Recurrent genetic changes in intestinal-type sinonasal adenocarcinoma

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Introduction

Sinonasal adenocarcinoma is a rare epithelial head and neck tumor located mainly in the ethmoid sinus. The most frequent histological type resembles adenocarcinoma of the colon and is called intestinal type adenocarcinoma or ITAC. The etiology includes professional exposure to wood dust. Little is known about the genetic changes in these tumors.

Objectives

The aim of this study was to identify genome-wide recurrent DNA copy number changes and to evaluate their relation to clinico-pathologic characteristics.

MATERIAL & METHODS

PATIENTS
44 patients with sinonasal adenocarcinoma - mean age: 64 years (range 40-92 years)
- stage I:15, stage II:7, stage III:15, stage IV:12
- Histopathology: 6 papillary, 13 colonic, 10 solid and 9 mucinous type
- no patient had metastases at the time of diagnosis.

MICROARRAY CGH

Tumor DNA and reference DNA were differently labeled by random priming and hybridized to the array. Hybridization and washing took place for two nights in a specialized hybridization chamber (GenetTAC Hybridize 12 hybridization (Genomic Solutions/Parker Elmer). Images were acquired using a Microarray Scanner G2505B (Agilent Technologies). Analysis and data extraction were quantified by BlueFuse (BlueGnome, Cambridge, UK). Gains and losses were defined as at least two neighboring clones with deviations of 0.2 or more from log2 ratio=0.0. High level amplification was considered when at least two neighboring clones reached a log2 ratio of 1.0 or higher.

MLPA

Overview of all gains (bars to the right) and losses (bars to the left)

RESULTS

Overview of the four histopathological types of ITACs

Results statistics

Three genetic alterations correlated to overall survival: loss TIMP2 (17p25), loss RENT2 (10p14) and gain TANK (2q24). Of these three, loss TIMP2 also correlated with clinical stage (Chi2 p=0.029) and with histopathological type (Chi2 p=0.052).

CONCLUSION

1. Sinonasal adenocarcinoma have their own pattern of chromosomal abnormalities and probably also their own multistep pathway of cancer development and progression.
2. Most frequent gains were at 5p15, 8q24 and 20q13 and most frequent losses were at 4q31-qter, 18q12-22, 8p12-pter and 5q11-qter. High level amplifications were detected at 11p11, 11q13.3, 11q22.1, 13q12.1 and 13q12.1.
3. Losses of TIMP2 was associated with worse survival (p=0.017), as well as losses of RENT2 (p=0.0012) and gains of TANK (p=0.019).
4. The stage T4 tumors presented a greater number of losses of TIMP2 (Chi2 p=0.003) and IL2 (Chi2 p=0.005), compared to T1-T3 stages. The solid and mucinous type tumors presented more gains of MYC (Chi2 p=0.039) and PTPN1 (Chi2 p=0.022) than the papillary and colonic type.
5. TIMP2, IL2, RENT2, TANK, MYC and PTPN1 could play a role in the tumorigenesis of the ITACs.

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Left: Analysis of PCR products of a MLPA experiment. Right: Final MLPA results after calculating copy number ratios between the sample and normal control. This case had a number of deletions, including TIMP2 (17p25, see arrow).