Myxedema

Volume VI Thursday, May 9, 1935 Number 27

UNIVERSITY OF MINNESOTA HOSPITALS
Volume VI Thursday, May 9, 1935 Number 27

INDEX

I. CASE REPORT

MYXEDEMA WITH HYPERCHROMATIC ANEMIA

, 51 years old, admitted 5-19-34. History from husband and son.

Present Complaints

1. Severe generalized pain since May 5,
2. Vomiting and loss of appetite since May 5,
3. Weakness for years; and
4. Fatigue for years.

Fainted

On May 5th, 1934, fainted suddenly. On regaining consciousness, she complained of severe pain in her arms, legs and back. From that time on, she remained in bed and for about 5 days had continual vomiting.

Just before being brought to the hospital, she was given a hypodermic of morphine sulphate. On admission, she was in a semicomatose condition. 7½ gr. sodium benzoate brought about marked improvement.

Past history

Her son stated that for the past 15 years she has been suffering from weakness, and easy fatigueability. For the past 4 to 5 years, her voice has become deeper and speaking increasing difficult. She has suffered from impaired hearing for 5 years. One year previous to admission, a diagnosis of pernicious anemia was made and she was given liver extract by mouth. She was sensitive to cold and noted that her hair has become thinner, nails became brittle and skin dry. There has been no loss in weight. About one year previous to admission, noted numbness and tingling of extremities.

Physical examination

Hair - thin and scanty, marked thinning of eyebrows. Skin - dry and thick. Impaired hearing. Generalized weakness. Vibratory sense absent below knees. Marked impairment in position sense of toes.

Laboratory

Blood (5-17-34) - Hemoglobin 65%, erythrocytes 2,480,000, leucocytes 5,800, Hemogram: eosinophils 10%, basophils 2%, young forms 2%, band 4%, segmented neutrophiles 50%, monocytes 8%, lymphocytes 24%. Hyperchromatic anemia, slight anisocytosis, poikilocytosis. No outspoken macro- or microcytes present. Marked increase of eosinophils, neutrophiles show toxic granulations. There is slight shift to right, however, neutrophiles are not of pernicious anemia type. Hematological impression - hyperchromatic anemia. (Dr. Stasney)

Basal Metabolism Rate (5-19-34) --42%; (5-21-34) -45%. Urine (5-25-34) - urobilinogen trace. Feces (5-29-34) - urobilinogen 22.5 mg. per day. Icterus index 10.4 units. Urine - trace of albumen, few leucocytes. Serologic test for syphilis - negative. Creatinin - 1.0 mg. %. Gastric analysis - free Hcl acid present after histamine injection. Blood cholesterol (5-26-34) - 273.2 mg.%. (Note: Patient had already received some thyroid extract.) Electrocardiogram - P.R. interval prolonged, partial A-V block. T diphasic and very low in D I and D II. Suggestion - coronary insufficience T in D III positive and very low. Tendency for left axis deviation. X-ray of Chest and Gastro-Intestinal Tract - negative.

Thyroid therapy

Course: Placed on thyroid extract.

5-23-34 - Condition improved. Strength returning. Can hear and speak better. Receiving thyroid extract grains II t.i.d.

5-28-34 - Condition much better. Looks brighter. Strength increasing.

6-2-34 - Thyroid extract increased to grains IV daily.

Reaction

6-4-34 - Complains of severe headaches. Numbness of fingers. Stiffness of muscles of face. Unable to close eyes tightly.

6-11-34 - "Burning" feeling in chest. Nauseated. Pulse 110. Skin warm. Complains of headache. Thyroid extract reduced to grains I b.i.d.

Better

6-17-34 - Unable to close eyes tightly. Paresis of left lower face. Puffiness of lids disappeared. Appears brighter and talks more than she used to.

Discharged

7-15-34 - There has been marked improvement in the mental state. B.M.R. has risen to -5%. Edema has disappeared. Feels stronger. Maintenance dose 4 grains thyroid extract daily.

Follow-up in Out-Patient Department: 8-10-34 - Feels better. Able to walk. Blaud's pills for anemia. Maintenance dose reduced to grains III t.i.d.

11-26-34 - Still some weakness but is gradually improving.

2-7-35 - Basal Metabolism Rate -18%. Hemoglobin 73%. Thyroid increased to grains IV. daily.

4-8-35 - Remarkable improvement. Hair of scalp is increasing. Puffiness of face has disappeared. Memory is better. Maintenance dose grains IV daily.

Comment

This is a characteristic story with usual findings and response. It has been reported that myxedema patients cannot readily tolerate morphine sulphate. (Int. Med. Musser, 2d. edition).

II. ABSTRACT

MYXEDEMA

"A constitutional disease, occurring in adults, due to decrease or absence of the secretion (thyroxin) of the thyroid gland as a result of its atrophy or removal, characterized by a markedly decreased basal metabolic rate, a myxedematous condition of the tissues, a slowed, impaired mental condition, a typical facial expression and other secondary manifestations." (Boothby)

Nomenclature

The condition is frequently called Gull's disease. Cachexia strumipriva is a term used to designate the post-operative form.

Historical note

Sir William W. Gull in 1873 read a paper "On a Cretinoid State Supervening in Adult Life in Women." He gave a lucid description of two cases and mentioned that he had seen three other cases. In the cases which he saw he felt that the intellect was unimpaired, although there was a "placid indifference, corresponding to the muscular languor."

Distribution

Myxedema occurs sporadically and has no known geographic distribution. (Boothby).

Etiology

Most cases are idiopathic. Myxedema following partial thyroidectomy rarely occurs unless there was a wound infection. Plummer in a series of 51 cases had 3 patients with a history suggesting mild thyroiditis. The disease has been reported in association with colloid goiter.

Clinical pathology

There are no characteristic post-mortem findings aside from changes in the thyroid gland. "The thyroid gland is small and atrophied and shows microscopically a marked increase in fibrous connective tissue with a decrease in the vesicles. Frequently the walls of the vessels show a round cell infiltration.

Age and Sex

The condition is very much more frequent in men than in women (4 to 5 to 1). (Boothby) It usually occurs between the ages of 30 and 60.

Clinical Course

The onset is slow and gradual. There is a feeling of lassitude, lack of energy and a general slowing down of activities usually accompanied by some increase in weight with decrease in appetite and the development of hard,

non-pitting edema. The skin is thick, dry and scaly and there is a marked decrease in perspiration. The hair may fall out, especially about the eyebrows. The hair is often fine and dry. "The features are broad, coarse and mask-like with thick lips and puffiness around the eyes." There is a characteristic non-pitting edema of the skin, most noticeable in the face, hands, feet and supradavicular fossae. The tongue is large and is maneuvered awkwardly by the patient. The joints and muscles are often painful. The symptoms are accentuated during cold weather. The patient complains of a chilly sensation and objects to room temperatures which are comfortable to healthy subjects.

Nervous and Mental Symptoms

Disturbances in the intellect may be absent or very mild. The speech is slow and thick. Visual and hearing acuity may be decreased. The patients are apathetic and lose interest in ordinary affairs. They are somnolent, their recent memory is poor and in some instances the general intellectual ability may deteriorate. "Hallucinations appeared in 16 cases out of 109 investigated by the English Myxedema Commission. In 16 instances, also the latter found a frank psychosis, usually of depressive type." (Henderson and Gillespie).

In some instances, the disturbance in the mental state may be very profound and yet there will be a marked improvement as the result of therapy. Parker and Haines report such an instance. A 53 year old woman was brought to the clinic because of her mental state. Five years previously, she was given a diet for anemia; 4 months before she was brought to the clinic, mental changes were noted.

"The outstanding feature of the case was the mental state. The patient lay in bed inert, paid no attention to her surroundings, and suffered from urinary and fecal incontinence. When she was spoken to, often no answer could be obtained, and if she replied at all, it was in monosyllables and what she said was irrelevant. She had to be fed and cared for, and did not make any attempt to assist. Her general attitude was one of profound apathy; there were no emotional reactions and practically no intelligence was shown in her face. She slept most of the time when she was not lying motionless in bed, vacantly gazing at the opposite wall." She was treated with dessicated thyroid following which her mental state returned to normal. She had a total amnesia for the 3 months preceding her treatment."

The Blood

Secondary anemia is often a pronounced feature and occasionally the blood resembles that of pernicious anemia. Baldridge and Greene state that myxedema is more often mistaken for pernicious anemia than any other disease. They list the following signs which might lead to confusion: yellowish pallor, absence of weight loss, achlorhydria, anemia, color index about 1, paraesthesias, difficulty in walking, increased serum bilirubin, leukopenia, urobilinogen in urine, and remissions.

Cases have been reported in which myxedema and pernicous anemia co-existed in the same patient. (Sturgis and Isaacs) Baldridge and Greene state there is no response to liver extract in the anemia of myxedema. In some of their patients, there was neither reticulocyte increase nor increase in hemoglobin. In one case in which the initial hemoglobin was 54% and color index unity, there was a reticulocyte response to 5.2%. The response lasted until the 24th day and did not correspond to the usual reticulocyte crisis. After 41 days, the hemoglobin had not increased.

Blood cholesterol

Hurxthal states that thyroid deficiency produces hypercholesteremia. In 30 cases of spontaneous myxedema, the average blood cholesterol was 355 mg. per 100 cc. (He gives 230 mg. as the upper limit of normal but he mentions that many laboratories have their own variations for the normal. In our laboratories, the variations for cholesterol in serum and plasma of normals are 150 to 185 mg. per 100 cc.; for whole blood, 140 to 175 mg.

He feels that the blood cholesterol

provides another variable which may be used as a guide in the treatment of thyroid disease. "The finding of hypercholesteremia, in the absence of its few other common causes, points more specifically to thyroid deficiency than does the finding of a low metabolic rate. Finding both renders the possibility of thyroid deficiency extremely likely." "Hypercholesteremia, when not explainable on any other basis, may be considered as possibly of thyroid origin, and is a rational indication for thyroid administration." Other causes of hypercholesteremia mentioned by the author are: nephrosis, diabetes mellitus, obstruction of common bile duct, xanthomatosis and Shuller-Christian's disease.

He describes his experience with a patient who suffered from aural hallucinations. She had symptoms of mild myxedema and her basal metabolic rate was -22%. Thyroid therapy brought about a return to normal. When thyroid was withheld, symptoms returned and there was hypercholesteremia.. He feels that a therapeutic trial of thyroid is indicated in "any mental case with hypercholesteremia, regardless of the metabolic rate."

"The relationship between the blood cholesterol and the basal metabolism is usually reciprocal when they undergo change as the result of variations in the activity of the thyroid gland or thyroid substance in the body."

Heart

Lerman, Clark and Means in a study of the heart in myxedema found a shrinkage in the transverse diameter in 20 of the 30 patients observed.

Patient	Age	B.M.R.	Half Trans. Chest Diam. Cm.	Trans. Heart Diam. before Medication Cm.	Max. Heart Change after Medication Cm.	Time Interval for Change	Blood Pressure before Medication	Blood Pressure after Medication
1	59	-30	13.2	18.9	4.6	11 mo.	190/120	208/112
	55	-42	12.9	16.8	4.4	4½ mo.	125/90	
	48	-37	14.4	15.6	3.6	1½ mo.	120/80	110/72
	36	-38	12.8	15.7	2.7	3½ mo.	88/64	106/68
	57	-41	12.3	15.5	2.5	2 mo.	130/80	120/56
	60	-23	12.3	14.5	2.0	7½ mo.	170/100	128/66
	47	-46	13.1	14.6	2.0	1 yr.	110/65	142/90
	18	-45	12.6	11.5	1.9	2 wks.	105/78	
	39	-40	13.8	15.0	1.7	5 wks.	140/100	136/84
	55	-33	15.0	15.7	1.6	1 mo.	112/72	116/62
	67	-33	12.5	16.1	1.6	2 wks.	195/110	180/95
	16	-44	13.3	14.6	1.6	9 mo.	114/90	120/86
	42	-44	12.6	13.6	1.6	8 mo.	170/108	114/62
	46	-35	13.7	16.3	1.5	6 mo.	165/104	130/90
	44	-39	12.8	11.8	1.5	6 wks.	110/84	100/56
	46	-44	12.3	14.1	1.3	11 da.	110/80	104/66
	55	-27	12.5	15.1	1.3	14 mo.	170/110	216/128
	55	-29	13.8	13.1	-0.4	3 mo.	130/98	130/80

They mention one case of myxedema who died before treatment could be instituted. The heart showed hypertrophy. The myocardium was soft and friable. On histologic section, the muscle bundles and fibers and connective tissue were widely separated by interstitial edema.

Electrocardiogram

The most frequent findings are flattening and inversion of the T-waves, usually in leads I and II. In Fahr's series, "the majority of cases showed negative T-waves in leads I and II" (cited by Hallock). In 24 cases from the Massachusetts General Hospital, 9 showed low voltage and abnormal axis deviation besides changes in the T-waves.

Whether dyspnea, a not uncommon symptom in myxedema, signifies cardiac failure when associated with an increased transverse diameter of the heart is a matter of dispute amongst investigators.

Differential diagnosis

Besides pernicious anemia, myxedema may be confused with chronic glomerulonephritis. "Phenolsulphonephthalein, when injected subcutaneously, shows a low return and even when injected intravenously may be quite low." Albumen is not infrequently present in the urine and there may be pus cells. Basal metabolism in complete myxedema ranges between -30 and -40%. In 30 cases, reported by Hurxthal, the average basal metabolism rate was -26.2%.

Treatment

Boothby states "any good thyroid preparation may be used with equal benefit to the patient." The plan of treatment is to bring the amount of available thyroxin in the tissues up to normal and maintain this level for the remainder of the patient's life. The longer the patient has had the disease, the more intense will be the reaction to treatment.

Thompson, et al, formulate the following rule: "Because of the initial period of intoxication that follows the administration of a single large dose of thyroxine or of dessicated thyroid, and the fact that improvement in a patient with myxedema occurs only slowly, the ideal method of treatment is to raise the metabolism gradually by slowly increasing doses until the minimum amount is being administered that will maintain the basal metabolism at the normal level. In this way unpleasant symptoms are avoided. In particular, sudden changes in metabolism are to be avoided in patients with heart disease, notably those with angina pectoris. In patients with myxedema who are desperately ill there is great danger of death from large doses because of the period of intoxication and the slowness with which beneficial effects appear. They are unable to tolerate the sudden replacement of the very thing that their bodies lack. In the treatment of all patients with myxedema it should be remembered that adjustment to any dose may require many months, and changes should be made slowly."

Lerman and Salter determined the equivalent maintenance dosage on various commercial preparations of thyroid. They found considerable discrepancy in the strength of these preparations expressed per unit of weight. This fact must be taken into account in adjusting dosage. They are in accord with the method of standardization as required by the U.S.P.--total organic iodine rather than thyroxin content.

Impressions

1. Myxedema is a constitutional disease due to the decrease or absence of the secretion of the thyroid gland.

2. The disease is most frequent in adult women.

3. Most cases are idiopathic.

4. The onset is slow and gradual. There is a decreased basal metabolic rate, a typical facial expression, myxedematous condition of the tissues and a slowed, impaired mentality.

5. Occasionally, there is a profound disturbance in the mental state which responds to treatment.

6. Pernicious anemia and glomerulonephritis must be differentiated from

this condition. In some instances, there is a marked similarity to pernicious anemia even to the extent of hyperchromasia in the blood and paresthesias of extremities.

7. The blood cholesterol is as a rule elevated.

8. Studies of the blood cholesterol may be of some benefit in obscure mental disorders.

9. The English Myxedema Commission reported a fairly high incidence of hallucinations (16 of 109 cases).

10. The relationship between the blood cholesterol and the basal metabolism is reciprocal.

11. Increase in transverse diameter of the heart is a fairly frequent finding; and not infrequently there are changes in the electrocardiograph tracings.

12. There is nearly always a good response to thyroid medication. The ideal treatment is that which alleviates symptoms without producing toxic effects. There may be marked discrepancies in the strength of thyroid preparations expressed per unit of weight.

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III. STAFF MEETING

Date: May 2, 1935

Place: Recreation Room, Nurses' Hall

Time: 12:15 to 1:15

Attendance: 96

Program: February Autopsies

Discussion: L. G. Rigler
O. H. Wangensteen
A. Blumstein
Richard Johnson

Theme:

Case I - Ruptured Ulcer.

L.G.R. Many films following patient over long period of time. Films on admission show stomach filled with gas. Small bowel also distended. Some gas in the colon. Under diaphragm numerous gas bubbles suggesting perforation. Further examination week later in upright position, demonstrates gas in the stomach and very large encapsulated pocket containing fluid and gas. Next is taken a few weeks later. Suction tube in the stomach. Large subphrenic abscess shown. Fluid level at that point. This shows patient lying on his side and the shift in fluid level. Pleural effusion. Commonly seen in subdiaphragmatic abscess. Two weeks after admission -- communication between gastrointestinal tract and pocket shown by barium. Followed over long period of time. We were unable to demonstrate any further communication with the bowel but the barium remained. Size of the pocket smaller. Month or two later, pocket smaller. Last film made in February 18, 1935. You can see pocket under the diaphragm smaller than previous one. No particular changes in the lung of any consequences. Fluid level films made in prone position. Mixture of gas and fluid still shown in that area. Barium given few weeks before still shown, indicating how slowly absorbed.

O.H.W.: We have had experience with 4 cases which were treated for late perforations. One, a traumatic perforation, others perforated peptic ulcers. 4th unfortunately died. Diffuse peritonitis when admitted. We see many late cases of perforation. Traumatic factor important in perforation. Delay reflected directly in the mortality. From general literature one would get impression mortality runs from 70 to 90 per cent in late perforation of duodenal ulcer. Apart from element of time, factors of significance -- size of perforation, state of digestion, general condition of patient. This man 77. He came to us with story of pain starting 48 hours before admission, totally incapacitated. Pulse and temperature high. Impression was that he had perforation. Films shown by Dr. Rigler indicate localization. We treated him conservatively. Suction employed. Epigastric pocket subsequently closed off. Tube inserted later thru trochar. Unfortunately tube slipped out when patient was discharged. No attempt made to reinsert it, wound closed. Slow perforations are treated conservatively. We had one patient, kicked in abdomen by horse. Gas present under diaphragm. Treated conservatively, got well. Mrs. C. came in 28 hours after onset, treated conservatively, died. I am not prepared to advise conservative treatment for duodenal ulcer. Perforation should be closed as soon as recognized. We have treated 4 patients conservatively. One patient now in the hospital, Mr. M., typical history but no gas under the diaphragm. We have found that a small amount of gas can be visualized. Frequently takes 20 cc. Perforation may seal itself off and gas be absorbed. We have 4 cases of early perforations which were sealed? off soon after perforation. Patient comes in with late perforation, diffuse peritonitis, I think his chance is best with conservative treatment. Dr. Bowers experimented with dogs, guinea pigs, rabbits. 100% recovery when perforation made with stomach empty. 86% mortality with food in the stomach. First thing to do is empty stomach, close the stomach afterward.

Cases 2 and 3:

L.G.R.: Film on first case made before he came into hospital in January, 5 months after onset of symptoms, shows striking appearance. Diffuse irregular density through the left lung. No particular displacement of mediastinum. With a massive tumor of the lung, we expect such findings. The diaphragm is pulled up on the side of the lesion. By the time he came to the hospital 3 weeks later, some fluid in the pleural cavity. Iodized oil examination done.

Right lung filled up fairly well. Left main stem bronchus occluded. Impression, massive tumor of the left lung. We have been interested in this type of examination and find it helpful in making diagnosis of bronchogenic carcinoma.

Next Case:

First film made on entrance to hospital, January 24. Diffuse density is hilar, with an irregular character. Little pulling up of diaphragm, with displacement of mediastinum towards the side of the lesion. Iodized oil examination showed that the right middle lobe bronchus and the upper portions of the bronchus filled up. However, main stem bronchus not as well visualized. No definite obstruction. Latter developed more marked symptoms. Iodized oil examination, showed complete closure of main stem bronchus on that side. You can see marked atelectasis. Picture changes more as the atelectasis becomes more marked.

A.B.: In regard to metastasis in carcinoma of the bladder. One series reported is in contrast with that stated here. In series from Massachusetts General Hospital, in 50 postmortem examinations, 16 showed metastasis. The frequency of metastasis in this series apparently is independent of the microscopic picture of the bladder tumor.

Last Case:

L.G.R.: Chest entirely normal 1932. In July, 1934, showed typical picture of enlarged mediastinal lymph nodes. Classical picture of Hodgkin's disease. 2½ months later, nodes practically disappeared. Whole chest looks quite normal. 2 months later, no particular increase in size of nodes but questionable increase in size of heart. Diaphragm good deal higher than previously and heart may lie more transversely. In January 29, 1935, striking increase in size of heart.

R.J.: Where we have severe anemia, simulating hemolytic type. Bile pigments are high but excretion is not elevated. Reutilized in the body. Hemoglobin of 70 dropped later to 14. In pernicious anemia the heart is diffusely enlarged. As hemoglobin rises, heart goes back to normal. This may account for cardiac enlargement in this case. Certainly not aplastic type of anemia.

A.B.: Bone marrow was examined in the middle of the shaft of femur. Rather hyperplastic bone marrow.

Gertrude Gunn,
Record Librarian.

IV. MOVIES

Title: The Gem of the Sea

Released by: Fox Motion Picture Corporation.

V. ANNOUNCEMENTS

1. MINNESOTA STATE MEDICAL ASSOCIATION

will meet in Minneapolis at the Municipal Auditorium June 24th to 26th. It will be a joint meeting (in part) with the American Association for the advancement of science. All speakers on the general program will be from outside the state, with the exception of clinics by the staffs of the Mayo Clinic and the University of Minnesota. Special features will be: the largest exhibit in the history of the Association, many scientific movies, special demonstrations, and a time allotment for each speaker sufficient to cover the subject and allow for questions and discussion. It is expected that the attendance will also exceed that of any previous meeting. Be sure to keep these dates in mind as this will be a unique opportunity to get something out of the ordinary.

2. STAFF MEETINGS

will run until the final examination period, which starts June 7th. The last meeting will be held June 6th. We have appreciated your attendance and interest to date. Be sure to stay with us until the close.