Detection high-risk HPV DNA in chagasic megaesophagus with and without cancer

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BACKGROUND: Esophageal cancer (EC) is the 8th most common type of cancer worldwide and is often the squamous cell carcinoma type (SCC). The main risk factors related to EC development are smoking, alcohol consumption, the chagasic megaesophagus (CME), common digestive chronic manifestation of Chagas Disease, and HPV, although the role of the last is controversial. Our group previously detected mutations in the suppressor *TP53* gene (Lacerda, C dissertation), which are closely related to the development of EC and CME, with or without cancer. However, there are still no reports that demonstrate the relationship between the presence of HPV, EC and CME. Therefore, it is considered important to investigate whether there is HPV with or without cancer and to evaluate its relationship with proteins associated with the EC.

OBJECTIVE: To carry out the detection of high-risk HPV DNA in CME and evaluate the expression of proteins related to cancer and associated with HPV. Correlate the results with the clinical and demographic information related to molecular and mutation status of *TP53*.

METHODS: Samples retrospectively collected from the southeast region of Brazil obtained from patients treated in two participating hospitals Universidade Federal do Triangulo Mineiro (UFTM) e Hospital de Cancer de Barretos (HCB) and healthy control samples obtained from Barretos will be used. They are divided into three groups: SCC (n = 59), CME (n = 34) and SCC/CME (n = 23). DNA integrity analysis will be made by conventional PCR and detection of high-risk HPV by multiplex PCR (Luminex) and immunohistochemistry for markers p16 and p53.

RESULTS: The characteristics of our population are described below. For EC group: 84.7% men, mean age of 58.2 years and 62.5% with family history of cancer. For CME: 85,3% men, mean age of 52,85 years and without family history of cancer in 90%. For SCC/CME: 87,9% men, mean age 58,43 years and family history of cancer in not viewed in 75% of cases. Clinical characteristics: SCC 88.1% smoked 81.4% drank, had no CME, 79.5% had no esophagitis; CME 56.2% smoked 64.5% drank, 88.2% had CME degree III and IV, 81.3% had esophagitis; SCC/CME 77.4% smoked 83.3% drank, 72.7% had CME degree III and IV, 81.5% had no esophagitis. However, CME group showed a lower frequency of family history of cancer compared with other groups and the risk factors associated with the SCC/CME were smoking and alcohol. Molecular characterization/mutation profile of the *TP53* gene: non-silent mutations was higher in SCC (45%) followed by the SCC/CME (38.7%) and CME (10.3%); the missense mutations were frequent in the 3 groups; the distribution of *TP53* gene mutations in exon 8 SCC group was the most mutated (55%), CME occurred exclusively in exons 6, SCC/CME exons 5 and 8 were the most mutated. The data suggested that mutations in the *TP53* gene appears to be a critical event in carcinogenesis SCC/CME group; and in the CME group, although less frequent, they may occur at pre-malignant lesions in the esophagus, in the presence of other co-factors, may lead to the development of cancer.