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TREATMENT OF THYROIDITIS

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THE THREE main and distinct clinical types of thyroiditis are (1) the subacute (pseudotuberculous or giant cell) variety, (2) struma lymphomatosa (Hashimoto's thyroiditis) and (3) Riedel's struma.[1] Subacute thyroiditis resolves promptly and completely in response to roentgen therapy; some, and possibly most, cases of struma lymphomatosa respond favorably to roentgen rays, but Riedel's struma is unaffected by irradiation.

SUBACUTE THYROIDITIS

Subacute thyroiditis is a self-limited disease of unknown causation. It has a variable course of weeks or months and eventually subsides without treatment and without significant interference with the function of the thyroid.

This type of thyroiditis has been variously named tuberculous, pseudotuberculous or giant cell thyroiditis because of the histologic appearance of pseudotubercles with giant cells. Tubercle bacilli cannot be demonstrated in the lesions, and the cause of the disease is unknown. Bacteria have not been demonstrated in the thyroid. The possibility that it represents a virus infection has not been excluded. The pseudotubercle or giant cell reaction represents a reaction of wandering cells to colloid, which they appear to be phagocytosing. The sedimentation rate is consistently elevated.

Many surgeons do not operate on patients with subacute thyroiditis and hence are not aware that this well recognized clinical entity is, from the histologic standpoint, identical with pseudotuberculous or giant cell thyroiditis. In order to prove to my own satisfaction that the two diseases are the same, I have analyzed 15 cases of subacute thyroiditis in which roentgen therapy was given and compared the history and physical observations with those in 12 cases in which operation was performed and found that there was no significant difference in the clinical observations in the two groups.[1] To confirm further the fact that the clinical entity of subacute thyroiditis is indeed identical to the pathologic entity

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1. Crile, G., Jr.: Thyroiditis, Ann. Surg. **127**:640-654 (April) 1948.

of giant cell or pseudotuberculous thyroiditis, biopsy specimens of the thyroid were taken in 2 typical cases of subacute thyroiditis, and the patients were then treated with roentgen rays. The biopsy specimens showed typical giant cell or pseudotuberculous thyroiditis; the response to roentgen therapy was prompt, complete and typical of that of subacute thyroiditis.

TREATMENT

Subacute thyroiditis responds promptly and completely to roentgen therapy. Six hundred to 800 r usually suffices to effect resolution in a few weeks. The pain and tenderness subside in a few days. The average time at which 15 patients treated with roentgen rays were considered to be entirely well was nineteen days after the start of treatment. By this time the thyroid is rarely either tender or palpably enlarged. In 2 of our cases, two or more courses of treatment over a period of three months were required before a complete cure was effected. In 3 cases the patients considered themselves well in one week.

Thyroidectomy is a satisfactory means of controlling subacute thyroiditis, but since the disease is essentially self limited and since roentgen rays effect such prompt and complete resolution, operation is not often indicated.

REPORT OF CASES

CASE 1.—The patient (previously reported [1]) was a woman, 32 years old, who had a hard tender painful enlargement of the thyroid gland, of two months' duration. Biopsy showed chronic thyroiditis, with decided granulomatous reaction to colloid (so-called pseudotuberculous thyroiditis). Foreign body giant cells were present.

A diagnosis of subacute thyroiditis was made, and roetgen therapy was started. Seven hundred roentgen units were given to the region of the thyroid in five treatments. Nine days after the first treatment the patient stated that he felt entirely well. There was no pain or tenderness of the thyroid. Although the gland had returned to normal size the right lobe was still fairly firm. Four weeks later, palpation of the thyroid revealed no abnormalities and the patient remained well.

CASE 2.—The patient was a woman, 35 years of age, who complained of a painful tender lump in the left lobe of the thyroid, which had been present for three weeks. The pulse rate was 150 and the basal metabolic rate + 18 per cent. The thyroid was enlarged to twice its normal size and was hard.

A diagnosis of subacute thyroiditis was made, and 700 r was given over the thyroid. A month after the last treatment the right lobe of the thyroid was normal to palpation and the left lobe was a little smaller but was still hard. Biopsy specimens were taken of both lobes of the thyroid and showed the typical picture of subacute thyroiditis with focal granulomatous reaction to colloid, slight to decided fibrosis and moderate lymphoid hyperplasia (so-called pseudotuberculous thyroiditis).

A month after the biopsy and two months after roentgen therapy was started, the thyroid was no longer palpable and the patient felt well.

COMMENT

The clinical features of these cases and the response of the thyroid to roentgen therapy are typical of those encountered in other cases of

subacute thyroiditis. Biopsy of the thyroid showed changes characteristic of the so-called pseudotuberculous or giant cell thyroiditis. There can be little doubt that the clinical disease, subacute thyroiditis, is from the pathologic point of view pseudotuberculous or giant cell thyroiditis. This disease responds promptly to roentgen therapy and does not necessitate thyroidectomy.

STRUMA LYMPHOMATOSA

Struma lymphomatosa is a progressive disease of the thyroid, possibly associated with systemic disorders.[2] There is extensive acidophilic degeneration of the epithelial elements of the thyroid and replacement by lymphoid and fibrous tissue. Hypothyroidism, or at least a peculiar type of hypometabolism that does not always respond specifically to treatment with thyroid, is likely to develop. The cause of the disease is unknown. It does not progress to Riedel's struma,[3] nor is it the end result of subacute thyroiditis. An excellent description of this disease was given by Joll in 1939.[4]

Until recently the diagnosis of struma lymphomatosa was rarely established prior to operation, and hence there was little opportunity to study its response to irradiation. Schilling [5] reported a case of struma lymphomatosa that responded to roentgen therapy.

In the last 3 cases that I have seen the diagnosis of struma lymphomatosa was established before operation, and in the last 2 cases I have performed only a biopsy and have treated the patient with roentgen rays. In the first case there was no immediate effect on the thyroid, but in six months the gland was not palpable. In the second there was prompt and complete resolution of the enlarged thyroid.

REPORT OF CASES

CASE 1.—The patient, a woman, 44 years of age, entered the clinic with complaints referable to nearly every system of the body. She had been receiving medical care constantly for fifteen years. For four years prior to this examination she had noted an intermittent tender swelling of the neck, with pain radiating up to the ears. Among her other complaints were headache, fatigue, gain of 50 pounds (about 23 Kg.) of weight, swelling of the entire body, tightness of the shoulders, numbness of the extremities, dizziness, nervousness and shortness of breath.

2. Graham, A.: Struma Lymphomatosa (Hashimoto), Tr. Am. A. Study Goiter, 1940, pp. 22-251.

3. Graham, A., and McCullagh, E. P.: Atrophy and Fibrosis Associated with Lymphoid Tissue in Thyroid; Struma Lymphomatosa (Hashimoto), Arch. Surg. **22**:548-567 (April) 1931.

4. Joll, C. A.: Pathology, Diagnosis, and Treatment of Hashimoto's Disease (Struma Lymphomatosa), Brit. J. Surg. **27**:351-389 (Oct.) 1939.

5. Schilling, J. A.: Struma Lymphomatosa, Struma Fibrosa, and Thyroiditis, Surg., Gynec. & Obst. **81**:533-550 (Nov.) 1945.

Results of examination were essentially negative except for a blood pressure of 148 systolic and 112 diastolic, obesity and a hard enlargement of the entire thyroid to about twice its normal size. The left lobe was larger than the right. The gland was only slightly tender. She was a little hoarse.

Examination of the larynx showed thickening of the anterior end of the right vocal cord, consistent with chronic laryngitis. Results of urinalysis, blood counts, the level of blood sugar, Wassermann and Kahn tests and a roentgenogram of the chest were within normal limits. The basal metabolic rate was —22 per cent, and the level of blood cholesterol was 120 and on a later test 179 mg. per cubic centimeter.

A diagnosis of struma lymphomatosa was made and confirmed by biopsy. The specimen showed dense fibrous tissue with several broad patches of lymphocytes and plasma cells intermingled with a few epithelial elements resembling thyroid epithelium. Other fragments showed similar architecture with broad patches of dense lymphocytic infiltration, one area including some patches of acidophilic epithelium.

Roentgen therapy was advised, and 700 r was given to each lobe of the thyroid. The symptoms of pressure were relieved promptly, but, two months after treatment was started, there was little diminution in the size of the thyroid and it was still firm.

Six months after the beginning of treatment, the thyroid was not palpable and the patient remained free of local symptoms. The systemic symptoms persisted and did not respond to treatment with thyroid and amphetamine.

CASE 2.—The patient was a woman, 53 years of age, who complained of a "tight choking bursting" sensation in the throat, dating back to an injury sustained three months before entering the clinic. She had also noted lack of energy, drowsiness, sensitivity to cold, thickness of speech, constipation and flatulence.

Examination showed typical myxedema and a firm diffuse enlargement of the entire thyroid. The basal metabolic rate was —31 per cent, and the cholesterol level 316. A clinical diagnosis of struma lymphomatosa with associated myxedema was made and confirmed by biopsy. The pathologist reported observing rare thyroid follicles which were small, and had epithelial cells which were larger than usual with eosinophilic-staining characteristics. Little recognizable colloid remained. There was decided infiltration by lymphocytes and plasma cells, with occasional formation of lymph follicles. The stroma consisted largely of dense collagenous fibers.

A total of 1,550 r was given to the thyroid in eight treatments. The choking sensations subsided promptly and eight days after the beginning of treatment the gland was much softer and was considerably reduced in size. A month later, it was barely palpable and the patient, who was taking thyroid, felt much improved and had no symptoms other than nervousness and fatigue.

COMMENT

Neither roentgen therapy nor thyroidectomy have any effect on the systemic symptoms associated with struma lymphomatosa. The tendency to hypometabolism and its associated symptoms of weakness and exhaustion are not specifically corrected by feeding thyroid. Struma lymphomatosa appears to be a systemic disease. Roentgen therapy of the thyroid and thyroidectomy are nothing more than symptomatic treatment, which alleviates the local symptoms arising from the goiter. Thyroidec-

tomy does no more to alleviate the systemic symptoms than does roentgen therapy, and if the local symptoms can be controlled by irradiation there is no need to remove the goiter. How frequently struma lymphomatosa will respond to irradiation has not been established.

RIEDEL'S STRUMA

Riedel's struma is a chronic proliferating fibrosing inflammatory process, involving usually one lobe, but sometimes both lobes, of the thyroid and extending to involve the trachea and the muscles, fascia, nerves and vessels in the vicinity of the thyroid. It produces a bulky tumor that may be indistinguishable preoperatively from an inoperable carcinoma. It is not the end result of either subacute thyroiditis or struma lymphomatosa, but is a separate entity the cause of which is unknown. No specific organisms have been isolated from this lesion. In many instances the inflammatory reaction appears to center about a degenerating adenoma, and this may be a clue to its cause. Riedel's struma affects women more often than men and tends to occur beyond the age of 50.

TREATMENT

An adequate trial of roentgen therapy was made in 3 of the cases of Riedel's struma, without significant results. In 2 cases in which one lobe had been removed and a recurrence later took place on the other side, the roentgen therapy seemed to prevent further proliferations, although there was no change in the size of the tumor. In a third case, in spite of treatment with 2,550 r, pain and symptoms of compression continued, hypothyroidism developed and the process extended to involve the parathyroids and produced tetany. One must assume, therefore, that roentgen rays have little to offer in the treatment of this disease.

Complete surgical removal of the involved portion of the thyroid may be rendered utterly impossible by the extent of the extracapsular fibrosis. Serious damage to the trachea, carotid sheath or recurrent nerves may take place if the true nature of the lesion is not recognized and radical extirpation is attempted. In this disease one must often be content to do the best one can, within the bounds of safety, to relieve obstruction.

On the other hand, if one remembers the fact that at the center of the fibrosed lobe there is often a degenerating adenoma and that around this adenoma the fibrous tissue is deposited in concentric laminations which afford natural cleavage planes, it is often possible, without jeopardizing the vital structures adherent to the capsule of the thyroid, to split the lobe open and enucleate this central core. The results following this simple procedure have been excellent in the 3 cases in which I have found it practicable. Pressure symptoms have been relieved; the bulk of the tumor has been strikingly diminished, and the progress of the inflam-

matory and productive process appears to be arrested. It is well to remember that the severest obstruction to respiration usually is associated with retrotracheal adenomas that compress the trachea from behind and that this can be demonstrated before operation by a lateral roentgenogram of the trachea. If the surgeon is not aware of the retrotracheal tumor he is likely to overlook it in a thyroid which cannot be mobilized and rotated from its bed.

REPORT OF CASES

CASE 1.—The patient (previously reported [1]) was a woman 46 years old. She had noticed an enlargement of the left lobe of the thyroid two years before entry, and a few months later she became hoarse. Three months before entry an attempt was made to do a thyroidectomy, but the surgeon stated that the tumor was an inoperable carcinoma. From a biopsy specimen the lesion was diagnosed as either Riedel's struma or carcinoma.

Symptoms of pressure continued, but there was no loss of weight and no symptoms of systemic disease. Examination showed a stony hard fixed tumor, involving the left lobe of the thyroid and the cervical musculature. The left vocal cord was paralyzed. The basal metabolic rate was + 2 per cent.

A diagnosis of Riedel's struma or inoperable carcinoma was made. At operation it was observed that the left side of the neck was involved in a dense proliferation of fibrous tissue which had invaded the trachea and the prethyroid muscles. The lobe was exposed and the anterior half removed. It was white, brittle and avascular. The cleavage plane surrounding the central adenoma was located, and a degenerating adenoma was shelled out of its capsule of fibrous tissue. The right lobe was normal.

The pathologist reported chronic inflammation and complete replacement of thyroid tissue with fibrous tissue. There was a colloid adenoma in the center of the fibrous mass. Convalescence was uneventful, and the symptoms of pressure were relieved.

Comment.—This case is typical of Riedel's struma, in that (1) the initial diagnosis was carcinoma of the thyroid; (2) there was no systemic reaction or alteration of thyroid function; (3) there was extensive fibrosis of the thyroid and of the perithyroid structures; (4) there was a degenerating adenoma in the center of the fibrous mass, and (5) the symptoms were relieved by enucleation of the adenoma from the surrounding fibrous tissue.

CASE 2.—The patient was a Negro woman 42 years old. Seven years prior to entry a biopsy specimen of the thyroid had shown Riedel's struma. Following this she had been free of symptoms until five weeks before entry, when pain and tenderness developed in the region of the thyroid.

Physical examination showed a hard enlargement of the entire thyroid to four time its normal size. A diagnosis of chronic thyroiditis was made, but no treatment was given..

During the next four years the patient experienced a number of episodes of pain and tenderness of the thyroid and was treated with a total of 4,050 r to the thyroid over a period of twenty-two months. Roentgen therapy appeared to relieve the pain, but did not relieve the sensation of pressure or alter the consistency of the thyroid. Finally the sensation of pressure became intolerable, and the patient

became dyspneic from tracheal obstruction. Dr. R. S. Dinsmore removed enough of the thyroid to relieve the compression on the trachea and observed that the muscles, trachea and all the tissues around the thyroid were involved in dense fibrosis consistent with Riedel's struma. The pathologist confirmed the diagnosis of Riedel's struma, having observed that the thyroid was entirely replaced with fibrous tissue showing evidence of chronic inflammation.

Treatment with 2,050 r did not effect any improvement in this patient's symptoms or in the progress of the disease.

CONCLUSIONS

1. Roentgen therapy is the treatment of choice for subacute thyroiditis, and thyroidectomy is rarely, if ever, indicated.

2. When the diagnosis of struma lymphomatosa is made before operation roentgen therapy should be given a trial.

3. If struma lymphomatosa is recognized at the time of operation a very conservative resection of both lobes of the thyroid is recommended.

4. In Riedel's struma, roentgen therapy is of little or no value.

5. In Riedel's struma it is unwise, unnecessary and often dangerous to attempt to remove the entire lobe. If the onion-like concentric laminations in the fibrous tissue surrounding the central degenerating adenoma can be found, these avascular planes can be followed by blunt dissection and the core of the lobe shelled out without disturbing its capsule. Following this procedure, the symptoms are relieved and there is no further proliferation of fibrous tissue.

6. In 2 cases of subacute thyroiditis and 2 cases of struma lymphomatosa proved by biopsy, roentgen therapy was followed by complete resolution of the palpably enlarged thyroid.

7. Three patients with proved Riedel's struma were not benefited by roentgen therapy.

DISCUSSION

Dr. Joseph A. Witter, Detroit: I would like to comment on Dr. Crile's paper "Thyroiditis." During the last two years I have seen 5 cases of the subacute variety of the disease. I do not have a lot to offer, but I would like to state briefly my experience, because it has been at variance with that of Dr. Crile. The lesion in these cases was usually begun unilaterally as a tender, enlarged gland, with considerable systemic malaise, and has progressed slowly. As the original side improved in each case, the other lobe became involved. It is of interest that the second side became involved during the time that the patients were receiving penicillin in large doses and also were taking antithyroid drugs. I feel that perhaps these methods of therapeusis are not too valuable. My patients also received roentgen rays, but treatment was less intensive than recommended by Dr. Crile. The second side became involved during the course of the treatments with roentgen rays.

From this brief experience, I have come to the conclusion that subacute thyroiditis has a clinical course of from four to eight weeks.