AUTO-IMMUNITY IN CHRONIC ADRENAL INSUIFFICIENCY

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The success achieved in combating tuberculosis over the past several years has greatly reduced its role as an etiological factor in chronic adrenal insufficiency. As a consequence, the relative incidence of idiopathic adrenal atrophy has shown an increase. A great number of authors assume that one half (and even more, according to some of them) of the cases with Addison's disease are caused by idiopathic adrenal atrophy (6, 7, 10). Recently, in a number of studies it has been established that in this particular condition very often adrenal antibodies occur, whereas in cases with tuberculosis of the adrenals no such antibodies are discovered or they are observed in isolated cases only (3, 4, 6, 8, 12).

We made it our aim to investigate the presence of adrenal antibodies in a series of patients with chronic adrenal insufficiency.

Material and Methods

Investigations were conducted on a total of 22 patients — 11 with Addison's disease (Table 1) and 11 controls: 3 with melanoderma and 8 with various affections in whom the presence of organ-specific antibodies was suspectable (Table 2).

Table 1

№	Name	Age	Sex	Concomitant diseases	Mantoux	Antibodies			
						adrenal	thyroid	gastric	other organs
1	V. A. M.	38	f	Schizophrenia	+	+	—	—	
2	F. A. S.	25	f	—	+	+	—	—	
3	I. I. M.	28	f	—	+	—	—	—	
4	P. V. N.	49	f	Thyrotoxicosis	+	—	—	—	
5	M. D. M.	56	m	—	+	—	—	—	
6	N. A. B.	27	f	—	—	—	—	—	
7	M. I. S.	60	f	Pyelonephritis, hypertension, rheumatoid arthritis	—	+	—	—	Myocardial
8	M. N. A.	38	f	Rheumatoid arthritis.	—	+	+	+	
9	H. I. S.	35	m	—	—	+	—	—	Antinuclear
10	I. N. I.	28	m	Diabetes mellitus, hypogonadism.	+	—	—	—	
11	R. B.	44	m	Rheumatism, heart defect, diabetes mellitus.	—	—	—	—	

The diagnosis Addison's disease was established on the basis of the clinical picture and routine laboratory investigations, the test of Robinson and the spontaneous 17-ketogenic and 17-ketosteroids discharge via urine, inclusive. In cases running a lighter course, the above investigations were

Table 2

№	Name	Age	Sex	Disease	Antibodies
1.	N. I. I.	36	f	Melanoderma, hypoplasio uteri, adnexitis chronica dextra.	gastric thyroid
2.	K. T. K.	39	m	Toxic melanoderma from lubricating oils. Tonsillitis chronica.	gastric
3	S. S. K.	47	f	Melanoderma. Tonsillitis chronica. Hyperacidity.	gastric
4.	S. D. K.	46	m	Alcoholic hepatic cirrhosis. Vitiligo.	adrenal thyroid hepatic
5.	G. K. Tz.	44	f	Acromegaly; eosinophil adenoma of the hypophysis, proved histologically; anemia.	adrenal thyroid
6.	A. H. K.	11	f	Diabetes mellitus.	—
7.	R. M.	59	f	Toxoplasmosis.	—
8.	P. Sh. A.	33	f	Hypopituitarism.	—
9.	N. Sh. A.	29	f	Acromegaly. Anemia.	thyroid renal
10.	D. N. I.	36	f	Diabetes mellitus.	thyroid gastric
11.	M. A. A.	20	f	Iron-deficiency anemia.	antinuclear.

supplemented by adrenocortical reserves' determination with the aid of the 8-hour venous ACTH test. Six of the patients with chronic adrenal insufficiency had familial history data of tuberculous affections. In five of them, evidence was found of past tuberculous process and positive tuberculin tests at the time of investigation, while in one patient whose parents were affected with tuberculosis, data of tuberculous process in the organism were absent and the tuberculin tests were negative. In the latter group of patients, it was accepted that tuberculous form of Addison's disease was concerned. In the remainder (five cases), tuberculous etiology of the affection was not proved and therefore it was accepted that idiopathic Addison's disease was concerned. In any of the patients of this series were roentgenological evidence of calcifications in the adrenals found.

The female patient P. V. N. (N° 4, table 1) in whom tuberculous etiology of adrenal insufficiency is considered, suffers from concomitant thyrotoxicosis, while patient V. A. M. (N° 1, table 1) — from schizophrenia.

Among the group of patients with idiopathic Addison's disease, case M. I. S. (N° 7, table 1) suffers from pyelonephritis, hypertension and rheumatoid arthritis, case M. N. A. (N° 8, table 1)— rheumatoid arthritis, case I. N. I. (N° 10, table 1) — diabetes mellitus and hypogonadism and case R. B. (N° 11, table 1) — rheumatism, heart defect and diabetes mellitus.

All patients underwent examination by resorting to indirect immune-fluorescent technique for adrenal and thyroid antibodies, as well as for antibodies against the parietal cells of the gastric mucosa. In a number of patients, antibodies against other organs were also searched for.

Results

The results of our studies revealed the presence of adrenal antibodies in the serum of three patients with idiopathic Addison's disease and in two with proved tuberculous infection in the organisim.

In the group of patients with idiopathic Addison's disease and presence of adrenal antibodies in the serum, the additional findings disclosed: in case M. N. A. (N° 8, table 1) — thyroid and gastric antibodies; in case M. N. S. (N° 7, table 1) — myocardial and in case H. I. S. (N° 9, table 1) — antinuclear antibodies.

One of the female patients (N° 2, table 1) with tuberculous form of Addison's disease and presence of adrenal antibodies in the serum had concomitant schizophrenia.

In the sera of the three cases with melanoderma, gastric antibodies were discovered, and in one of them (N° 1, table 2) also thyroid antibodies. In the control group, adrenal antibodies were established in two patients only. One of the latter (N° 5, table 2) was affected with acromegaly against the background of histologically proved eosinophil adenoma of the hypophysis and macrocytic anemia, whilst the other (N° 4, table 2) — with alcoholic cirrhosis and vitiligo. In the serum of the former, also thyroid antibodies were present, whilst in the serum of the latter — thyroid and hepatic antibodies.

However, it should be stressed that in none of the patients with thyroid antibodies in the serum were clinical evidence of thyroid gland affection established.

Discussion

The results of the studies, although carried out on a rather limited series, corroborate the literature data according to which, in the past several years, about 50% of all cases with chronic adrenal insufficiency are attributed to the idiopathic form of Addison's disease, and also, that adrenal antibodies are being established in about 50% of the patients with idiopathic form of the Addison's disease (4, 8, 12).

Irvine and co-workers (5, 6) and many others (5, 8, 12) emphasize the higher incidence of adrenal antibodies among female patients with Addison's disease, pointing out that in the same patients, very often, thyroid antibodies are also discovered (4, 8, 12). In our case material, females prevail among the patients with adrenal antibodies, whereas among the patients without antibodies, the female to male ratio is equal. In three cases there is a simultaneous combination of adrenal and other organ-specific antibodies. Attention is called to the female patient with adrenal and myo-

cardial antibodies. In the latter, chronic adrenal insufficiency is developed against the background of rheumatoid arthritis and diabetes mellitus. A year ago a female patient was referred to us with proved at dissection rheumatic defect and idiopathic adrenal atrophy (2). Recently, Zabriskie and co-workers (20) reported the finding of myocardial antibodies in a patient with acute rheumatism.

In the pertinent literature, particularly in the past few years, often the combined occurrence of idiopathic Addison's disease and various endocrinopathies is stressed, in which there is sufficient reason to suspect autoimmunity of the condition (6, 17). In some of the latter patients also the respective antibodies have been demonstrated (11). According to Solomon and co-workers (17), the results of studies on 15 patients with Schmidt's syndrome point to the presence of a correlation between the antibodies found, on the one hand, and the thyroid and adrenal dysfunction, on the other.

In three patients of our series in whom the Addison's disease runs a course characterized by concomitant affection with thyrotoxicosis — in P. V. N. ((N° 4, table 1), with diabetes mellitus and hypogonadism — in I. N. I. (N° 10, table 1) and with diabetes mellitus and rheumatism — in R. B. (N° 11, table 1), no antibodies were established in the serum. Anyway, the latter fact is still not sufficient to rule out the auto-immune character of the affection in similar instances. Recently, Nerup and co-workers (14, 15, 16) demonstrated, although on the basis of certain tests only, the presence of organ-specific antiadrenal hypersensibility of cellular type in patients with Addison's disease and in patients with diabetes mellitus without clinical evidence of Addison's disease but with circulating adrenal antibodies. It is by no means excluded that antibodies would be demonstrated also in cases similar to ours after the introduction of new technical facilities and methods.

Apart from that, Irvine and co-workers (9) found a complex of IgG antibodies in patients with idiopathic chronic adrenal insufficiency, entering in reaction with the adrenal and with the steroid producing cells in the ovary, testis and placenta as well.

Adrenal antibodies were disclosed in our series also in two cases with tuberculous etiology of the Addison's disease. Goudie and co-workers (8) similarly established antibodies in two out of a total of 27 patients investigated with tuberculous Addison's disease. In their opinion, similar cases point to the possibility for the existence of an odd relationship between the tuberculous and idiopathic forms of the disease.

In the control group of patients, adrenal antibodies were discovered in two cases — one female with acromegaly at histologically proved eosinophil adenoma of the hypophysis and macrocytic anemia, and the other concerning a male with alcoholic cirrhosis and vitiligo. The latter patient merits special attention, since apart from adrenal and thyroid, hepatic antibodies were also discovered in him. Notwithstanding the paradox, vitiligo is observed in about 15% of the patients with Addison's disease (7). In all likelihood, it is exactly in the idiopathic form of the disease that vitiligo occurs. Against the background thus outlined, the establishing of adrenal antibodies in our case is worth of special notice.

It is worthwhile noting also that thyroid antibodies were found in both patients with acromegaly investigated by us.

In the group of patients with pronounced melanoderma, which justified to suspect Addison's disease, no adrenal antibodies were established. However, although clinical data for gastro-intestinal involvement were absent, gastric antibodies were found in the sera of all three patients.

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АВТОИММУННОСТЬ ПРИ ХРОНИЧЕСКОЙ НЕДОСТАТОЧНОСТИ НАДПОЧЕЧНИКОВ

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РЕЗЮМЕ

При помощи индиректного иммунофлюоресцентного метода исследовали 22 человека больных, в том числе 11 аддисоновой болезнью и 11 контрольных лиц, в отношении наличия антител против надпочечников, щитовидной железы и слизистой желудка. У 6 больных аддисоновой болезнью была обнаружена туберкулезная этиология заболевания, а у 5 считается наличие идиопатической атрофии надпочечников. В первой группе больных были обнаружены у 2 больных надпочечниковые антитела, а во второй — у 3 больных. Кроме того во второй группе установили: у 1 больной — тиреоидные и желудочные антитела, у 1 — миокардные и у 1 — антиядерные.

Группа контроля включала 3 больных меланодермией и 8 — другими заболеваниями. У больных меланодермией не обнаружено надпочечниковых антител, но у всех трех установлено наличие желудочных антител. У 1 больного алкогольным циррозом печени и витилиго обнаружены надпочечниковые, тиреоидные и печеночные антитела, а у 1 больной акромегалией и анемией — надпочечниковые и тиреоидные антитела.