ONCOLOGY

Soluble Fas Antigen (sFAS) in the Serum from Patients with Adrenal Tumors

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Serum content of soluble Fas antigen was measured by enzyme immunoassay in 60 healthy donors, 31 patients with adrenal tumors, and 16 patients with diffuse-and-nodular hyperplasia of the adrenal cortex accompanying primary aldosteronism and Cushing's disease. sFas was more often detected in the serum from patients with tumors of the adrenal cortex and medulla and diffuse-and-nodular hyperplasia of the adrenal cortex and its content varied in a wider range in patients compared to healthy donors. No correlations were found between the incidence of sFas, its content, sex, and age of healthy donors and patients. The highest content of sFas was found in patients with pheochromocytoma and primary aldosteronism. sFas probably plays a role in the pathogenesis of adrenal tumors and hyperplasia.

Key Words: *apoptosis; soluble Fas antigen; adrenal tumors; diffuse-and-nodular adrenal cortex hyperplasia*

Apoptosis or programmed cell death is an important physiological process necessary for the maintenance of cell composition in organs and tissues and removal of autoreactive cells and cells completing their life cycle [10].

Various factors, including the key receptor Fas/APO-1/CD95 [8,11] and its ligand FasL [11,14,15], are involved in apoptosis. Fas belongs to the tumor necrosis factor receptor family [3] and is expressed in the heart, lungs, kidneys, thymus, and liver and in virus-infected or tumor cells. FasL is expressed in activated lymphocytes and natural killer cells [11,12]. The interaction between Fas receptors and FasL or monoclonal anti-Fas antibodies triggers enzyme reactions leading to biochemical and structural changes and culminating in cell death [9].

Overproduction of soluble Fas (sFas) in some cells probably determines their resistance to Fas-dependent apoptosis. sFas is an alternative splicing product of full-length Fas mRNA, an inhibitor of the cytotoxic effects of FasL [4,5]. Plasma sFas content increases in systemic lupus erythematous [7], viral hepatitides [6], diffuse toxic goiter, autoimmune thyroiditis [6,13], and osteosarcoma [2].

Here we measured serum sFas content in healthy donors and patients with adrenal tumors and hyperplasia.

MATERIALS AND METHODS

We examined 31 patients with adrenal tumors, including aldosterone-producing adenoma (n=16), pheochromocytoma (n=5), hormonally inactive myeloli-

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poma (n=4), corticosteroma (n=3), and adrenocortical cancer (n=3), and 16 patients with diffuse-and-nodular hyperplasia of the adrenal cortex accompanying primary aldosteronism (n=7) and Cushing's disease (n=9). There were 16 men and 31 women (21-75 years). The history of the diseases before the start of treatment varied from 6 months to 10 years (average 3.0±2.4 years). Clinical diagnoses were made for the first time and confirmed by endocrinological tests and morphological examination of the adrenal glands after adrenalectomy. The patients received no antitumor therapy before examination.

The control group included 60 healthy donors (5 men and 55 women, 19-70 years).

Serum concentration of sFas was measured by enzyme immunoassay [1].

The results were analyzed by Student's t test.

RESULTS

sFas was found in 28% serum samples of healthy donors (Table 1). No correlations were found between the incidence of sFas, its content, sex, and age of healthy donors.

In the total group of patients sFas was found in 39 serum samples (83%). Thus, the incidence of sFas in patients was 2.9 times higher than in healthy donors. In 28 samples from patients (60%) the concentration of sFas surpassed the maximum sFas concentration in healthy donors. sFas concentration varied from 0.6 to 9.9 ng/ml (average 3.32±2.53 ng/ml). We revealed no correlations between the incidence of sFas, its content, sex, age, and history of the disease.

sFas was found in 75% male patients (41.9±9.5 years); its concentration varied from 1.01 to 9.90 ng/ml (average 4.49±3.20 ng/ml). We revealed sFas in 87% female patients (51.1±10.3 years); its concentration was 0.60-7.54 ng/ml (average 2.79±1.90 ng/ml). We found no significant differences between sFas concentrations in female and male patients.

In 60% patients with pheochromocytoma, sFas content surpassed its maximum concentration in healthy donors. The mean sFas content was the highest in these patients (Table 1). A positive correlation was found between sFas concentration in the serum and age of patients with pheochromocytoma (r=0.8).

sFas was found in most patients with primary aldosteronism (Table 1). We revealed no correlations between the incidence of sFas, its content, sex and age of patients, and duration of primary aldosteronism. No correlations were revealed between the incidence of sFas, its content, and clinical manifestation of Cushing's disease. sFas was found in 2 of 4 serum samples from patients with myelolipoma (Table 1). In 1 of 3 patients with adrenocortical cancer the tumor was hormonally inactive (72 year-old woman). Hormonally active tumors were found in 2 women with adrenocortical cancer: virilism (43 years) and Cushing's syndromes (48 years). It should be emphasized that in 1 woman with adrenocortical cancer and Cushing's syndrome the primary tumor growth was characterized by generalization of the process (multiple metastases in the liver). In this patient sFas content was 1.85 ng/ml. The lowest sFas content was found in a woman with adrenocortical cancer and virilism (0.6 ng/ml). sFas concentration in woman with hormonally inactive adrenocortical cancer did not differ from the control (1 ng/ml).

Our results indicate that sFas was more often detected in the serum of patients with tumors of the cortical and medullar layers and hyperplasia of the

TABLE 1. Incidence and Content of sFas in the Serum of Patients with Tumors of the Cortical and Medullar Layers and Diffuse-and-Nodular Hyperplasia of the Adrenal Cortex

Disease	Number of patients	Age, years	sFas incidence		sFas content, ng/ml	
			abs.	%	limit of variations	M±m
Adrenocortical cancer	3	57.7±21.4	3	100	0.60-1.85	1.15±0.64
Pheochromocytoma	5	51.8±11.9	3	80	0.72-9.90	4.86±4.22
Aldosterone-producing adenoma	16	52.9±7.6	16	100	0.70-7.54	3.22±2.03
Corticosteroma	3	39.3±2.9	2	67	2.22-8.00	2.22±8.00*
Myelolipoma	4	41.8±12.4	2	50	0.60-3.58	0.60±3.58*
Diffuse-and-nodular hyperplasia of the adrenal cortex						
Cushing's syndrome	9	41.7±13.7	6	67	0.80-3.44	2.18±1.09
primary aldosteronism	7	45.0±12.9	6	86	1.06-9.90	4.61±3.03
Control (healthy donors)	60	38.1±7.4	17	28	0.62-1.34	0.83±0.30

Note. *Individual values.

adrenal cortex than in healthy donors. Serum content of sFas in these patients varied in a wider range than in healthy donors. In most patients sFas concentration surpassed the control. These data suggest that sFas expression can be associated with the pathogenesis of adrenal tumors and hyperplasia.

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