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WARTHIN TUMOR

Dr Puja Bansal (professor) , Muskan Roria, Tanushi Dixit, Anjali verma

Affiliated by : school of dental sciences sharda University

ABSTRACT

Warthin tumor is the second most common tumor of salivary gland. This tumor was first recognized by Albrecht in 1910 and later described by warthin in 1929. It represents about 2% to 15% of all primary epithelial tumors of the parotid gland. Warthin tumor is histologically characterized by a dense lymphoid stroma and a double layer of oncocytic epithelium with a papillary and cystic architectural pattern. Its etiology remains controversial.

Key Words- Histopathology,pathophysiology,complications

Introduction

Initially described by Hildebrand in 1895, Warthin tumor (also known as cystadenolymphoma), is a benign and frequent salivary gland neoplasm. It represents about 2% to 15% of all primary epithelial tumors of the parotid gland. Extra-parotid Warthin tumor is very rare and may occur in the periparotid lymph node, nasopharynx, eyelid, and oral cavity. Warthin tumor is histologically characterized by a dense lymphoid stroma and a double layer of oncocytic epithelium with a papillary and cystic architectural pattern. Its etiology remains controversial.[1]

Etiology

The etiology of Warthin tumor has not yet been fully established. Some authors stipulated that this benign neoplasm arises as a result of some tumourigenic effect on epithelial inclusions located in the lymph nodes adjacent or the parotid gland.[2] Etiologic factors of Warthin tumor have been said to encompass Epstein Barr virus infection, tobacco, autoimmune disease, ionizing radiation, and chronic inflammation.[3] However, several questions remain regarding the male predominance in Warthin tumors and why tobacco should predominantly affect the parotid gland rather than the intraoral minor salivary glands.[3] Malignant transformation of Warthin tumor is extremely rare and accounts for 0.3% of the cases.[4]

Epidemiology

Warthin tumor is the most common 'monomorphic' adenoma of the major salivary glands. It accounts for about 2% to 15% of all parotid tumors.[5] It is the second most frequent benign neoplasm of the salivary glands after pleomorphic adenoma. Warthintumor occasionally occurs in young patients. In women, the peak incidence is in the 6th decade, whereas it is in the 7th decade in men. There is an apparent male predilection for the occurrence of Warthin tumor, although, with the recent reports, the difference in the sex ratio is declining.[6]

Pathophysiology

Warthin tumor is the only benign neoplasm of salivary glands associated with smoking.[7] The origin of this tumor is still debated despite the numerous theories concerning its histogenesis mentioned in the literature. [6] Numerous theories have been advocated, with each having different interpretations. Initially, *Hildebrand* proposed that the lesion may be remnants of the branchial pouches and a variant of the lateral cervical cyst. Later, *Albrech* and *Artz* proposed the heterotropic origin of Warthin tumor from the neoplastic proliferation of salivary gland ducts present within intra- or para-parotid nodes. This theory is widely accepted and was sustained by immunohistochemistry findings, which demonstrated that basal and luminal epithelial cells of Warthin tumor bear characteristics similar to those of the basal cells and striated duct cells of the excretory duct of the salivary gland.[6] Only a

small subset of Warthin tumors present the t(11,19)(q21,p13) translocation and expression of the chimeric genes. These Warthin tumors are often classified as infarcted or metaplastic Warthin tumors.[8] Some authors suggested that the different histologic subtypes of Warthin tumor (epithelial predominance, mixed, lymphoid predominance) may result from staged pathogenetic development in which the lymphoid predominance subtype constitutes the early stage, followed by the mixed and the epithelial predominance subtypes.[9] This spectrum of modifications could be triggered by different and mostly unidentified pathogenetic factors, such as tobacco smoking, autoimmune disorders, or Epstein-Barr virus infection.[3] Interestingly, the latter was detected in very close association with multiple/bilateral Warthin tumors, in comparison with solitary Warthin tumors.[10]

Histopathology

Macroscopic Findings

Grossly, Warthin tumor is a well-circumscribed spherical to oval mass. On cut section, there are solid areas and multiple cysts with papillary projections. The cystic spaces often contain mucoid creamy brown or white fluid.[11]

Cytology

Smears characteristically show oncocytic epithelial cells without atypia admixed with polymorphous lymphocytes and cellular debris. Mucinous differentiation and squamous cells with mixed inflammation and cytological are rarely encountered.[12] Fine needle aspiration cytology is a useful method for preoperative assessment of Warthin tumors. However, its accuracy is controversial compared with other methods. The confirmation of diagnosis with certainty relies on histopathological examination.

Microscopic Findings

Warthin tumors are composed of varying proportions of papillary- cystic structures lined by oncocytic epithelial cells and a lymphoid stroma with germinal

centers. The epithelial component is formed of inner columnar and outer cuboidal cells. Some foci of mucous, ciliated, sebaceous, and squamous cells can be present in Warthin tumors. A granulomatous reaction can be seen in some cases. infarcted or metaplastic tumors may have marked mucinous or squamous metaplasia and stromal reaction, which may present diagnostic challenges.

The diagnosis of malignant transformation of Warthin tumor to carcinoma relies on :

- The presence of a Warthin tumor;
- The presence of transitional zones from a benign oncocytic to a malignant epithelium;
- The presence of an infiltrating growth in the surrounding lymphoid tissue;
- and the exclusion of metastasis to lymphoid stroma from another primary carcinoma.

Immunohistochemical study

- The epithelial component is immunoreactive for cytokeratin cocktail.
- The lymphoid portion shows kappa and lambda light-chain polyclonality

History and Physical

Clinically, Warthin tumor presents as a rounded or an ovoid nodular painless, slow-growing, fluctuant to firm at palpation. It can be unilateral, bilateral, or multicentric and is asymptomatic in 90% of cases. Warthin tumor induces little or no pain, ear ringing, ear pain, and hearing loss in some cases. The size of a Warthin tumor can be several millimeters to centimeters and two to four centimeters on average.

Treatment / Management

The optimal treatment of Warthin tumor relies on surgical removal, which can be easily realized due to the superficial location of the tumor. Some surgeons prefer the superficial parotidectomy to avoid the rupture of the tumor capsule, whereas others chose local resection with the surrounding tissue.[2] Some authors considered that the likelihood of malignant transformation of Warthin tumors is only 0.3% and that it is a frankly benign neoplasm of the salivary glands. Hence,

they certified that enucleation was the best treatment modality for this tumor. Another study stipulated that parotidectomy reduces the recurrence rate of Warthin tumor significantly because of its possible bilaterality and multicentricity.

Since the Warthin tumor is well-defined and because of its superficial location on the surface layer of the parotid gland, some authors prefer to perform superficial parotidectomy. The best treatment option for Warthin tumor located in the deep lobe is deep parotidectomy following superficial parotidectomy and confirmation of the facial nerves. According to some authors, since Warthin tumor is often located in the tail of the parotid gland, partial parotidectomy could be a relevant option. Partial parotidectomy excises not only the bottom branches of the facial nerves but also the tumor, including the neighboring normal tissues.

Differential Diagnosis

Histological differential diagnosis

- Lymph node metastases: usually there is marked cellular atypia. Lymph node metastases are devoid of the bilayered, oncocytic epithelial element
- Sebaceous lymphadenoma: it is devoid of the bilayered, oncocytic epithelial element
- Cystadenomas of the salivary glands: they can be oncocytic however, they are devoid of lymphoid stroma and usually have small, multilocular cystic spaces.
- Lymphoepithelial cysts

Prognosis

Warthin's tumor has a favorable prognosis and almost never recurs. Malignant degeneration of Warthin tumor is very rare. In such cases, a close follow-up of the patients is mandatory so as to detect metastases. According to some authors, the enucleation of Warthin tumor or follow-up without removal may be sufficient.

Complications

Local Recurrence

The local recurrence rate is low; when recurrence does occur, it is probably due to multifocal tumors or inadequate excision.

Malignant Transformation

Malignant transformation in a Warthin tumor is extremely rare; however, there are a few reported examples in both the epithelial and the lymphoid component. The most frequent histological types of malignant transformation in a Warthin tumor are mucoepidermoid carcinoma, squamous cell carcinoma, undifferentiated carcinoma, oncocytic adenocarcinoma, and adenocarcinoma.

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