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Conference report

Salivary gland disease. First International accord on modern management – Paris, July 4-5 2008

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The Conference, held in Paris, on the left bank in the famous Institute Pasteur, was attended by 177 participants from all over Europe and the USA. The Conference was graciously opened by Prof. Eugene Myers with an overview of the history of parotid surgery which was a wonderful introduction to the Proceedings of the Meeting.

The Conference had been designed with the intention of addressing questions on problematic areas in the management of salivary gland disease. Nineteen topics were selected for evaluation and a Lead Speaker with a particular interest in the topic under discussion was chosen for each. The Lead Speakers reviewed the topic, produced a manuscript and presented the data to a select panel of experts and the audience. The manuscript was circulated to the panel before the meeting to stimulate the discussion. The Conference was divided into three identifiable themes: *Management of benign parotid tumours*, *Malignant parotid disease* and *Inflammatory disorders of salivary glands* (*minimally invasive management of obstruction*).

The first topic to be presented was *The optimum tests for investigating salivary tumours* (Professor F. Heran, Fondation Rothschild Service d'Imagerie, Paris, France). It was refreshing to note that Prof. Heran took a very practical approach to this topic, pointing out that in superficial, easily palpable benign tumours, no imaging may be required. It was agreed that in the salivary gland the first and most practical imaging modality is ultrasound (US). It is more sensitive than computed tomography (CT) scan for identifying small lesions, it will distinguish between lesions arising within or outside the parotid parenchyma and vascularity can be assessed by Doppler imaging. The next investigation of choice is fine needle aspiration cytology (FNAC). All investigations have advantages and disadvantages, it was agreed that FNAC was operator dependent. Nevertheless, in appropriate hands, the diagnostic accuracy, in terms of benign and malignant disease, is excellent. Rapid advances are being made in more sophisticated imaging modalities such as helical acquired CT scans. It is now generally agreed that magnetic resonance imaging (MRI) gives better information than CT, in most instances. Both of these modalities are expensive and may not be available in all medical institutes. The CT or MRI scan should be reserved for malignant disease or complex tumours that are deep to the mandible or in the infra-temporal fossa. MRI spectroscopy, in the future, may have a role in distinguishing different types of salivary tumours and the high definition scanners may reliably identify the path of a facial nerve within the gland.

The topic *Role of electrophysiologic facial nerve monitoring during parotidectomy* (Prof. David W. Eisele, Chairman, Department of Otolaryngology, Head and Neck Surgery, UCSF, San Francisco, USA) produced a lively debate. The technique has been adopted by the ENT fraternity following experience with acoustic neuroma surgery. Two bodies of opinion emerged, one favouring the use of the monitoring apparatus, and the other considering it a distraction. There is no definitive data to resolve the debate and it is unlikely that any will become available. The incidence of permanent nerve injury is so low that it is impractical to undertake a prospective randomised study. It was agreed that nerve monitoring should be used for high risk cases. Monitoring may reduce the incidence of transient nerve injury by surgeons in training. Some of our American colleagues thought that, for optimum results, an independent person should monitor the electromyographic signals (a luxury not available in Europe). There was no consensus on the use of nerve monitoring. But the technique is simple, carries low morbidity, is relatively inexpensive and is likely to give some help from time to time. Under such circumstances, the medico-legal forces may decide the question of nerve monitoring for us.

The third topic of discussion of the morning was whether *It justifiable to move away from superficial and total parotidectomy as standard of care for benign parotid tumours* (Prof. H. Iro, Head of the Department of OtoRhino-Laryngology, Head and Neck Surgery, University of Erlangen-Nürnberg, Germany). A careful evaluation of the literature was undertaken for facial nerve injury, Frey's syndrome, and recurrent disease when adopting different surgical techniques. Convincing data showed that as the magnitude of the operative procedure became reduced so did morbidity and complications and without an increase in tumour recurrence. In Prof. Iro's experience, 40-60% of benign tumours can be treated by minimally invasive surgery. He routinely uses facial nerve monitoring. The benign nature of the tumour should be confirmed by FNAC. Paradoxically, small parotid tumours (< 2 cm) should be removed with extracapsular dissection (ECD) as they may be malignant tumours masquerading as benign lumps. There was a consensus within the audience that the practice of parotid surgery was starting to move down a conservative treatment pathway, and that large centres that have a significant workload of parotid tumours are likely to become proficient and the main providers of minimally invasive surgery in the future.

The fourth topic addressed in the morning was *Whether Warthin's tumour could be considered a neoplasm* (Prof. O. Gallo and Prof. A. Franchi, University of Florence, Italy). Warthin's tumour is a disease of the elderly, particularly those who smoke, and the condition is multifocal in up to

50% of patients. Yet (as one might expect with true neoplasms) local excision is not associated with a high incidence of second tumours. Prof. Franchi showed convincing data that both the epithelial and lymphoid components of these lesions are polyclonal supporting the hypothesis that Warthin's tumours are non neoplastic lesions. Genetic studies show multiple genetic alterations in Warthin's tumours and one distinct cytogenic abnormality is shared with mucoepidermoid carcinoma. The question is whether Warthin's tumour is a progenitor for mucoepidermoid carcinoma. These patients are not known for developing mucoepidermoid carcinoma. There was firm agreement that Warthin's tumour of the parotid gland can be removed by local surgery and if ruptured, there was no need to proceed to further maximal surgery for fear of recurrent disease, and if following FNAC it disappeared clinically, then a "wait-and-see" policy was acceptable. There was conviction within the audience that total parotidectomy on the pretext that this was a multifocal neoplastic disease was no longer tenable. It seems that Warthin's tumour cannot be considered a neoplasm.

In the afternoon, discussion was focused on malignant disease of the parotid gland. The first topic addressed was *Does the presence of malignant disease in the parotid gland demand a total parotidectomy?* (Dr. Gérard Mamelle, Chef de Service, Département de Chirurgie Cervico-Faciale, Institut Gustave Roussy, Villejuif, France). Dr. Mamelle listed the type of procedures applicable to parotid tumours and the aim of his presentation was to match the procedure to the stage of disease. Salivary gland staging is unique as it encorporates an element of biological grading of the tumour. This clinical grading system is both practical and more useful than histological grading for planning surgery. He reported on the French treatment protocols (Bensadoun RJ et al., Cancer Radiother 2003;7:280-95).

Facial nerve resection is mandatory in cases of direct involvement. Only a few series have reported a conservative approach to malignant tumours. Invariably, these tumours are mobile, low grade and limited to the superficial lobe of the parotid gland (stages I and II). In such circumstances, if an adequate excision margin can be obtained (ideally tumours in the periphery or tail of the gland) then it may be appropriate to remove the lesion with a less than total or a superficial parotidectomy. It is wise to routinely sample the digastric lymph nodes, and if they are positive, then, by definition, the tumour is > stage III and requires neck dissection. A conservative approach has to be highly selective and usually a superficial or total parotidectomy is still standard care for most cases of parotid cancer.

The second issue addressed was *Is it necessary to always resect the facial nerve in cases of parotid cancer?* (Dr. Fausto Chiesa, Director, Head & Neck Department, Istituto Europeo di Oncologia, Milan, Italy). The immediate response is that this issue was settled in the '60s and '70s in favour of nerve preservation. But what about a single branch of the facial nerve running in close proximity to the malignant tumour – should it be sacrificed? The rationale is that an independent risk factor for treatment failure is close or inadequate surgical margins. This finding argues in favour of radical surgical excision. But the data demonstrate that, in such cases, the site of failure is not at the primary site but distally. The close surgical margins are a feature of aggressive tumour biology. There was general agreement that a conservative approach (to the facial nerve) should be taken unless it was visibly involved in tumour or bodily entered a malignant tumour. A working nerve should be preserved.

The theme of the facial nerve was continued in the next Lecture *The evidence supports improved results with immediate repair of the facial nerve*. A traumatic radial nerve injury is considered an emergency and repaired within 24 to 48 hours. No such sense of urgency seems to accompany facial nerve injury during head and neck surgery. A nerve repair may be delayed for months. Prof. A.G. Salimbeni (Institute of Plastic Surgery, Casa di Cura San Rossore, Pisa, Italy) advocated early reconstruction. A wealth of studies pointed towards better regeneration with early repair but no definitive studies dealt with the facial nerve. This is because the case mix is never uniform (different tissue beds, chemotherapy, radiotherapy, different reconstructive techniques). There was general agreement, based mainly on intuition, that early repair was preferable to delayed reconstruction if only because, with time, it became increasingly difficult to find the nerve ends and there was atrophy of the motor end organ. A parotid surgeon should have the ability to repair an injured facial nerve immediately if the need arose.

Prof. J. Werner (Department of Otolaryngology, Head and Neck Surgery, University of Marburg, Germany) addressed the question of whether it was necessary to perform a neck dissection in every case of parotid cancer. A number of factors impact on this issue, not least of which the histological type of tumour. Certain families of tumours (squamous cell carcinoma, anaplastic carcinoma, high grade mucoepidermoid carcinoma ex pleomorphic adenoma) demonstrated an aggressive biological behaviour with a high incidence of cervical metastasis and elective neck dissection is advisable. Stage is important in the decision and this is another example of the advantage of the unique salivary (biological) staging system.

Tumours classified high stage, either because they are large or because they have an aggressive biological nature (local invasion), are candidates for neck dissection. It was generally agreed that small tumours (stages I and II) with few, if any, clinical features of malignancy did not require neck dissection. However, it is wise to sample digastric lymph nodes which are easily accessible during parotid surgery for frozen section examination. Negative results encourage a conservative approach.

Dr. N.J. Slevin (Christie Hospital, Manchester, England) discussed the role of adjuvant radiotherapy in the management of salivary gland tumours. The talk was divided into two sections, the management of malignant, and the management of benign, salivary disease. In the former, the role of adjuvant radiotherapy is well established. High grade tumours, or those with close surgical margins, warrant adjuvant radiotherapy. This reduces the incidence of local recurrence. But, in addition, there is emerging evidence that adjuvant radiotherapy may also improve long-term survival particularly in the subgroup of patients with high stage, or biologically aggressive, neoplasms.

The role of radiotherapy in the management of benign disease is more controversial. Dr Slevin briefly summarised the topic. The data suggest that the risk of recurrent tumour, following spillage, is approximately 8% (at 15+ years). This low recurrence rate did not merit the routine use of adjuvant radiotherapy following tumour spillage. However, once recurrent disease was established and in particular when it

was multifocal, then the addition of adjuvant radiotherapy following second surgery appeared to reduce further recurrence from 50% to 4%. Its application, in this context, seemed reasonable.

The focus then turned to the role of adjuvant chemotherapy in the management of salivary gland cancer (Dr. Lisa Licitra, Istituto Tumori, Milan, Italy). There is no accepted chemotherapy regime for the management of salivary gland cancer. Single agents such as 5 fluorouracil or doxorubicon have been used in small series of patients with variable success. No data from randomised trials are available. It is not known whether single or multi agent chemotherapy is more effective. At present, chemotherapy seems to be reserved for recurrent or metastatic disease, despite the absence of an apparent survival benefit. New targets are consequently being evaluated. KIT is over-expressed in up to 39% of salivary gland cancers, mostly in adenoid cystic carcinoma. The variation in expression might explain the lack of activity of imatinib in this disease. HER2 and EGFR have also been examined. EGFR is present in 70% of salivary gland cancers making it one of the most attractive targets. Nonetheless, preliminary results obtained with gefitinib, cetuximab and lapatinib are discouraging. Androgen blockade has also been studied and there are isolated incidences of response to such chemotherapy. The message is that this is an evolving field with the focus moving away from traditional chemotherapy to new targeted drugs.

The final lecture of the day was delivered by Prof. A. Franchi (Department of Human Pathology and Oncology, University of Florence, Italy) on the topic of *Has the new histological classification of salivary gland tumours been superseded by clinical stage in the management of salivary gland cancer?*. The issue at the heart of this debate is that salivary gland cancers are relatively rare and slow growing, consequently it takes many years to collect sufficient data to expose the natural history of most tumours. It may take two surgical lifetimes to establish the biological nature of the tumours in the new classification. The reclassification of tumours every 10 years consequently poses a problem to the clinician. But the introduction of a staging system, not based solely on size, but also incorporating a biological component based on clinical features of aggressive behaviour, has given staging primary importance over histology in planning initial surgery. Histological features govern the choice of adjuvant therapy.

The second day was dedicated to inflammatory disorders of the salivary glands. The first lecture was dedicated to inflammatory diseases of childhood (Prof. O. Nahlilie, Department of Oral & Maxillofacial Surgery, Barzilai Medical Centre, Ashkelon, Israel). The aetiology of this disorder remains unclear and there is probably more than one underlying cause for the condition. A subgroup of patients may have incompetent parotid ducts that allow air to be shown in the duct system at will. In others it may be an autoimmune or neurogenic reaction or an early manifestation of childhood Sjögren's syndrome. The advice was that the initial attack should be dealt with definitely by antibiotics, steroids and duct washouts. If the first attack is not dealt with appropriately, the risk of recurrent attacks increases. Advice is for frequent washouts, ideally combined with sialoendoscopy.

Dr. J.P. Meningaud (Department of Plastic and Aesthetic Surgery, CHU Henri Mondor, Paris, France) reviewed the management of drooling. Initial treatment relates to postural and behavioural management of the child. Anti-cholinergic agents have side-effects and it appears that botulinum toxin is the agent of choice, at present. Duct ligation or relocation of ducts is reserved for persistent cases.

Prof. Nahlilie then discussed the optimum investigation of obstructive diseases of salivary glands. A range of investigations are available (plain X-rays, sialograms, sialoendoscopy, US, scintigraphy, CT, sialo MRI and virtual endoscopy). In practice, the units with experience in treating obstructive disease rely mainly on US examination together with sialography (where available) and then, in turn, sialoendoscopy. Plain X-rays are of little value, scintigraphy carries a radiation hazard and CT scans are oversensitive with the risk of false positive results for calculi. Sialo MRI gives wonderful pictures but is expensive. Virtual endoscopy is a modality for the future.

Dr. F. Marchal (ENT HNS Department, University Hospital, Geneva, Switzerland) gave a Lecture on the treatment of parotid gland obstruction. A consensus is now developing on this topic. Small mobile stones (< 4 mm) can be retrieved by basket removal (either radiologically- or endoscope-guided). Larger or fixed stones are more problematic. If an extra-corporeal lithotripter is available then 60% of stones < 8 mm in diameter can be fragmented and washed from the duct system. It is possible to eliminate large stones by intraductal lasers or by crushing them with micro-forceps but the treatment is cumbersome and not very effective. Strictures can be dilated by balloon dilatation or freed by a hand rotated drill. High pressure balloon dilation under radiological control seems the most efficient method of treating strictures to date.

Professor J. Zenk (Department of ORL, Head and Neck Surgery, University of Erlangen-Nürnberg, Germany) discussed the management of submandibular obstructions. Strictures are uncommon in the submandibular glands. Presentation and theories of calculi formation were described as well as the distribution of stones within the duct system.

The majority of stones (60%) reside in the proximal duct or hilum of the submandibular gland. Small mobile stones (< 4 mm) are retrieved (as per parotid) by baskets (via endoscopes and radiologically-guided blind sweep of the duct system with a basket). The extracorporeal lithotripter is relatively inefficient in eliminating submandibular stones (30% clearance). These stones are dealt with by an intraoral surgical technique either under local anaesthetic or day case general anaesthesia.

Submandibulectomy, for obstructive disease, should be an uncommon event in 2008 based on a review of the treatment of 4600 salivary stones (< 3%). This point was emphasised by Dr. Pasquale Capaccio (Department of Otorhinolaryngological and Ophthalmological Sciences, Policlinico Foundation IRCCS, University of Milan, Italy). He described the advantages and disadvantages of gland removal and its complications.

Prof. M. McGurk (Guy's Hospital, King's College, London, England) discussed salivary ranulae. The increased interest in intra-oral surgery for submandibular calculi has rekindled interest in the anatomy of the sublingual glands. The sublingual gland consists of 2 functional separate units, the lesser sublingual gland (the head of the salivary gland) and the greater sublingual gland (the tail). The "lesser" is formed by numerous small ducts emptying directly into the floor of the mouth, the "greater" via a single duct. The minor salivary

glands have the unique ability to secrete against high pressure gradients. In contrast, submandibular and parotid gland atrophy. This combination (multiple small ducts and high secretion pressure) explains the genesis of the mucocele and ranulae. The treatment options were classified. If the ranula can be dissected back to its origin in the lesser sublingual gland, only a portion of the sublingual gland needs to be removed. Extirpation of the sublingual gland is not always necessary.

The management of Frey's syndrome was discussed (Dr. Capaccio) and the causes and management of this condition were described. Frey's syndrome is directly related to the magnitude of parotid surgery. Minimalist procedures almost eliminate this complication. There is some debate regarding the usefulness of barrier techniques. It was agreed they were not very effective. Natural barriers such as parotid fascia were the ideal method for avoiding Frey's syndrome. Once established, a wide range of techniques and pharmacological products have been used but, today, the most effective means of reducing gustatory sweating is by repeat botulinum injections.

The Conference ended with a demonstration of new minimally invasive equipment provided by Storz, Polydiagnost, Cook and ultrasound manufacturers (Philips & Sonosite). The commercial market is moving very rapidly with new endoscopes being produced every few years. Both Storz and Polydiagnost have new third generation endoscopes which can now be sterilised. Polydiagnost also has disposable canulae. A range of new catheters and baskets have been produced by Cook and the new Sonosite ultrasound machine has excellent image quality for a portable system. It is ideal for quick examination of patients in the clinic setting.

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