Sialadenitis following I-131 Therapy for Thyroid Carcinoma: Concise Communication

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During a 4-yr period, ten of 87 patients (11.5%) who received therapeutic doses of radioactive iodine (I-131) for thyroid carcinoma developed acute and/or chronic sialadenitis involving the parotid (five patients) or submandibular (four patients) glands, or both (one patient). Nine of the 10 patients had received prior I-131 therapy; the precipitating I-131 dose varied between 10 and 164 mCi. Onset of symptoms occurred between 1 day and 6 mo following therapy and the duration varied from 3 wk to 2½ yr. This complication occurs more often than has been appreciated.

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Acute, transient inflammation and altered function of the salivary glands has been reported to be an infrequent complication of radioiodine (I-131) therapy for thyroid carcinoma (*1–3*). Such radiation sialadenitis generally has its onset within 24 hr of I-131 administration and subsides within a week (*1,3*). Hilton et al. noted that following four to five therapeutic courses of I-131, some patients complained of periodic swelling of one or both parotid glands (*2*). However, neither the frequency nor the clinical features of this complication has been described in detail. During a 3-yr period, we encountered ten patients who developed acute or chronic sialadenitis following I-131 therapy for thyroid carcinoma, and their clinical characteristics form the basis for this report.

PATIENTS

From 1978 through 1981 a total of 87 patients received I-131 therapy for thyroid carcinoma at our medical center (n = 67) or through a private nuclear medicine office (n = 20). Our previously published treatment protocol was generally used in the treatment of those patients (*4*). We encountered ten patients (11.5%) from this group who subsequently developed subjective and objective findings compatible with acute or chronic sialadenitis. The condition was brought to our attention by the patients, who were not specifically questioned prospectively about salivary gland discomfort following the I-131. However, before administration of I-131, they were informed about the possible development of transient dry mouth and salivary-gland discomfort. All patients were examined by at least one of the authors, who checked salivary-gland tenderness and/or swelling.

RESULTS

The clinical characteristics of the patients are shown in Table 1. Salivary-gland abnormalities developed in both sexes, with an age range of 22–71 yr, reflecting the approximate distribution of all thyroid carcinoma patients seen by us. Four of the patients had a history of prior external irradiation of the head and neck, but denied sialadenitis following that therapy. Nine of the 10 patients had been treated with I-131 before the administration of the precipitating I-131 dose. The prior I-131 doses varied between 40 and 280 mCi, with a median of

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TABLE 1. CLINICAL CHARACTERISTICS OF PATIENTS

Case	Age	Sex	Prior external radiation	Thyroid histology	Total prior mCi I-131 (months)*	I-131 dose in mCi immediately before sialadenitis	Salivary gland(s) involved	Onset of symptoms following I-131 therapy	Duration of symptoms	Symptoms
1	57	M	x-ray therapy for acne age 13–15	papillary + metastases	100 (12)	10	left parotid	1 wk	3 wk	dry mouth, gland tenderness
2	37	F	none	papillary, + nodes	none	100	left parotid	5 days	1 yr	gland tenderness, swelling
3	35	F	none	papillary	102 (4)	164	left submandibular	3 days	2½ yr	one episode suppurative sialadenitis
4	60	M	x-ray therapy age 5 for tonsillitis	papillary, + nodes	100 (11)	100	right submandibular left parotid	6 mo	2 yr	gland tenderness and swelling
5	41	F	orthovoltage (66 roentgen) for keloid age 37	papillary, chronic thyroiditis	218 (12)	10	bilateral submandibular	1 day	2 yr	dry mouth, salivary-gland tenderness and swelling associated with eating
6	71	F	none	papillary, chronic thyroiditis	280 (4)	118	right parotid	1 wk	1½ yr	one episode suppurative parotitis, chronic gland tenderness and swelling
7	34	M	none	papillary-follicular	212 (9)	100	left submandibular	2 days	1½ yr	↓saliva, dry mouth, gland swelling while eating, ↑pain off thyroid in preparation for scan
8	70	F	none	papillary	60 (7)	100	left parotid	3 wk	2 yr	gland tenderness and swelling, narrowing of Stensen's duct, one episode of suppurative sialadenitis
9	56	F	none	papillary-follicular	10-0 (9)	100	bilateral submandibular	5 days	12 yr	gland swelling while eating
10	22	F	x-ray treatment for tonsillitis age 4	papillary-follicular	40 (11)	90	bilateral parotid	2 wk	2½ yr	gland tenderness and swelling, parotidectomy for relief

* Interval in months between the last prior dose of I-131 and the dose of I-131 precipitating the siladenitis.

100 mCi; they were administered 4 to 12 mo (median, 9 mo) before the precipitating dose. The median precipitating dose was 100 mCi (range 10 to 164 mCi). Five of the affected patients had serum TSH measurements made just before the radioiodine image; the mean was 56 μU/ml (range 34–155). This was not significantly different from the concentrations (mean 61 μU/ml) found in the sera from 45 patients who received I-131 for thyroid carcinoma but did not develop sialadenitis.

The parotid gland was involved in five patients, the submandibular gland in four, and both a submandibular and parotid gland in one patient. The sialadenitis was bilateral in three patients. The symptoms included dry mouth (three patients), bitter taste (three patients), recurrent salivary tenderness (nine patients), and swelling (nine patients). Three of the patients noted that the swelling of their submandibular glands occurred only during eating. Onset of symptoms generally occurred within 1 week of treatment (median 6 days, range 1 day to 6 mo). The symptoms lasted between 3 wk and 2 ½ yr, with a median of 2 yr at the time that these data were compiled (June, 1982).

Three patients developed suppurative sialadenitis, with fever, pain, and salivary-gland swelling requiring antibiotic therapy. One (Patient 8) developed narrowing of Stensen's duct, which required dilatation. A parotidectomy was performed in Patient 10 because of intractable salivary-gland discomfort and enlargement. Microscopic examination of the excised gland revealed reduced numbers of serous cells, proliferation of the ducts, and inspissation of secretions, compatible with atrophic sialadenitis.

DISCUSSION

Both acute and chronic sialadenitis was found in 11.5% of our patients treated with therapeutic doses of I-131 for thyroid cancer. This frequency is much greater than that found in the general population or even in high-risk groups of patients (e.g., during the first week following gastrointestinal tract surgery) (*5*). The probable cause of sialadenitis in our patients was radiation injury due to concentration of I-131 by the glands. It has been well documented that salivary glands concentrate iodide from the blood, the iodide concentration in mixed saliva being 30–40 times the plasma level (*3,6–8*).

Radiation induces histologic alterations in the salivary glands, and changes in the chemical composition of saliva. In patients with intact thyroid glands, a 5-mCi oral dose of I-131 delivers a radiation dose of ~250 rad to the salivary glands (*9*). Goolden and co-workers measured the salivary and plasma concentrations of I-131 after tracer doses in two athyreotic patients who had developed radiation sialadenitis from doses of 100–200 mCi radioactive iodine (*3*); they estimated the radiation dose to the salivary glands to be ~700 rad during the first 12 hr of therapy. A decrease in salivary amylase has been noted following 8–51 mCi of I-131, indicating a reduction in salivary-gland function (*10*). This effect was found approximately 4 days after the radioiodide treatment, and lasted an average of 10 days.

Most of the studies concerning the effects of radiation on salivary-gland histology and function have been performed on patients who received therapeutic external irradiation of the head-and-neck for benign and malignant conditions. Both inflammation and neoplasia have been observed in salivary glands in these irradiated patients (*11*). Indeed, even the relatively low doses of external radiotherapy used for treating a variety of benign conditions, such as tonsillar enlargement or acne, have been associated with sialadenitis and salivary neoplasms (*11*). Approximately 70% of such patients received less than 750 rad of external radiation (*11*).

A surprising feature of our study is the relatively high frequency (11.5%) of sialadenitis following I-131 therapy for thyroid carcinoma. This may reflect the increased awareness of our patients of this possible complication, since they were all warned that transient salivary gland discomfort and dry mouth may occur following such therapy. Although prior external head-and-neck irradiation may predispose patients to the subsequent development of radiation sialadenitis, a history of such exposure was present in only four of our ten patients. However, nine of them had received prior I-131 therapy, which may have initiated the injury in the salivary glands. We have generally opted not to give further I-131 therapy to patients who have developed chronic salivary-gland enlargement or dysfunction, unless the patients' serum thyroglobulin concentrations progressively rise while they are on adequate suppressive doses of thyroxine, or there is unequivocal evidence of distant metastases of the thyroid carcinoma demonstrated by radioiodine scanning. We note that Goolden et al. treated one of their two sialadenitis patients with additional I-131 therapy, without a recurrence of the sialadenitis (*3*).

We were unable to perform objective measurements of salivary-gland function following I-131 therapy, due to the retrospective nature of our study. A carefully conducted prospective study—with assessment of the signs and symptoms of salivary dysfunction and serial measurements of objective parameters of salivary function—will be needed to define accurately the prevalence and natural history of salivary-gland abnormalities following I-131 therapy.

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