Lecture (4)

SALIVARY GLAND DISEASES

There are four main salivary glands—two parotids and two submandibular glands—and multiple minor salivary glands which occur throughout the upper respiratory tract, notably in the oral cavity and oropharynx. Patients with enlargement of these glands or sialomegaly can pose an interesting diagnostic dilemma.

Pathology

1. Infection.

(a) Viral: mumps virus, coxsackie virus, echovirus, human immunodeficiency virus (HIV).

(b) Bacterial: staphylococcal, actinomycosis, tuberculosis, leprosy.

2. Neoplasm.

(a) Benign: pleomorphic adenoma, adenolymphoma.

(b) Malignant: adenoid cystic carcinoma, adenocarcinoma, squamous cell carcinoma.

(c) Variable: mucoepidermoid carcinoma, acinic cell tumour.

(d) Non-epithelial: haemangioma, lymphangioma, neurofibroma, lymphoma.

3. Inflammatory. Sjögren's syndrome is an autoimmune disease which is characterized by periductal lymphocytes in multiple organs. The salivary glands are affected in approximately 40% of all cases. In one in six patients the disease will progress to a lymphoma. Sjögren originally described xerostomia, keratoconjunctivitis sicca and rheumatoid arthritis, with no mention of salivary gland swelling. Now the disease can be classified into:

(a) Primary Sjögren's syndrome (or sicca complex) consisting of xerostomia and xerophthalmia with no connective tissue component.

(b) Secondary Sjögren's syndrome, which consists of xerostomia, xerophthalmia and a connective tissue disorder, usually rheumatoid arthritis.

4. Metabolic. Myxoedema, diabetes, Cushing's disease, cirrhosis, gout, bulimia, alcoholism.

5. Drug induced. Coproxamol (dextropropoxyphene and paracetamol), oral contraceptive pill, thiouracil, phenylbutazone, isoprenaline.

6. Sialectasis. Progressive destruction of the alveoli and parenchyma of the gland accompanied by duct stenosis and cyst formation. Many cases are thought to be congenital. Epithelial debris or calculi may be found in the main ducts.

7. Pseudoparotomegaly. These should be kept in mind as they may mimic sialomegaly: hypertrophic masseter, winged mandible, mandible tumours, dental cyst, branchial cyst, preauricular lymph node, sebaceous cyst, lipoma and neuroma of the facial nerve.

History

The diagnosis is often obvious from the clinical findings. The history should include the age of the patient (think of mumps or congenital sialectasis), the number of glands affected (tumours are unilateral apart from Warthin's on rare occasions), whether the swelling is exacerbated by eating (calculus disease secondary to sialectasis), duration of symptoms (benign tumours grow slowly and malignant ones fairly rapidly) and any related pain (infection, calculus or adenoid cystic carcinoma). There should be a thorough review of systemic symptoms (metabolic causes), and any medication the patient is taking should be noted. The social history including alcohol intake and risk of HIV infection may be relevant in some cases.

Examination

Inspect the enlarged gland and then all the other salivary glands. Inflamed skin over the swelling should make one consider an infection or skin involvement from a malignant lesion. The facial nerve should be tested as facial weakness also raises the suspicion of a malignant lesion. Before palpating the lesion be sure to ask if it is tender; this is kind to the patient and a good habit in clinical medicine—it is essential in an examination! Palpation should determine whether the lesion is local or diffuse, solid or cystic, mobile or fixed and whether or not other glands are affected. Inspect the oral cavity and palpate all of the glands bimanually. In the floor of the mouth a submandibular calculus may be felt or pressure on a parotid gland may express pus from the parotid duct. Then examine the pharynx to look for a parapharyngeal lesion (in particular one arising from the deep lobe of the parotid), which may push the tonsil medially. Complete the

ENT examination and perform a general examination if systemic or disseminated neoplastic disease is suspected.

Investigations

1. Blood tests. Rheumatoid factor, antinuclear factor and abnormal electro-phoresis are sometimes found in Sjögren's syndrome. Specific Sjögren's antibodies are usually also present (SSrho and SSla). Tests for the relevant endocrine disorders may be appropriate.

2. Radiography. A plain film is useful as it may reveal a radiopaque submandibular calculus. Most submandibular gland calculi are radiopaque, but most parotid calculi are radiolucent. A sialogram is

probably the most useful investigation of benign salivary gland disease. Duct stenosis, calculi and sialectasis can all be diagnosed if sialography is possible. MRI scanning is usually the preferred investigation in neoplastic disease to delineate any potential deep lobe involvement and to assess the tumour's relationship to the facial nerve.

3. Biopsy. Incisional and Trucut biopsy should not be performed as there is a risk of seeding neoplastic disease. Fine-needle aspiration biopsy is safe and often useful, but the results have to be interpreted in conjunction with clinical suspicion as incorrect reports are not uncommon, especially with cystic lesions. A parapharyngeal mass should never be biopsied through the pharynx because there may be uncontrollable bleeding if the patient has a vascular lesion. Sublabial biopsy is the definitive investigation to confirm the diagnosis in Sjögren's syndrome (periducatal lymphocytic infiltration found).

Management

The management and specific treatment of the patient depends on the cause of the salivary gland swelling.

SALIVARY GLAND NEOPLASMS

Pathology

Neoplastic lesions are divided into benign or malignant, and malignant lesions can be primary or secondary. In addition, if one can remember the epithelial and the non-epithelial histology of the organ, an excellent framework for working practice is easily established. Salivary gland tumours are no exception in this respect, except that some such neoplasms have variable biological behaviour.

Classification

The WHO histological classification of salivary tumours now includes over 35 variants and also includes tumour-like lesions (e.g. salivary gland cysts). A simplified classification is presented below:

1. Benign. Pleomorphic adenoma, Warthin's tumour (papillary cystadenoma lymphomatosum),

monomorphic adenoma, oncocytic adenoma, ductal papilloma.

2. Malignant. Adenoid cystic carcinoma, adenocarcinoma, squamous cell carcinoma, undifferentiated carcinoma, carcinoma expleomorphic adenoma.

3. Variable. Mucoepidermoid carcinoma, acinic cell carcinoma.

4. Non-epithelial. Haemangioma, lymphangioma, neurofibroma, lymphoma.

A good approximation to remember is that 80% of all salivary tumours are in the parotid, 80% of parotid tumours are benign and 80% of the benign tumours that arise in the parotid are pleomorphic adenoma. One in three tumours arising in the submandibular gland and one in two tumours that arise in the minor salivary glands are malignant.

Clinical assessment

All patients with a mass in a salivary gland should have: an inspection and palpation of the mass itself, oral examination with particular inspection of the relevant salivary gland duct, peroral palpation, inspection of the oropharynx for parapharyngeal extension assessment, facial nerve assessment and neck node palpation.

Investigations

1. Radiography. CT scanning of a parotid tumour is useful in the assessment and delineation of anatomical structures, extension to the deep lobe and relation to the facial nerve. MRI has significant advantages. Using STIR sequencing appears to add to the sensitivity in detecting lesions of the parotid gland, delineating the facial nerve and in identifying the tumour edge.

2. Fine-needle aspiration biopsy (FNA). The role of FNA in the diagnosis of benign and malignant salivary gland disease is a controversial issue. Proponents of the technique argue that FNA provides diagnostic information which may allay a patient's anxiety and aid in preoperative counselling and planning of surgery. However, those against the routine use of FNA argue that one cannot rely on the sensitivity or specificity of the procedure. This is particularly true in patients with cystic lesions of the parotid, in whom the aspirates often yield straw-coloured fluid, which is almost invariably hypocellular or acellular, and thus non-diagnostic. FNA is a relatively painless procedure, has few complications (seeding of the tumour does not appear to occur) and may prevent an ill-advised and often ill-fated incisional or excisional biopsy of a parotid mass. If the result of FNA is at variance with other findings then clinical judgement should prevail.

Staging

With malignant tumours of the parotid gland, a significant correlation exists between tumour stage and survival. The stage of the disease has been shown to be a more important prognostic parameter than its histological grade. The UICC system is summarized below:

T0 No clinical evidence of tumour.

T1 < 2 cm in diameter, without extraparenchymal extension (skin, soft tissues).

T2 2–4 cm in diameter, without extraparenchymal extension.

T3 4–6 cm in diameter, and/or extraparenchymal extension (but not facial nerve).

T4a > 6 cm in diameter, and/or base of skull or facial nerve invasion.

T4b A tumour of any size with significant local extension.

Benign tumours

1. Pleomorphic adenoma is the commonest benign salivary tumour. The sex distribution is equal and the peak age incidence is in the fifth decade. It has a pseudocapsule of compressed parotid tissue into which the tumour usually has many protuberances. It arises from intercalated duct cells and myoepithelial cells. Microscopically it comprises epithelial and mesodermal elements with a mucopolysaccharide stroma giving rise to a characteristic mixed staining pattern. If the capsule is ruptured during removal, then tumour may implant, causing recurrence. They are therefore excised with as large a margin as possible to reduce the risk of capsule rupture. Superficial parotidectomy or hemisuperficial parotidectomy when the lesion is small is now the preferred procedure. Management of recurrent tumour is difficult as the facial nerve may be

involved and its sheath may need to be stripped. The facial nerve should if at all feasible not be sacrificed; rarely radical surgery is needed with resection of the facial nerve. Many surgeons advocate adjuvant postoperative radio-therapy in these situations.

2. Warthin's 's tumour (papillary cystadenoma) is a benign tumour, usually seen in elderly men. The peak incidence is the seventh decade and the male-female ratio is 7:1. They are soft and cystic tumours which are thought to arise from heterotopic parotid tissue in the lymph nodes within the parotid gland. Ten per cent are bilateral, but rarely synchronously. Treatment is by excision and, unlike pleomorphic adenoma, recurrence almost never occurs.

3. Monomorphic adenomas arise from ductal epithelium and are treated by surgical excision with a cuff of tissue.

4. Oncocytoma is a benign eosinophilic tumour (also called oxyphil adenoma) that arises from

intralobular ducts or acini. It is usually found in the superficial lobe of the parotid. It can undergo malignant change and treatment is also by excision with a cuff of tissue.

Malignant tumours

1. Adenoid cystic carcinoma is the commonest malignant tumour and may arise from any salivary tissue, but is more common in minor than in major salivary glands. The sex incidence is equal and they are seen most often in patients in their sixth decade. The tumour is slow-growing and tends to spread along nerve sheaths. The patients often complain of facial pain and may present with a facial paresis. The incidence of lymph node metastases is low and distant metastases occur late. Treatment is usually by radical excision and adjuvant radiotherapy. If the facial nerve is free of tumour it may be dissected out and left intact.

However, it is often involved, and in this situation it needs wide excision and anastomosis with a nerve graft. The sural nerve is preferred as the greater auricular nerve may be involved and should also be excised. Postoperative radiotherapy will not affect the graft. Radiotherapy in the curative and palliative treatment of patients with adenoid cystic carcinoma of salivary gland origin is useful in some cases, but is still being assessed.

2. Adenocarcinoma accounts for about 3% of parotid tumours and 10% of submandibular and minor salivary gland tumours.

3. Squamous cell carcinoma. Some pathologists doubt their existence, regarding them as high-grade mucoepidermoid tumours; true malignant pleomorphic adenomas are rare.

Tumours with variable behaviour

1. Mucoepidermoid carcinoma arises in any salivary tissue but predominantly the parotid gland. It is the commonest salivary neoplasm in children. Low-grade or well-differentiated tumours usually behave in a benign fashion, intermediate ones are more aggressive and high-grade or undifferentiated tumours metastasize early and carry a poor prognosis. However, the behaviour is not always accurately predicted by the histological appearance.

2. Acinic cell carcinoma is similarly difficult to classify. They are, however, much more benign than mucoepidermoid tumours.