stered amount of Na⁺. Furthermore, fluid shifts to a "whirl space" do not take place. Finally, ECV can be maintained at preoperative values by relatively small amounts of crystalloid solutions.

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Lymphocytic adenohypophysitis

A review and a case

Flemming Find Madsen, Ole Dahr & Erik Ludvigsen

Abstract
Madsen FF, Dahr O, Ludvigsen E. Lymphocytic adenohypophysitis. A review and a case.


An unconscious, 29-year-old woman was taken to hospital where, 28 hours after admission, she succumbed to an intractable shock. Autopsy disclosed a lymphocytic adenohypophysitis (LAH).

Judged by experiments on animals and by antibody examinations in women during puertera, LAH is probably an autoimmune disease belonging to a group of autoimmune endocrinopathies, from which one or more is seen with LAH.

The description of the present case is accompanied by a description of the disease in eight cases, all women; in only one patient was the diagnosis not made by autopsy.

The patients can be divided into two groups, one group consisting of postmenopausal women, another who all became ill approximately one year after giving birth.

It is suggested that this histopathological diagnosis also has a clinical significance.

From: Departments of Neurology and Pathology, Sønderborg Hospital.

Reprint requests to: Flemming F. Madsen, Nordvestpassagen 76, DK-8200 Århus N.

Lymphocytic adenohypophysitis (LAH) is a condition which until now has almost exclusively been seen as a fatal insufficiency of the hypophysis. Histologically, the disease is characterised by infiltration of the adenohypophysis by lymphocytes which can form lymph follicles and plasma cells. Furthermore, an interstitial fibrosis is seen.

LAH was described first by Goudie & Pinkerton (1) in 1962. LAH clearly differs histologically from other conditions with insufficiency of the hypophysis such as Sheehan's syndrome, granulomatous conditions, hypophysis apoplexia, tumour infiltration, and lymphocytic infiltration in pars intermedia and the neurohypophysis (2, 3, 4, 5, 6).

In seven patients, the diagnosis was made by autopsy and only in one patient clinically, seen by coincidence and found at an operation performed because of a presumably hormonally inactive tumour of the hypophysis (7). With our information, the disease is described and histologically verified in eight patients.

CASE REPORT

A 29-year-old woman was admitted unconscious to hospital 11 months after delivery. Her temperature was 40.7°C, the systolic blood pressure 100 mm Hg. A neurological examination and ophthalmoscopy were found to be normal. Blood sugar values, serum sodium, serum potassium and spinal fluid were normal. Electrocardiogram and X-ray of the chest were normal. A carotid arteriography on the right side was normal.

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Because of increasing circulatory failure and suspicion of incipient sepsis, treatment was started with ampicillin, aminoglycosides, methylprednisolon, phenemal, and hyperventilation.

Twenty-eight hours after admission, without regaining consciousness, the patient died of circulatory failure with intractable heart arrhythmia.

Three days before admission, her physician had measured serum thyroxin to 21 mmol/l (65-135 mmol/l), serum resin-triiodothyronin uptake 0.79 U/l (0.82-1.08 U/l), free thyroxin index 17 U/l (58-138 U/l). These values were not known during the admission.

Throughout her three pregnancies, the patient was bothered by pruritus, for which reason an abortion was carried out in the third month of her second pregnancy. During the last pregnancy there was raised serum alkaline phosphatase 197 U/l (20-90 U/l). All other laboratory tests were normal. The last delivery was complicated by haemorrhage of 1,000 ml, without the patient showing signs of shock.

Breast-feeding was not established and upon the gestagen-induced bleeding seven months after delivery, there was secondary amenorrhoea. Ten months after delivery, the patient complained of pruritus and increasing tiredness. A somatic examination at this time found her pale, but otherwise normal. ESR 24 mm per hour (<10), aspartate-aminotransferase 62 U/l (<40). Follicle stimulating hormone 24 mIU per ml (follicular phase 8-22, median cycle 16-43, luteal phase 4-20). Luteinising hormone 15 mIU per ml (basal value 3-40 mIU per ml, during ovulation 40-240 mIU per ml). Prolactin was 2.6 µIU/ml (3.9-21.4 µIU/ml). A liver biopsy showed slight portal fibrosis. Haemoglobin, leucocytes and differential cell count, bone marrow examination, coagulation status, serum creatinine, serum LDH, electrolytes and X-rays of thorax were all normal. At the autopsy a severe hyperaemia of all the organs and oedema of the lungs were found. The thyroid and the suprarenal glands were atrophic, the pituitary was normally sized but had a firm consistency, and all other organs were normal. Microscopically, an interstitial fibrosis with a diffuse infiltration by lymphocytes and plasma cells were found in the adenohypophysis, and several lymphofollicles were seen; granulomas could not be detected (Figs. 1 and 2). The neurohypophysis was normal. The thyroid gland showed slight interstitial fibrosis and consisted of small follicles with a low cubic epithelium, and no Hürthle cells were seen. There was a moderate diffuse infiltration by lymphocytes and plasma cells, sometimes forming larger infiltrates, as well as lymphofollicles (Fig. 3). The suprarenal glands showed bilateral cortical atrophy with all three zones equally affected, and they were without inflammatory infiltrates. Corpora lutea were not seen in the ovaries. In a mediastinal lymph node, two small epitheloid cell granulomas were seen. The liver had a normal structure with a modest portal and centrilobular fibrosis and a slight lymphocytic infiltration of the portal areas.

**DISCUSSION**

The case history and the histological findings in our patient are similar to previously described cases with

Fig. 1. Haematoxylin-eosin stain. 15×. Section through adenohypophysis.

Fig. 2. Haematoxylin-eosin stain, 60×. Section through hypophysis, lymphoid follicle with germinal center formation seen in the middle.

Fig. 3. Haematoxylin-eosin stain, 60×. Section through thyroid gland. Small follicles with low epithelium and lymphocytic infiltration.

LAH, and in spite of insufficient laboratory data, there is no doubt that our patient suffered from insufficiency of the hypophysis.

The gonadotrope hormones, measured three months before her death, were normal. Retrospectively, one could have expected far higher values in a woman with normal ovaries ten months after giving birth when
breast-feeding was not established and at the same time there was a secondary amenorrhea. The bleeding at the delivery could suggest Sheehan’s syndrome (2) as an explanation of her pituitary insufficiency, but the histological picture does not correspond.

Tables I and II show symptoms and pathological findings in patients with LAH. Pathological changes compatible with an autoimmune disease were found in several cases in other endocrine organs: (17), (8), (10), (12), (15), (16). One patient had a retrobulbar neuritis without this being recognised as an autoimmune disease (9). Gleason et al (11) took unexplained severe arthralgia as a possible expression for an autoimmune disease.

Botazzo et al (4) discovered antibodies against prolactin-producing cells of the adenohypophysis in the serum in 19 out of 287 patients with autoimmune endocrine disease. Ludwig & Schernthaner (12) and Mayfield et al (7) both described a patient with LAH and circulating pituitary antibodies. Ludwig & Schernthaner examined 23 patients with idiopathic Addison’s disease for antibodies against endocrine organs and found in a 55-year-old woman with LAH, hypophysitis antibodies and antibodies against microsomal thyroid antigens. The authors did not find that the patient had pituitary insufficiency. The values of TSH were not raised, which indicates a relative insufficiency of the pituitary gland. These authors also found hypophysitis antibodies in a 48-year-old woman with insufficiency of the suprarenals, diabetes mellitus, and myxoedema. This patient had antibodies against the steroid hormone producing cells in the suprarenals, pancreas island cells and the thyroid microsomes. A histological diagnosis was not made.

The patient described by Mayfield et al (7) had pituitary insufficiency and antibodies against the hypophysis. The histological diagnosis was made after a transphenoid hypophysectomy was carried out because of a presumed pituitary tumour without endocrine activity. Her normal menstruation cyclical.
after the operation is explained by the fact that she had been taking oral anticonception after her last delivery, which is thought to have yielded protection by suppressing the gonadotrope cells of the hypophysis during the development of the disease. Postoperatively, the patient was given thyroid- and corticosteroid substitutions. Antibodies against the suprarenals, the pancreas, the thyroid gland, the ovaries and the ventricular mucous membrane could not be detected, whereas antibodies against the adenohypophysis were present pre- as well as postoperatively.

Levine (5) found adenohypophysitis in rats on the thirteenth and the twentieth day after injection of autologous hypophysis extract and found a stronger reaction in more rats when the injection was given immediately post partum.

Engelberth & Jezkova (13) found hypophysis antibodies in 18 percent of 128 women on the fifth or seventh day post partum (all sera were without antibodies before and at delivery). A quarter of these 18 percent developed signs of decreased function of the hypophysis during the following year such as missing lactation, amenorrhea, decreased libido, loss of weight, tiredness and intolerance to cold. Only four percent of the patients without antibodies had the same symptoms.

The coexistence of LAH with other autoimmune diseases, findings of antibodies against adenohypophysis, and the animal experimental findings indicate that LAH is an autoimmune disease (5), (7), (12), (13), (14).

On the basis of the few described patients, LAH can be divided into two groups, one group consisting of postmenopausal women (aged 42-74) and one in which the disease apparently is triggered in the period of the puerperal involution.

The disease should be considered in patients with rapidly abating function of the hypophysis. In women post partum with signs of decreased function of the hypophysis, the endocrine parameters should be measured so that a substitutional therapy can be started. Examination for hypophysis antibodies could make possible the diagnosis of LAH in vivo, and this presumably not insignificant group of patients could thus be examined further.

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