

## THE REACTION OF MAST CELL IN THE PAROTID GLAND ON CHAIN ALCOHOL INTOXICATION

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The parotid gland is a major salivary gland in many animals. In humans, the two parotid glands are present on either side of the mouth and in front of both ears. They are the largest of the salivary glands. Each parotid is wrapped around the mandibular ramus, and secretes saliva through the parotid duct into the mouth, to facilitate mastication and swallowing and to begin the digestion of starches. The parotid glands are a pair of mainly serous salivary glands located below and in front of each ear canal, draining their secretions into the vestibule of the mouth through the parotid duct [1]. Each gland lies behind the mandibular ramus and in front of the mastoid process of the temporal bone. The gland can be felt on either side, by feeling in front of each ear, along the cheek, and below the angle of the mandible [2]. The gland is roughly wedge-shaped when seen from the surface. The parotid duct, a long excretory duct, emerges from the front of each gland, superficial to the masseter muscle. The duct pierces the buccinators muscle, then opens into the mouth on the inner surface of the cheek, usually opposite the maxillary second molar. The parotid papilla is a small elevation of tissue that marks the opening of the parotid duct on the inner surface of the cheek [3]. The gland has four surfaces – superficial or lateral, superior, anteromedial, and posteromedial. The gland has three borders – anterior, medial, and posterior. The parotid gland has two ends – superior end in the form of small superior surface and an inferior end (apex). Chronic and frequent alcohol (ethanol [EtOH]) intake has been associated with an increased incidence of several types of cancers including breast, mouth, throat, esophageal, stomach, and colorectal (CRC). The underlying mechanism of this deleterious carcinogenic effect of alcohol has not been clearly established but inflammation may be one unifying feature of these cancers. We have recently shown that parotid mast cells play a central role in parotid carcinogenesis. In this study, we tested our hypothesis that mast cell-mediated inflammation is one underlying mechanism by which chronic alcohol promotes parotitis tumorigenesis.

**Keywords:** Adenoid cystic carcinoma, mast cell, mucoepidermoid carcinoma, pleomorphic adenoma, salivary gland tumor

Cells in labial salivary glands obtained from patients with xerostomia with or without focal sialadenitis/Sjogren's syndrome were studied.

There was no significant correlation between the intensity of local lymphocyte infiltration and the morphometrically analysed number of mast cells staining positive with toluidine blue.

Histamine staining with heterologous IIC antiserum showed significantly fewer positive cells than staining with toluidine blue. This suggests heterogeneity of the mast cell population.

Furthermore, there was a correlation between the focus score and the number of mast cells containing histamine.

This suggests that the proliferation of mast cells containing histamine may be locally regulated by the immune inflammation, possibly through mediators from macrophages and fibroblasts.

Mast cells were previously studied by metachromatic toluidine blue staining of the labial salivary glands of patients fulfilling the 1958 criteria of the American Rheumatism Association for RA. The study showed that the number of mast cells was higher in patients than in healthy controls.

### Parotitis

*Main article: Parotitis*

Inflammation of one or both parotid glands is known as parotitis. The most common cause

of parotitis is mumps. Widespread vaccination against mumps has markedly reduced the incidence of mumps parotitis. The pain of mumps is due to the swelling of the gland within its fibrous capsule [1].

Apart from viral infection, other infections, such as bacterial, can cause parotitis (acute suppurative parotitis or chronic parotitis). These infections may cause blockage of the duct by salivary duct calculi or external compression. Parotid gland swellings can also be due to benign lymphoepithelial lesions [*clarification needed*] caused by Mikulicz disease and Sjögren syndrome. Swelling of the parotid gland may also indicate the eating disorder bulimia nervosa, creating the look of a heavy jaw line. With the inflammation of mumps or obstruction of the ducts, increased levels of the salivary alpha amylase secreted by the parotid gland can be detected in the blood stream.

### Salivary stones

Salivary stones mainly occur within the main confluence of the ducts and within the main parotid duct. The patient usually complains of intense pain when salivating and tends to avoid foods which produce this symptom. In addition, the parotid gland may become enlarged upon trying to eat. The pain can be reproduced in clinic by squirting lemon juice into the mouth. Surgery depends upon the site of the stone: if within the anterior aspect of the duct,

a simple incision into the buccal mucosa with sphincterotomy [*clarification needed*] may allow removal; however, if situated more posteriorly [*clarification needed*] within the main duct, complete gland excision may be necessary.

### Injury

The parotid salivary gland can also be pierced and the facial nerve temporarily traumatized when an inferior alveolar local anesthesia nerve block is incorrectly administered, causing transient facial paralysis [2].

### Materials and methods of research

Patients Labial salivary gland biopsy specimens were obtained from 12 patients, who had all given their informed consent to the biopsy. The project was also accepted by the local ethical committee.

Eight patients had Sjogren's syndrome according to the Copenhagen criteria<sup>9</sup>- two had primary Sjogren's syndrome and six secondary Sjogren's syndrome associated with RA according to the 1987 criteria of the American Rheumatism Association.

The remaining four patients had other diseases-two patients had RA, one systemic lupus erythematosus, and one sialolithiasis.

The patients who did not, in the final evaluation, have Sjogren's syndrome, were suspected of having that condition on clinical grounds.

### Demonstration of mast cells with toluidine blue staining

For staining with toluidine blue the frozen glands were cut in a cryostat. The specimens (6, mm thick) were fixed in cold (4°C) acetone for five minutes. After fixation the specimens were washed in phosphate buffered saline (PBS), pH 7-2, and then stained with toluidine blue for five minutes. After staining, the specimens were washed in running water for 10 minutes, dehydrated in alcohol, cleared, and then mounted.

### Immunohistochemical staining for mast

CELLS The frozen specimens (6 mm thick) were fixed in paraformaldehyde for five minutes and then washed in PBS. Intrinsic peroxidase was inhibited by pretreating the specimens

The tissue sections were incubated in 3,3-diaminobenzidine tetrahydrochloride (50 mg in 150 ml PBS) with 0.003% H<sub>2</sub>O<sub>2</sub> substrate for seven minutes and then washed in PBS. Counterstaining was performed with haematoxylin.

The specimens were finally washed, dehydrated, cleared, and mounted. To test the specificity of the immunoperoxidase staining the first antiserum was replaced by either PBS or normal rabbit serum. TRANSMISSION ELECTRON MICROSCOPY Several small (about 1 mm<sup>3</sup>) pieces were cut for ultrastruc-

tural study from three patients with Sjogren's syndrome.

### Results of research and their discussion

After staining with toluidine blue the metachromatic mast cells were seen as violet, granular mononuclear cells. Histamine staining using 1 IC antiserum in the peroxidase-antiperoxidase method stained mast cells brown. Mast cells were usually located in the periphery of the lymphocyte foci or diffusely scattered in the salivary tissue stroma. Staining controls confirmed the specificity of immunoperoxidase staining.

In this study the presence of mast cells in labial salivary gland biopsy specimens was shown by histochemical toluidine blue staining, immunohistochemical histamine staining, and transmission electron microscopic evaluation of the fine structure.

Toluidine blue staining shows the proteoglycan matrix of the mast cell granules, the heterologous 1 IC antiserum labels mast cell mediator histamine, and transmission electron microscopy demonstrates the typical ultrastructure.<sup>5 16</sup> Although mast cells show heterogeneity in their histochemical, functional, and morphological criteria,<sup>7</sup> our study, based on three different, independent methods, established beyond any doubt that mast cells are present in diseased salivary glands in Sjogren's syndrome.

Mast cells have been implicated in various diseases, particularly allergic rhinitis, asthma, and anaphylaxis. Mast cells modify homeostatic regulation and effect functions, such as mucus production, microcirculation and blood vessel growth, and bone remodelling.

They have also been implicated as markers of inflammatory disorders.<sup>6 18</sup> In particular, mucosal type mast cells-easily overlooked in routine histological analysis owing to poor visualisation after formalin fixation-depend on T cell derived interleukin-3 for their proliferation.<sup>17-19</sup> The factors regulating the proliferation of connective tissue mast cells are less clear but they seem to be derived from macrophages and fibroblasts.

Therefore, one would expect that active focal sialadenitis would be accompanied by extensive proliferation of mast cells in situ. The extent of labial salivary gland participation can be assessed by focus score counting according to Greenspan.

### Conclusion

SGTs showed greater MC counts compared to normal SGs but benign neoplasms

were similar to malignant ones. MCC counts in minor normal and neoplastic SGs were more than those in major glands, maybe due to anatomical variations.

Further studies are suggested to determine the type of MCs in these neoplasms and its relationship to behavior of the tumor.

Lymphoma of Salivary Gland is a slow-growing malignancy with a generally good prognosis with early diagnosis and treatment

The prognosis is mainly dependent upon the tumor stage and lymphoma subtype. Also, primary lymphomas have better prognoses than secondary or recurrent lymphoma

In general, the prognosis depends upon a set of several factors, which include:

- Stage of tumor: With lower-stage tumors, when the tumor is confined to site of origin, the prognosis is usually excellent with appropriate therapy. In higher-stage tumors, such as tumors with metastasis, the prognosis is poor

- Overall health of the individual: Individuals with overall excellent health have better prognosis compared with those with poor health

- Age of the individual: Older individuals generally have poorer prognosis than younger individuals

- The size of the tumor: Individuals with small-sized tumors fare better than those with large-sized tumors

- Individuals with bulky disease have a poorer prognosis

- Involvement of vital organs may complicate the condition

- The surgical respectability of the tumor (meaning, if the tumor can be removed completely) – it is a rare option

- Whether the tumor is occurring for the first time, or is a recurrent tumor. Recurring tumors have worse prognosis compared to tumors that do not recur

- Response to treatment: Tumors that respond to treatment have better prognosis compared to tumors that do not respond to treatment

- Progression of the condition makes the outcome worse (progressive Salivary Gland Lymphoma)

- Cancer and tumours

- About 80% of tumors of the parotid gland are benign [11]. The most common of these include pleomorphic adenoma (70% of tumors, [11] affecting predominantly females (60% [11])) and Warthin tumor (i.e. adenolymphoma) more in males than in females. Their importance is in relation to their anatomical position and tendency to grow over time. The tumorous growth can also change the consist-

ency of the gland and cause facial pain on the involved side [12].

- Around 20% of parotid tumors are malignant, with the most common tumors being mucoepidermoid carcinoma and adenoid cystic carcinoma. Other malignant tumors of the parotid gland include acinic cell carcinoma, carcinoma expleomorphic adenoma, adenocarcinoma (arising from ductal epithelium of parotid gland), squamous cell carcinoma (arising from parenchyma of parotid gland), and undifferentiated carcinoma. Metastasis from other sites like phyllodes tumour of breast presenting as parotid swelling have also been described [13]. Critically, the relationship of the tumor to the branches of the facial nerve (CN VII) must be defined because resection may damage the nerves, resulting in paralysis of the muscles of facial expression.

#### Note

The combination chemotherapy drugs used, may have some severe side effects (such as cardio-toxicity).

This chiefly impacts the elderly adults, or those who are already affected by other medical conditions. Tolerance to the chemotherapy sessions is a positive influencing factor.

Progression to bone marrow failure is usually associated with short survive.

#### Diagnosed

Inflammatory swelling of the glands may present a serious diagnostic challenge. Parotitis presents in many forms and the symptoms vary from modest to prostrating.

Reading the numerous journal on parotitis articles reveals frequent contradictions in the classification, etiology, and treatment of the disorders.

A pure viral or bacterial infection, an autoimmune inflammation, or a combination of these can be the etiology.

In this article, evolution of the knowledge of parotitis, as well as the diagnosis and treatment, is discussed. Parotid gland cancer is most often diagnosed when a person goes to a doctor because of symptoms he or she is having.

If you have signs or symptoms that might be caused by a salivary gland tumor, your doctor will do exams and tests to find out if it's cancer or some other condition.

If cancer is found, other tests may be done to find out if it has spread.

#### Surgery

Surgical treatment of parotid gland tumors is sometimes difficult because of the anatomical relations of the facial nerve parotid lodge,

as well as the increased potential for postoperative relapse. Thus, detection of early stages of a parotid tumor is extremely important in terms of postoperative prognosis [11]. Operative technique is laborious, because of relapses and incomplete previous treatment made in other border specialties [11].

After surgical removal of the parotid gland (Parotidectomy), the auriculotemporal nerve is liable to damage and upon recovery it fuses with sweat glands. This can cause sweating on the cheek on the side of the face of the affected gland. This condition is known as Frey's syndrome [14].

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