A hyperkeratotic papilloma, with a dual aetiology of retroviral disease and smoking, presenting with stridor, the lesion being negative for HPV infection makes it uncommon from other laryngeal lesions.

Keywords
Papilloma, Hyperkeratotic; Larynx; HIV; Smoking
A 55-year-old male patient presented to ENT outpatient department with difficulty in breathing since 3 months aggravated since 3 days and hoarseness of voice since 3 years which increased over time. Patient is on Anti Retro-viral treatment (Atazanavir, Ritonavir, Lamivudine and Tenofovir) since 10 years. CD4 cell count done 2 months before presentation was 182 cells per cubic millimeter. There is significant history of smoking with a smoking index of 60 pack years and history of occasional alcohol consumption around two times in a month. No other co-morbidities like diabetes mellitus hypertension, bronchial asthma. On presentation, patient had inspiratory stridor. On laryngoscopic examination, a whitish, horny lesion was noted occupying whole of the glottis and obscuring the ventricle (Fig. 1a). The lesion was wide based with restricted movements of left hemilarynx.

Patient was taken up for surgery, primary goal was to establish the airway as the patient was in stridor due to complete blocking of the rima glottidis by the lesion. Since the lesion was extensive, THRIVE or spontaneous ventilation were not considered. The other alternative was to debulk the tumor to establish the airway and proceed with endoscopic excision, but as the tumor was very horny, it was not taken into consideration and hence the airway was established by tracheostomy. On examination, lesion was noted involving entire left vocal cord and subglottic region. It was a firm, horny lesion which was not easily separating from the left vocal cord. Right vocal cord was normal. Endoscopic complete excision of the lesion was done (Fig. 1b).

Histopathological examination of the lesion showed hyperplastic laryngeal mucosa with extensive orthokeratosis and papillomatosis (Fig. 1c). There was no evidence of atypia / malignancy and a diagnosis of hyperkeratotic papilloma was made. Further molecular examination revealed negative for human papilloma virus. Post-operative period was uneventful. There is no
evidence of recurrence till date.

Discussion

Among the Otorhinolaryngological manifestations in HIV infected individuals, the most common are oral/pharyngeal candidiasis, chronic sinusitis, serous otitis media, cervical lymphadenopathy. HPV infections can be benign and malignant. Low risk subtypes HPV 6 and 11 has certain manifestations in the head and neck, the most common among those are condyloma acuminatum, focal epithelial hyperplasia, Verruca vulgaris, oral squamous papilloma. Due to recurrent nature of HPV laryngeal papillomas, they are referred as recurrent respiratory papillomatosis. HPV negative papillomatous lesions in the larynx are not frequent as majority of the lesions are tested positive. In our patient, the specimen tested negative for human papilloma virus.

The most common predisposing factors are tobacco smoking and alcohol. Cigarette smoke contains various harmful chemicals which includes nitrosamines, radioactive compound like arsenic, cadmium, benzopyrene. Nicotine is the most harmful agent in smoke. Chronic laryngeal exposure to these harmful substances will cause alteration in the laryngeal mucosa and epithelial lining of vocal folds leading to variety of laryngeal pathologies. In a retrospective study done by Santhosh et al., on laryngeal manifestations due to smoking, the most common manifestation was laryngopharyngeal reflux (LPR) (40.62%) followed by chronic laryngitis (25%), vocal fold keratosis (18.75%), Reinke’s edema (12.50%), and malignancy (3.12%). HIV infection causes dysregulation of the immune system at various sites, in particular causes irreversible damage to the mucosal barriers. In our patient, chronic smoking could have precipitated the mucosal damage caused by underlying immunosuppressed status.

Majority of the laryngeal pathologies present with hoarseness of voice which affects the quality of life and loss of participation in social communication and development. A study by Ximenes Filho et al., on laryngeal papillomatosis found that 54.54% of patients had dysphonia and 4.54% had dysphagia and bleeding. In our case, patient had progressive change in voice since 3 years, patient had difficulty in breathing due to huge size of the lesion completely obstructing the airway resulting in stridor.

The nearest differential diagnosis of papillomatous lesion is Verruca vulgaris. It is differentiated from hyperkeratosis on histopathological examination where presence of koilocytosis in the spinous layer and atypia are present along with papillary structures, hypergranulosis and hypergranulosis. Siebal et al., reported a case of verruca vulgaris, HPV negative in a 55 year old male patient with history of smoking who presented with a nodular keratotic lesion over right vocal cord. Histopathological examination showed hyperkeratosis, hypergranulosis, koilocytes in the spinous layer confirming the diagnosis of Verruca vulgaris.

Keisuke et al reported a case of vocal cord actinomycosis where a 49 year old male patient presented with voice change since 2 years and has an irregular lesion over vocal cord which mimicked a laryngeal papilloma or tumor. Histopathological examination showed actinomycosis with vocal nodule which was treated with appropriate antibiotics. This adds on to differential diagnosis of vocal cord lesion.

In cases presenting with a laryngeal lesion obscuring the airway, the primary goal is to establish the airway and then address the underlying lesion. In this case, the huge lesion was completely occupying rima glottidis resulted in stridor which prompted the need for tracheostomy. Micro/microendolaryngeal complete excision is the treatment of choice. Patients should be under constant follow up to watch for any recurrence. They also need to be advised regarding smoking cessation and de-addiction centres.

To conclude, A dual aetiology of smoking and retroviral disease positivity could have precipitated the laryngeal mucosal damage. Immunosuppression caused by HIV infection added upon by the laryngeal mucosal damage caused by chronic exposure to various harmful carcinogenic substances would have led to development of hyperkeratotic papilloma. In this case, patient had a huge papilloma obstructing the airway resulting in stridor along with hoarseness of voice. The nearest differential that is usually considered in such a presentation is
malignancy, hence histopathological diagnosis should be established as early as possible. Endoscopic excision is the choice of treatment and the patient should be under regular follow up to watch for any recurrence. Hyperkeratotic papilloma is differentiated from the most common type verruca vulgaris on histopathological examination where the later shows presence of atypia and koilocytosis in the spinous layer. This case also emphasizes on the differential diagnosis of laryngeal papillomatous lesion and the effect of chronic exposure to smoke in an immunosuppressed individuals.

References
1. Sulyman A, Kazeem S, Abdulrahman A, David D, Kayode A, Oluwayemisi O et al., Otolaryngologic manifestations among HIV/AIDS patients in a Nigerian tertiary health institution: an update. Arquivos Internacionais de Otorrinolaringologia 2010;14(4):398-403
2. Yoshihama K, Kato Y, Baba Y. Vocal cord actinomycosis mimicking a laryngeal tumor. Case Reports in Otolaryngology 2013; 2013:1-2
3. Unsal O, Turk B, Akpinar M, Bagli M, Coskun B. Human Immunodeficiency Virus (HIV) Positive Case with Squamous Cell Larynx Cancer: Difficulties in the Choice of Treatment. Turkish Archives of Otorhinolaryngology 2015; 53:136-8
4. Purina B, Pantanowitz L, Seethala R. A review of carcinomas arising in the head and neck region in HIV-positive patients. Pathology Research International 2011; 2011:1-12
5. Swain SK, Behera I, Mohanty J. Laryngeal manifestation due to smoking among the pediatric age group–Our experiences at an Indian teaching hospital. Archives of Medicine and Health Sciences 2019; 7:186
6. Longubuco CE, dos Reis HL, Cavalcante FS, de Pinho CR, et al. Dysphonia as a sign of HPV laryngeal infection: a case report. BMC Research Notes 2014;7(1):898. doi: 10.1186/1756-0500-7-898
7. Oliveira LH, Cavalcanti S, Andrade DD, Fonseca EC. Laryngeal papillomatosis in an AIDS patient. Memórias do Instituto Oswaldo Cruz 1998; 93:827-9
8. Kariche N, Hortal MT, Benyahia S, Alemany L, et al. Comparative assessment of HPV, alcohol and tobacco etiological fractions in Algerian patients with laryngeal squamous cell carcinoma. Infectious Agents and Cancer 2018;13(1)
9. Ximenes Filho JA, Simoceli L, Imamura R, Tsuji DH, Sennes LU. Papilomatose laringea recorrente: experiência de 10 anos. Revista Brasileira de Otorrinolaringologia 2003; 69(5):599-604
10. Yildirim S, Tezcaner ZÇ, Fatullayev T, Dursun G. Laryngeal verruca vulgaris Presenting with Dysphonia: A Case Report. Turkish Archives of Otolaryngology 2017; 55(4):184-6.