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ORIGINAL ARTICLE

Sialadenitis following radioiodine therapy – a new diagnostic and treatment modality

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OBJECTIVES: To explore the usage of salivary gland endoscope technique as a diagnostic tool as well as a novel treatment modality for sialadenitis following radioiodine therapy.

SUBJECTS AND METHODS: Fifteen patients suffering from sialadenitis of the major salivary glands after I^{131} therapy for thyroid carcinoma underwent a single procedure of sialoendoscopy under local anesthesia.

RESULTS: All the patients were free of sialadenitis after one sialoendoscopy procedure with no complications accompanied.

CONCLUSIONS: Sialoendoscopy is an efficient technique with low morbidity as well as a relatively simple surgical method for diagnosing and treating sialadenitis induced by radioiodine therapy for thyroid cancer patients.

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Introduction

Radioactive iodine (I^{131}) is a well-known adjunct treatment of thyroid carcinoma, especially in patients with high risk of recurrence (Freitas *et al*, 1985; Samman *et al*, 1992; Rodrigues *et al*, 1998; Newkirk *et al*, 2000). The average dose of radioiodine administered for ablative therapy ranges from 0.81 to 4.05 MBq (30–150 mCi) (Alexander *et al*, 1998; Newkirk *et al*, 2000).

The thyroid and salivary glands possess a mechanism for selectively concentrating iodine. It is estimated that *c*. 2% of the administered radioactive iodine is absorbed by the salivary glands (Becciolini *et al*, 1994) at a tissue to serum gradient ratio of 50:1 respectively (Newkirk *et al*, 2000; Solans *et al*, 2001; Caglar *et al*, 2002). The parotid glands often show more severe dysfunction than the submandibular and sublingual salivary glands because of greater ability of the serous cells to concentrate iodine compared with the mucous cells (Mandel and Mandel, 1999).

The rate of salivary gland dysfunction behaves as a dose and time-dependent manner manifested mainly by recurrent episodes of sialadenitis (Alexander *et al*, 1998; Newkirk *et al*, 2000; Caglar *et al*, 2002). However, salivary gland dysfunction does not always have subjective clinical implications.

Maier and Bihl (1987) hypothesized that injury of the acinar and ductal cells is secondary to damage of the vasculature of the gland following radiation damage to the dividing endothelial cells.

A second theory about the mechanism of salivary gland injury is based on its ability to concentrate iodine (Stephens *et al*, 1991; Mandel and Mandel, 1999; Newkirk *et al*, 2000; Solans *et al*, 2001; Caglar *et al*, 2002) through a selective sodium/iodine symporter. This symporter is mostly prevalent in the ductal cells (Jhiang *et al*, 1998). Mandel and Mandel (2003) noted that the first symptom is obstructive in nature because of duct lumen narrowing secondary to inflammatory process. Salivary stagnation and mucus precipitation ends in jelly-like plaque formation, which causes pain and swelling until its extrusion. Duct stricture is evident in parotid sialogram with concomitant proximal dilatation (Mandel and Mandel, 2003).

At present, the two imaging techniques helping in diagnosis of tissue damage following I^{131} therapy to the salivary glands are scintigraphy and sialography (sialogram). Tc-99m pertechnetate salivary gland scintigraphy plays a vital role in evaluating parenchymal damage of the salivary glands (Bohuslavizki *et al*, 1996; Solans *et al*, 2001; Caglar *et al*, 2002). Caglar *et al* (2002) and Alexander *et al* (1998) noticed that decreased uptake of Tc-99m by the salivary glands becomes evident especially more than 1 year postoperatively indicating a fibrosis process of the salivary parenchyma (Alexander

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et al, 1998; Newkirk *et al*, 2000; Solans *et al*, 2001; Caglar *et al*, 2002).

Sialography provides demonstration of the ductal system of salivary glands by inflating a radiopaque contrast agent into this system before imaging. The purpose is to opacify the ductal system all the way down to the acini. Sialography is indicated for the evaluation of chronic inflammatory diseases and ductal pathologies of the gland (White and Pharoah, 1996). The two above-mentioned techniques have their limitations mainly because of the lack of three-dimensional representation of the complexity of salivary ductal system.

Sialoendoscopy is a novel technique that has promoted a significant new dimension to the surgeons' armamentarium for diagnosis and management of inflammatory salivary gland diseases. Konigsberger *et al* (1990), were the first to introduce a mini flexible endoscope combined with an intracorporeal lithotriptor for fragmentation of calculi. Katz (1991), published his technique using a mini flexible endoscope into the ductal system of the major salivary glands. Nahlieli *et al* (1994) described the use of a mini rigid endoscope for diagnosis and treatment of salivary gland obstruction. Intermediate- and long-term experiences with this technique were reported subsequently (Zenk *et al*, 1998). Marchal *et al* (2000) reported a similar experience with sialoendoscopic techniques. Zenk *et al* (2004) reported experience with a new flexible endoscope.

Sialolithiasis is the most common cause of salivary gland infections (Zenk *et al*, 2001). Until recently, the main use of sialoendoscopy was to confirm the diagnosis of obstructions and to remove sialoliths by different techniques (Nahlieli and Baruchin, 1999).

As the ductal compartment of the salivary gland is the prominent one regarding salivary gland impairment because of radioiodine therapy, we decided to utilize our previous knowledge with the sialoendoscope technique for this pathology. Here we describe the first time, to our knowledge, the use of endoscopic technique as a diagnostic tool as well as a therapeutic device for patients suffering from chronic sialadenitis following radioiodine therapy for thyroid cancer.

Subjects and methods

Fifteen patients (13 women and two men) who had received radioiodine therapy following total thyroidectomy because of metastatic papillary carcinoma of the thyroid gland were admitted to the maxillofacial outpatient clinics in Barzilai Medical Center during the past 4 years. Their major complaint was recurrent episodes of swelling and tenderness of the buccal and/or submandibular region. All patients underwent salivary gland sialography of the suspected impaired gland followed by sialoendoscopy.

Upon detection of the impaired gland, a local infiltration anesthetic was injected with lidocaine 2% to the orifice region followed by lavage of the inner aspect of the duct via the orifice. Thereafter, a gradual dilatation of the duct orifice was established with increasing diameter lacrimal probes usually reaching 1.3 mm diameter matching the outer diameter of the sialoendoscope diagnostic unit. Thereafter, the diagnostic unit was diagnosed intraductaly and was advanced forward until reaching the end point of the ductal system. The advancement was performed under continuous lavage with isotonic saline solution.

When stricture was encountered, a first attempt of dilatation was performed with saline torrent. If no improvement was established, a sialobaloon (Sialotechnology, Ashkelon, Israel) was inserted and inflated as previously described (Nahlieli *et al*, 2001).

After the dilatation step was established, an intraductal wash with 100 mg hydrocortisone was made. Postoperatively, Augmentin® (GlaxoSmithKline, Petach Tikua, Israel) 1.5 g day^{-1} for a week was prescribed.

Results

All the patients were free of salivary gland sialadenitis symptoms during 1–4 years of follow up. All the patients were treated by saline lavage hydrostatic pressure except one patient who was also treated with sialoballoon. No complications were observed after treatment except immediate swelling of the affected gland postoperatively (in all patients), which resolved spontaneously after 12 h.

Clinical findings

The most prevalent symptoms were swelling and pain in the parotid glands followed by the submandibular glands.

Sialographic results

Preoperative sialography revealed one to multiple strictures in the ductal system of the affected gland (Figure 1) and in some cases a total atrophy of the gland observed.

Endoscopic results

The endoscopic appearance of the ductal system in sialadenitis following radioiodine therapy showed avas-

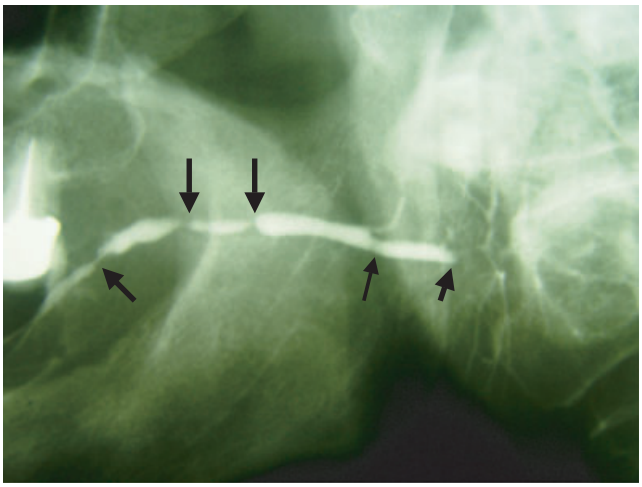

Figure 1 Sialographic view of multiple ductal stricures (black arrows)

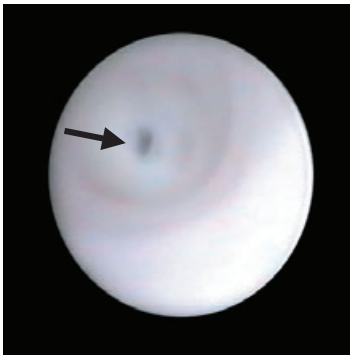

Figure 2 Endoscopic view of avascular lining mucosa and ductal stricture (black arrow)

cular lining mucosa (mat appearance of the ductal layer) without the typical proliferation of blood vessels. Multiple mucus plaques and narrowing of the main duct performing strictures were also observed (Figure 2).

Discussion

External beam irradiation therapy usually cause irreversible damage to salivary glands affecting primarily the acinar compartment followed by destruction of the whole parenchymal tissue (Newkirk *et al*, 2000). In contrast, radioiodine therapy to thyroid cancer patients primarily damage the ductal system and in severe cases cause total atrophy of the gland (Mandel and Mandel, 1999). In some cases, one or both of the parotid glands are affected followed by the submandibular glands (Mandel and Mandel, 1999; Aframian *et al*, 2005).

Consequently, residual secretory ability is available enabling the usage of sialogogous as pilocarpine hydrochloride as a mode of treatment (Aframian *et al*, 2005).

The rate of silaladenitis ranges from 8.3% to 11.5% with xerostomia being a long-term symptom (Allweiss *et al*, 1984; Dirusso and Kern, 1994), which causes progressive susceptibility to dental caries and periodontal diseases.

Other clinical signs and symptoms of salivary gland impairment include mucositis in the immediate postoperative period, taste and smell disturbances, alteration of nutritional status as well as higher risk for secondary malignancies, all of which decrease considerably the quality of life of the patients (Alexander *et al*, 1998; Newkirk *et al*, 2000).

Mandel and Mandel (2003) noted about the evidence of ductal obstruction in parotid sialogram. Following multiple endoscopic and sialographic evaluation, we believe that the cause of glandular injury is secondary to ductal injury. Here, we used sialography to provide accurate anatomic view of the injured ductal system of the gland.

Sialoendoscopy has gained great popularity for diagnosis and treatment of obstructive salivary gland diseases. This is a minimal invasive technique for the diagnosis of sialadenitis following radioiodine therapy as well as treatment of ductal system constrictions and plaques secondary to radioactive injury. The finding of avascular lining mucosa of the luminal ductal system in this study (Figure 2) is parallel with previous works suggesting the main target of damage in these patients is the ductal cells (Jhiang *et al*, 1998; Mandel and Mandel, 1999). Sialoendoscopy serves as much as an excellent toileting for this kind of damage rather than repairing it and provides secession of the viscous cycle of pain and swelling. We do not always manage to dilate all of the strictures, especially in severe cases, but symptomatic improvement is always achieved. Because of improving surgical skills, we are able to introduce the endoscope into the ductal system more easily, thus shortening time of treatment with minimal discomfort for the patients. Moreover, this is an outpatient procedure which can be performed under local anesthesia with minimal complications.

It is important to stress that the effect of I^{131} is dose dependent and time dependent, which means that long-term dysfunction may occur and most likely may aggravate at least during first 3 years postoperatively and probably may become irreversible and permanent. The patients whom we treated were admitted to our clinic with a permanent parenchymal damage. Endoscopic stricture dilatation can manage successfully symptoms of acute sialadenitis following one session only, but it cannot provide healing of the avascular changes of the lining mucosa. As long as patients are totally free of symptoms, this finding is of less importance.

In conclusion, sialoendoscopy is a promising method for diagnosis of sialadenitis following radioiodine therapy and may provide a better solution for this pathology and become the treatment of choice as more surgeons are involved with this treatment modality.

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