Rev Esp Patol 1999; Vol. 32, N~ 3: 43 1-435

Short Course 9

Update on salivary gland tumors

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Head and neck pathology incorporates aspects of anatomical and surgical pathology, otorhinolaryngology, as well as oral surgery, medicine and pathology. Over the past few years immunohistochemistry and molecular biology have contributed to greater understanding in this area, especially in the classification and prognostic evaluation of salivary gland tumors. Therefore, this short course will review some practical diagnostic problems and give insights into the relevance of molecular biology in this field. The main topics will be:

- Criteria for the diagnosis of malignancy in pleomorphic adenoma.
- Characteristics to distinguish between the different types of clear cell tumors.
- Oncocytic lesions and squamous differentiation in salivary gland tumors.
- The progression of low-grade carcinomas to high-grade neoplasms.
- Relevant recent advances in molecular biology and immunohistochemistry.

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Malignancy in pleomorphic adenoma

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Introduction

Pleomorphic adenoma (PA) (benign mixed tumor) of the salivary glands is clinically and pathologically benign but the concept of malignancy in it is much more complex than appears at first sight. The multinodular and pseudoinfiltrative growth pattern can make complete surgical excision difficult and can lead to recurrences. Microscopically, benign PA may display hypercellularity, cellular atypia, necrosis and capsular and vascular invasion (1), whereas there are PAs that contain genuine histological evidence of malignancy, either *in situ* or minimally invasive, but which behave in a benign fashion after excision.

Incidence

The frequency of malignancy in a PA *(i.e.,* malignant mixed tumor) varies in different surveys (2, 3); the average of several large series was 3.6% of all salivary tumors, 11.7% of malignancies and 6.2% of PAs (range 1.9-23.3%).

Forms of malignancy in a pleomorohic adenoma

Three entities are recognized (in order of frequency): carcinoma in pleomorphic adenoma, carcinosarcoma (true malignant mixed tumor) and metastasizing pleomorphic adenoma.

Carcinoma in a oleomorphic adenoma

This typically presents with a long history of a salivary gland nodule that suddenly gets bigger. The incidence of malignancy increases with the length of history of the PA but the time interval can still be short (2). The main histological finding is the simultaneous presence of a benign PA and a carcinoma. The proportion of the malignant component varies from minute foci to major parts of the PA. The most common types of carcinoma are poorly differentiated adenocarcinoma and undifferentiated carcinoma [many ot which were found to be myoepithelial by K. Nagao *et al.* (2), and also by us in Milan (4)], but others can occur, *e.g.,* squamous, mucoepidermoid, polymorphous low grade adenocarcinoma and ductal carcinoma (3).

The criteria for a diagnosis of malignancy are capsular invasion, infiltration into neighboring tissues, vascular involvement and abnormal mitotic figures (2). Minor findings are the presence of hyalinization, necrosis and increased mitotic activity, with occasional transitional changes made up of cells sharing features intermediate between frank malignancy and PA. A recent practical development may be the use of the proliferation marker Ki-67 (MIBi); carcinoma within a PA usually shows a markedly increased MIBi index.

Once a carcinoma has been identified in a PA, it is important to assess its relationship to the capsule of the PA. If the malignant element has invaded into the capsule but does not extend beyond it, the prognosis should be similar to that of ordinary benign PA – this is minimal capsular invasion. This is the case even when the malignant component is an aggressive neoplasm, such as salivary duct carcinoma, provided there is no extension through the capsule (1). However, there are practical problems when the capsule is incomplete or inadequately sampled. When a carcinoma invades beyond the capsule, its extent is important: Tortoledo *et al.* (3) found that