Gallium-67 Scanning in Sjögren's Syndrome: Concise Communication

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We performed gallium-67 scans in 12 patients with primary or secondary Sjögren's syndrome (SS). Salivary-gland uptake of gallium-67 was noted in four of five patients with primary SS. Pulmonary uptake was observed in ten of 12 patients. Chest radiographs were essentially normal in all patients, although 60% complained of significant dyspnea with exertion. The gallium-67 scan may prove to be a sensitive noninvasive diagnostic test for lung and mediastinal involvement by either primary or secondary SS, and for salivary-gland involvement in primary SS.

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Sjögren's syndrome (SS) is defined by clinical and laboratory parameters, but a sensitive noninvasive anatomic test for salivary-gland inflammation is still lacking. The pertechnetate scan correlates roughly with salivary-gland biopsy findings, but is a direct test of secretory function rather than of glandular infiltration (*1*). Sialography, while demonstrating ductal and acinar anatomy (*2*), detects destructive changes occurring relatively late in the inflammatory process. Neither test is entirely specific nor sensitive for the diagnosis of SS (*3,4*). The minor salivary-gland biopsy—which is currently the most accurate test for the lymphocytic salivary-gland inflammation of SS (*3*)—is invasive and ill-suited for use as a follow-up procedure. There have been scattered reports of gallium-67 uptake in the lacrimal and salivary glands of patients with SS (*5,6*), as might be expected from the known affinity of gallium for lymphocytes in vitro (*7*) and for lymphomas in vivo (*8*). As part of a prospective study of SS, we therefore performed gallium scans as well as minor salivary-gland biopsies to determine whether a correlation might exist in this group of patients.

MATERIALS AND METHODS

Patient sample. Patients from the clinic population with suspected or known SS were offered the opportunity to participate in the study. SS was defined as previously described (*3*) by two of these three criteria: xerostomia, xerophthalmia, and another well-defined connective-tissue disease. We studied five patients with primary SS (sicca syndrome alone) and seven with secondary SS: five of seven with classical or definite rheumatoid arthritis (RA), and two of seven with systemic lupus erythematosus (SLE) as defined by ARA criteria (*9,10*)). Informed consent was obtained and the patients were hospitalized in the General Clinical Research Center. Salivary-gland biopsies were graded as described by Tarpley et al. (*11*).

Scintigraphy. Each patient received 4–5 mCi of gallium-67 citrate, and 48 hr later was imaged on either a single- or dual-probe rectilinear scanner or a multicrystal scanning device, using an 85-325 keV window and appropriate collimation. Anterior and posterior full-body images were obtained. The pulmonary uptake of gallium was graded as follows (*12*): 0 = normal, 1+ = bone > lung, 2+ = lung-bone, 3+ = liver > lung > bone, 4+ = lung ≥ liver.

RESULTS

Selected clinical and laboratory results are listed in Table 1. Two of ten patients were receiving corticosteroids and three of ten received gold salts (*2*) or hydroxychloroquine (*1*) for RA at time of study. Seven of ten patients had anti-SSA (Ro) antibody (four of seven with primary SS) and four of ten had anti-SSB (La) antibody (4/4 with primary SS). Precipitating antibodies to SSA

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TABLE I

Patient	Age	Sex	Diagnosis	D.O.D.†	SSA*	SSB*	Biopsy‡	CXR§	Gallium uptake¶			
									S	L	P	M
1	54	M	RA, 2°SS	11	+	−	III	N	−	−	2+	+
2	51	M	RA, 2°SS	5	−	−	III	N	−	−	1+	+
3	61	F	RA, 2°SS	5	−	−	III	N	−	−	1+	−
4	53	F	RA, 2°SS	5	−	−	I	Blunt CPA	−	−	2+	−
5	64	M	RA, 2°SS	10	−	−	II	N	−	−	2+	+
6	40	F	SLE, 2°SS	3	+	−	II	N	−	−	0	−
7	46	F	SLE, 2°SS	1	+	−	I	N	−	−	1+	−
8	61	F	1°SS	5	+	+	IV	N	+	−	1+	+
9	26	F	1°SS	1	+	+	III	N	+	+	0	−
10	76	F	1°SS	13	−	−	IV	N	+++('75)			
									++	−	1+	−
11	61	F	1°SS	8	+	+	IV	N	+++	−	2+	−
12	73	F	1°SS	15	+	+	IV	N	+++('77)		3+('77)	
									+('81)			
									−	−	0	−

* Anti-SSA and SSB antibodies.

† Duration of disease (SS), yr.

‡ Minor salivary gland, class (see text).

§ Chest radiograph, N = normal, CPA = costophrenic angle.

¶ Date of study = 1982–83 unless otherwise specified.

S = salivary (submandibular and/or parotid), L = lacrimal, P = pulmonary, M = mediastinal.

During the time of the studies, certain patients were being treated with hydroxychloroquine or corticosteroids, namely: Patient 2: aurothioglucose 50 mg i.m. weekly, Patient 3: hydroxychloroquine 200 mg twice daily; prednisone 10 mg daily, Patient 4: prednisone 5 mg daily, Patient 5: aurothioglucose 50 mg i.m. weekly, Patient 6: prednisone 10 mg every other day.

react with antigens obtained from a human lymphoid cell line as well as with the soluble cytoplasmic antigen termed Ro. SSB is a similar lymphoid nuclear antigen thought to be identical to the cytoplasmic antigen termed La. A high but variable percentage of patients with Sjögren's Syndrome have antibodies to SSB. Antibodies to SSA are less common and still less specific. No patient had known pseudolymphoma or malignancy. Note that Patients 10 and 12 both had more intense parotid and pulmonary uptake of gallium in 1977 than in 1983; uptake disappeared from both lungs and parotid glands in Patient 12. No significant changes in Patient 12's clinical status or therapy occurred during this interval, although her serum gamma globulin dropped from 3.27 to 2.31 g/100 ml, and her Westergren ESR fell from 99–105 mm/hr (1975–1981) to 55 mm/hr (1982). Representative scans are shown in Fig. 1.

DISCUSSION

There are no striking differences between primary and secondary SS, in duration of disease or salivary-gland enlargement, by which to explain the absence of glandular gallium uptake in the seven patients with secondary SS, although the number of patients is too small for statistical analysis. Five out of five patients with primary SS have had positive salivary scans at some time (4/5 at this analysis). As is usually the case, our patients with primary SS tended to have more extensive lymphocytic infiltration on biopsy than did those with secondary SS; nevertheless, Patients 1 and 3 had Grade III biopsies but negative scans, and Patient 12, whose salivary gland is currently the most severely infiltrated of all, has had a reversion of her salivary scan to negative. Furthermore, four patients with secondary SS had significant parotid-gland swelling at the time of negative salivary scans; two of the four patients with primary SS and positive scans also had parotid enlargement at this examination. Differences between primary and secondary SS in subsets of infiltrating leukocytes (which might by inference account for differing affinities for gallium) have not been found consistently (*12*), and typing was not performed on these biopsies. In this small sample, the sensitivity of the gallium scan in primary SS (~80%) appears to be similar to that of the anti-SSB antibody (60–75%), a sensitive noninvasive laboratory test for primary SS (*13*). While one is unlikely to confuse sarcoidosis and primary SS, salivary uptake of gallium in the former (*14*) mandates study of a population in which SS is part of the differential diagnosis before commenting on specificity. In addition, the sensitivity and anatomic accuracy of this procedure might be improved further by detailed imaging of the head region with lateral and oblique views, as has been described for pertechnetate (Tc-99m) scans (*15*).

The high incidence of pulmonary parenchymal uptake of gallium, not only in secondary (six of seven) but in primary SS (four of five), is intriguing and not previously reported. Three of our ten patients complained of chronic bronchitis, and six of the ten had one-block dyspnea on exertion. Only two patients smoked or had coronary heart disease (Killip Class I). Our data suggest that subclinical lung disease may be much more common in primary SS than the 10% that is recognized clinically (*16*). Although all of the chest radiographs were interpreted as normal, 10% of patients with abnormal pulmonary function tests and biopsy-proven interstitial lung disease may have normal chest radiographs (*17*). Furthermore, previous reports have documented the sensitivity of gallium for subclinical pulmonary disease (*18*). More extensive longitudinal investigation of lung function and anatomy will be required to establish the significance both of the pulmonary parenchymal and the mediastinal uptake of gallium-67 noted in our patients.

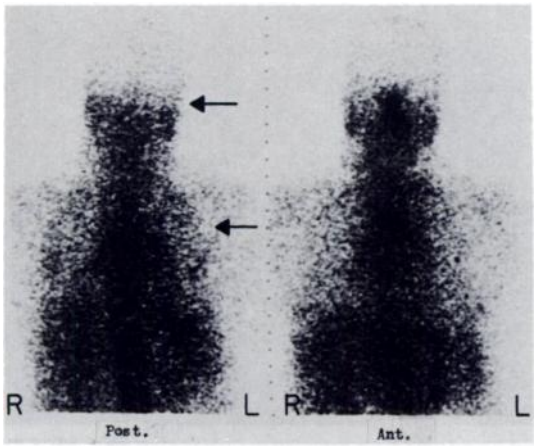

FIG. 1. Patient 10: Whole-body scans at 48 hr after injection of 5 mCi Ga-67. Note left submandibular and parotid uptake (upper arrow), and 1+ pulmonary uptake (lower arrow).

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