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CHRONIC SIALODENITIS¹

By

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A case of chronic sialoadenitis with unusual localization is recorded. Since it has been suggested lately that chronic sialoadenitis (Sjögren's syndrome) might be due to an auto-immune mechanism, a series of serological examinations have been carried out with special reference to the possibility of finding organ specific antibodies directed against salivary glands.

METHODS

Complement fixing reactions were performed as described by Roitt *et al.* (14) using 2 minimum hemolytic doses of complement and extracts of human post mortem liver, kidney, salivary glands, and adrenals as antigens. Thyroid extracts were made from surgically removed toxic goitres. Differential centrifugation was performed as described by Hagebom & Schneider (7). Serum was tested for the presence of thyrocytotoxic factor by means of cell cultures obtained by trypsinization of surgical specimens of toxic goitres as described by Pulvertaft *et al.* (13) and Irvine (8). The method was standardized as described by Halberg (6). Agar-gel diffusion precipitin tests were carried out as described by Anderson *et al.* (1). Serum was examined for the presence of thyroglobulin antibody by means of thyroglobulin sensitized sheep cells (obtained from Burroughs Wellcome & Co.). Immune fluorescence tests were performed on unfixed sections of surgical specimens of parotid glands, adrenals and thyroids as de-

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scribed by *Coons & Caplan* (4), on ethanol fixed sections of thyroid tissue as described by *Beutner & Witebsky* (2) and on acetone fixed He-La cells, *i.e.* an old strain of carcinoma cells maintained in cultures.

CASE HISTORY

The patient was a 68 year old woman whose daughter had died at the age of 25 from disseminated lupus erythematosus with hemolytic anemia, thrombocytopenia, rheumatoid arthritis, pericarditis, chronic hepatitis, nephritis and a non specifically positive Wasserman reaction. The patient herself had had a goitre which disappeared spontaneously. In 1948 she developed fever and swelling of both parotid glands. After this episode she developed constant dryness of the mouth and she had difficulty in swallowing. Moreover she noticed intermittent dryness of the eyes. She has never had arthralgia.

In 1960 she noticed a swelling of the palate. It was not painful or tender, but it persisted when in 1963 she was seen in the dental clinic and the medical department A of the University Hospital in Copenhagen. At that time she was found to have pronounced dryness and atrophy of the mucous membrane of the cheek. The back of the tongue was dry, red, and shiny and the papillae were atrophic. The mucous membrane of the hard palate was normal, but on the right side of the soft palate a swelling was found. A groove with a decubital ulcer was seen in the swelling at the back of the denture, but otherwise the mucous membrane over the swelling was normal. No swelling of the parotid, submaxillary, sublingual or lacrimal glands could be detected. The joints were normal and she had no goitre. A biopsy of the swelling revealed salivary glands with pronounced round cell infiltration and epithelial proliferation (Fig. 1 and 2).

SEROLOGICAL EXAMINATIONS

In the patient's serum complement fixing antibody was found in a high titer (512) against extracts of salivary glands, toxic thyroid tissue, liver- and adrenal tissues, but not against extracts of kidney tissue. The extracts of salivary glands and of thyroid tissue were fractionated by means of differential centrifugation, and the microsomal fractions were isolated. The antigenicity of both extracts was found in the supernatant after removal of the microsomal fractions which were not antigenic. The serum was found not to be toxic to thyroid cell cultures. Thyroglobulin antibody was found in a low titer (250).



Fig. 1.

Histological section of the tumour on the palate. 32 $\times$.

No precipitins were found against extracts of salivary glands, thyroid or kidney tissues. Using an immune fluorescens technique a very bright nuclear staining was found in unfixed sections of salivary glands, thyroid- and adrenal tissues, and also in acetone fixed He-La cell cultures. No cytoplasmatic fluorescence could be discerned in any of the sections. In aethanol fixed thyroid sections a faint colloid staining could be found.

OTHER INVESTIGATIONS

ESR 20 mm. Hb 12.6gms. per 100 cc. Leucocytes 4.400. Thrombocytes 286.000. No L.E. Cells. Coombs' test negative. Serum electrophoresis: albumin 4.82, α_1 0.27, α_2 0.39, β 0.68, γ 1.85 gms. per 100 cc. Thymol turbidity 0.24. (Normal < 0.15). Rose Waaler negative. R.A. test positive.

Examination of the production of saliva revealed complete

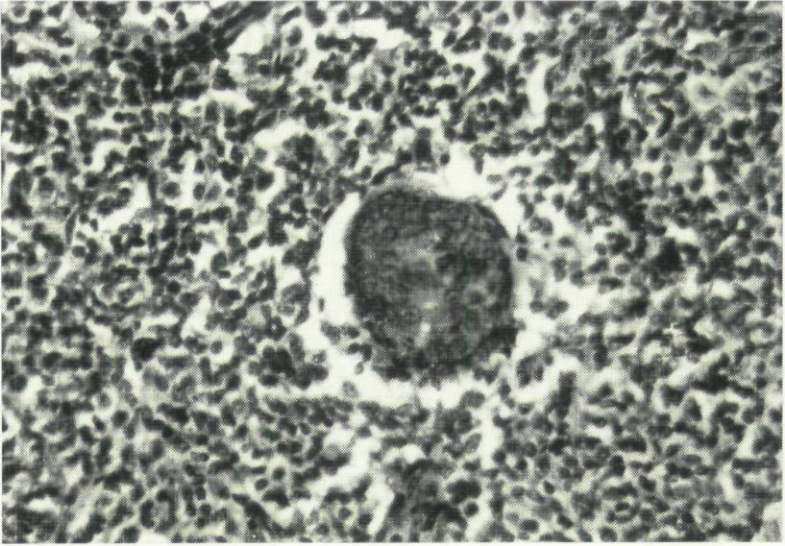


Fig. 2.

Same as 1. Notice epi-myoeptithelial cell island, 100 $\times$.

xerostomy on two occasions. Sialography showed signs of bilateral parotitis. Examinations of the eyes including Schirmer's test was normal. Examinations of protein bound iodine and tracer tests with J-131 were inconclusive because the patient had recently had sialography done using a dye with iodine in it. A biopsy of the thyroid revealed perfectly normal thyroid tissue.

DISCUSSION

The symptom which was the reason for the examination of the patient was the swelling of the palate, which by biopsy was found to be due to chronic sialoadenitis. This localization of the disease is unusual. Similar cases have been described by *Nelson et al.* (12) and *Lancaster & Hughes* (10). However, further examinations showed that the disease was not exclusively localized in the palate. The patient had previously had a swelling of both parotid glands and sialography revealed changes also in these glands. Moreover the xerostomy could

not be explained merely by a defective function of the salivary glands in the palate. The function of other salivary glands would have to be impaired as well.

The etiology of the disease is unknown. The assumption that an auto-immune mechanism is involved is based on a number of observations: The histological picture of the affected salivary glands is predominated by a dense round cell infiltration, hypergammaglobulinemia is almost always present, serological phenomena are regularly present which may represent auto-antibodies, and other auto-immune diseases as for instance disseminated lupus erythematosus are over represented in the patient's families.

Jones (9), Anderson et al. (1) and Bloch & Bunim (3) found precipitating antibodies against extracts of salivary and lachrymal glands in sera from patients with Sjögren's syndrome. However, the reactions were not specific since extracts of various other organs were also active as antigens. Serum from our patient did not contain a precipitating antibody, even though several sera from patients with disseminated lupus erythematosus produced distinct precipitin reactions in the systems used. Serum from our patient contained complement fixing antibody against extracts of salivary glands in a high titer. However, the reaction was not specific, since the serum could fix complement in an equally high titer with extracts of liver, adrenal and thyroid tissues. The serum was not anti-complimentary. *Mosbech & Østergaard Kristensen (11)* have described a case of chronic sialoadenitis with complement fixing antibody directed against extracts of salivary tissue present in the serum. This antibody was not specific either since similar reactions could be obtained using extracts of adrenal and kidney tissues. *Anderson et al. (1) and Bloch & Bunim (3)* also found that the complement fixing antibodies against extracts of salivary tissue demonstrable in sera from patients with Sjögren's syndrome were non specific.

Serum from our patient contained a complement fixing thyroid antibody. It should be emphasized that this thyroid antibody is not identical to the much more specific complement

fixing antibody found in sera from patients with Hashimoto's disease. The antigen corresponding to the specific complement fixing thyroid antibody is localized in the microsomal fraction of the extract, whereas the antigen in this case could be demonstrated exclusively in the supernatant after removal of the microsomal fraction. Testing for the thyro-cytotoxic factor may be used as a control of the specificity of the thyroid antibody because the cytotoxic factor and the microsomal complement fixing antibody are probably identical, *Irvine* (8) and *Halberg* (6). The fact that the serum from our patient was not cytotoxic indicates that the complement fixing antibody against thyroid tissue is not specific. A biopsy of the patient's thyroid revealed perfectly normal thyroid tissue. The complement fixing antibody found in the serum from this patient is identical with the phenomenon described by *Gajdusek* (5). It can be demonstrated regularly in sera from patient with disseminated lupus erythematosus, cirrhosis of the liver, rheumatoid arthritis, *i.e.* diseases with a possible autoimmune etiology.

The anti nuclear factor found in the serum from our patient was also non specific since it could be found in sections from thyroid- and adrenal tissues as well as in sections of salivary glands. Even cell cultures of He-La cells gave a bright nuclear fluorescens when treated with serum our patient. No cytoplasmatic fluorescence could be demonstrated using sections of salivary glands.

None of the serological phenomena demonstrable in sera from patients with Sjögren's syndrome are specific. Even though this disease has features in common with auto-immune diseases it has not been possible to demonstrate organ specific antibodies against extracts of salivary glands in sera from patients with the disease.

SUMMARY

Chronic Sialoadenitis. A case history.

A 68 year old woman whose daughter had died from disseminated lupus erythematosus was admitted because of a

tumour in the palate. A biopsy of the tumour revealed chronic sialoadenitis. No swelling of other salivary glands could be found, but the patient had xerostomy and sialography showed changes also in the parotid glands. The patient had diffuse hypergammaglobulinemia, and in her serum, complement fixing antibody directed against extracts of salivary glands was found. The antibody was, however, not specific since the serum could also fix complement with extracts of various other organs. The serum contained anti nuclear factor demonstrated by immune fluorescence technique, but no cytoplasmatic fluorescence could be obtained in sections of salivary glands. It is emphasized that even though chronic sialoadenitis (Sjögren's syndrome) has features in common with auto-immune diseases all attempts to demonstrate organ specific antibodies against salivary antigens in sera from patients with this disease have so far been unsuccessful.

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