

Penetapan potensi metastasis kelenjar getah bening lokoregional pada karsinoma sel skuamosa laring: pemeriksaan ekspresi biomarka HPV, EGFR, MMP-9, timp-1, vegf, e-kaderin, dan kolagen tipe IV = Potential metastatic locoregional lymph nodes on squamous cell carcinoma larynx examination of biomarker expression HPV, EGFR, MMP 9 timp 1 vegf e cadherin and collagen type IV / Fauziah Fardizza

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Abstrak

ABSTRAK

Biomarka untuk memprediksi metastasis KGB lokoregional sampai saat ini belum akurat. Angka metastasis tersamar pada karsinoma laring bervariasi yaitu 165%. Dibutuhkan biomarka tumor yang dapat memberikan informasi adanya metastasis KGB lokoregional pada pasien KSS laring stadium lanjut tanpa keterlibatan KGB lokoregional (N0), sehingga diharapkan menjadi acuan untuk dilakukan diseksi leher selektif. Beberapa biomarka yang berhubungan dengan agresivitas dan prediksi metastasis yaitu Epidermal Growth Factor Receptor (EGFR), Matrix Metallo-proteinase (MMP)-9, Tissue Inhibitor Metallproteinase (TIMP)-1, Vascular Endothelial Growth Factor (VEGF), Epithel Calcium Adhesi (Ekaderin) dan kolagen tipe IV serta HPV dapat digunakan untuk memprediksi luaran pada status pasien tumor dengan dan tanpa metastasis.

Penelitian ini ingin memeriksa peran infeksi HPV sebagai faktor onkogenesis dan kejadian metastasis KGB leher pada keganasan laring berdasarkan biomarka sebagai penetapan diagnosis metastasis KGB lokoregional.

Dilakukan Cross-sectional, double blind study dengan pengumpulan data sekunder dari rekam medis di Departemen THT-KL FKUI-RSCM. Pemeriksaan ekspresi biomarka dan status HPV dilakukan terhadap jaringan berupa blok parafin dari pasien karsinoma laring. Ekspresi biomarka dilakukan dengan pemeriksaan imunohistokimia, dan identifikasi virus HPV dengan nested PCR, dilanjutkan dengan flow-through hybridization.

Didapatkan proporsi HPV KSS laring sebanyak 28,7% dengan infeksi HPV risiko tinggi sebanyak 9,15% dan HPV 16 merupakan tipe yang terbanyak. Analisis multivariat Mantel-Haenszel didapatkan ekspresi tinggi biomarka EGFR, MMP-9 dan VEGF berperan terhadap kejadian metastasis KGB pada KSS laring stadium lanjut tanpa infeksi HPV dengan OR 3,38; 5,14. Keadaan tersebut tidak berperan lagi bila terdapat infeksi HPV. Dari penelitian ini didapatkan suatu algoritma penatalaksanaan KSS laring stadium lanjut khususnya untuk penentuan tatalaksana diseksi leher pada N0.

Infeksi HPV didapati pada KSS laring stadium lanjut, HPV 16 merupakan tipe HPV yang terbanyak. Biomarka penanda metastasis didapatkan pada EGFR; MMP-9; VEGF dengan kekuatan 2;1;6.

ABSTRACT

Biomarkers to predict locoregional lymph nodes metastasis is not yet accurate until now. The number of occult metastasis in laryngeal carcinoma varies between 165%. A tumor biomarker that can give information on the existence of locoregional lymph node involvement in patients with or without signs of clinical locoregional lymph node involvement, as guidelines whether selective neck dissection is needed in N0 cases. For patients that need additional treatment biomarkers that are correlated with aggressivity and metastasis prediction such as EGFR, MMP-9, TIMP-1, VEGF, E-cadherin, collagen Type IV and HPV are also needed to predict the outcome of patients with or without lymph node metastasis.

This study aimed to investigate the evidence of HPV infection in laryngeal carcinoma and the role of biomarkers EGFR, MMP-9, TIMP-1, VEGF, E-cadherin and collagen type IV, in a late stadium laryngeal SCC observed clinically, especially in N0 and also to predict diagnosis of a locoregional lymph node that has potential for metastasis. Cross-sectional, double blind study with planned data collection was performed in the Department of ENT FKUI-RSCM. Data were taken from Formalin Fixed Paraffin Embedded (FFPE) of laryngeal cancer specimen after laryngectomies. Samples were analysed by nested Polymerase Chain Reaction (PCR) and continuous flow-through hybridization for genotyping. Expression of EGFR, MMP-9, TIMP-1, VEGF, Ecadherin, and collagen Type IV as metastasis biomarker were evaluated by immunohistochemistry.

Overall HPV proportion in laryngeal cancer was 28.7%. A total of 9,15% laryngeal cancer patients were infected with high risk HPV type and HPV 16 was the most frequently observed. Mantel-Haenszel multivariate analysis found that HPV infection did not play role in neck metastasis eventhough there were positive evidence of metastasis biomarker. In contrast, the absent of HPV infection, positif metastasis biomarker of EGFR and VEGF have risk for neck nodes metastasis with OR 3.38; 5.14 fold consecutively. The algorithm was formed from the PM model to determine the metastasis potential to locoregional lymph nodes of late stadium laryngeal SCC with N0.

HPV was found to be the oncogenic factor of the laryngeal SCC and HPV 16 was the most frequently observed type in laryngeal SCC. Biomarkers to predict locoregional lymph nodes metastasis are EGFR; VEGF with strenght 2;1;6.