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COMBINATION OF AUTOIMMUNE ENDOCRINOPATHY AND NON-ENDOCRINE DISEASE OF AUTOIMMUNE GENESIS: A RARE CASE IN PEDIATRIC PRACTICE

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Abstract

Comorbidity is a combination of several diseases in patient. Cases of two or more endocrine glands affection with different organospecific non-endocrine diseases of autoimmune genesis combination are rarely observed in endocrinological practice. Mutual influence of the present pathologic processes which can significantly change the typical clinical disease picture concealing or exacerbating the manifestation of separate glands dysfunction are necessary to be taken into account in such health states. The combination of the 1st type diabetes with the thyroid gland autoimmune affection in children is mentioned in the literature data. The prevalence of the 1st type diabetes with the autoimmune affection of the thyroid gland is amounted from 18% to 24% according to the various researchers' data. However, the combinations of endocrine glands' two autoimmune affections with different organospecific non-endocrine diseases of autoimmune genesis are rarely observed.

The 1st type diabetes combination, thyroid gland autoimmune affection and sclerodermia in pediatric practice are discussed in the present article. A 12 years old girl complaining of polydipsia, dryness in mouth, polyuria, weight loss of 4 kg was presented to the Department of Endocrinology of "Mouratsan" University clinic. The diagnosis of 1st type "Diabetes mellitus, manifestation, ketosis on admission" was made based on the anamnesis, clinical picture, the laboratory data and instrumental studies.

Intensive rehydration and insulin therapy in insulin daily dose 30-34 Un, later gradually decreasing up to 16-18 Un daily under glycemia control was initiated. The insulin daily dose decreased amounting up to 10.

Energy increase and 3 kg weight gain was noticed by the patient in the conducted therapy process. Hormonal and biochemical indices as well as those of glycemia were/became normalized.

Thus, it should be mentioned that autoimmune endocrinopathies develop not simultaneously, that's why it is necessary to remember the possibility of polyendocrine syndrome in one endocrine gland autoimmune affection and conduct targeted studies for earlier revelation of other endocrine glands affection.

Keywords: *comorbidity autoimmune endocrinopathies, 1st type diabetes.*

Introduction

Comorbidity is a combination of several diseases in patient. Cases of two or more endocrine glands affection with different organospecific non-endocrine diseases of autoimmune genesis combination are rarely observed in endocrinological practice. Mutual influence of the present pathologic processes are necessary to be taken into account in presence of such state, which can significantly change the typical clinical disease picture conceiving or exacerbating the manifestation of separate glands dysfunction.

The combination of the 1st type diabetes with the thyroid gland autoimmune affection in children is mentioned in the literature data. The prevalence of the 1st type diabetes with the autoimmune affection of the thyroid gland is amounted from 18% to 24% according to the various researchers' data [*Schatz D,Winter W, 2002; Navasardyan L, Tadevosyan A, 2013*]. However, the combinations of endocrine glands' two autoimmune affections with different organospecific non-endocrine diseases of autoimmune genesis are rarely observed [*Garcha-Hernández F, Ocaca-Medina G et al., 2006; Alimohammadi A, Dubois N et al., 2009*]. The 1st type diabetes combination, thyroid gland autoimmune affection and sclerodermia in pediatric practice are discussed in the present article.

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Case presentation

The 1st type diabetes combination, thyroid gland autoimmune affection and sclerodermia in pediatric practice are discussed in the present article.

A 12 years old girl complaining of polydipsia, dryness in mouth, polyuria, weight loss of 4 *kg* was presented to the Department of Endocrinology of "Mouratsan" University clinic. The anamnesis revealed that the complaints appeared two weeks prior hospitalization.

The child from the 1st pregnancy, proceeding with toxicosis during the 1st half, unassisted labor in term. Body mass was 3200 *g*, height – 51 *cm* at birth. Breast-feeding was up to 5 months. Early development was without specific features. Vaccinations were according individual schedule.

Past medical history: Acute respiratory infection – 2-3 times a year. Allergic anamnesis and heredity of endocrine pathology weren't aggravated.

Circinate focuses of skin induration with purple staining appeared on the anterolateral surfaces of the abdomen and on the femoral surfaces as well as on the lateral surfaces of knee joints of the patient in December, 2014 according to her mother's information. Dermal picture completely disappeared over the affected area, and hair shedding was observed. Later, swelling and induration of these areas were added, thereat the color changed into white. The diagnosis of focal sclerodermia was made after the consultation of dermatologist and rheumatologist. Complaints of weakness, rapid fatigue, constipation, memory worsening, hair shedding appeared in May, 2015. Clinical-hormonal study for thyroid gland pathology presence was carried out. Autoimmune thyroiditis in hypothyrosis stage with the increased level of antibodies to thyreoperoxydase and thyreoglobuline was revealed. Thyroid hormone therapy was administered.

Anamnesis of the disease: Complaints of excessive thirst, dryness in mouth, frequent urination appeared 2 weeks prior hospitalization. The girl lost 4 *kg* during this period. Blood glucose level was studied. Hyperglycemia of 24.7 *mmol/l*, ketonuria were revealed. Due to hyperglycemia the girl was hospitalized in the endocrinology department of "Muratsan" University clinic.

During the admission the patient's state was of medium gravity. Body build was normostenic. Height –weight indices corresponded to normative indexes for that age and gender. Skin integuments were pale, slightly dry, poorly developed subcutaneous fat. Single areas of hypopigmentation and skin induration were noticed over the abdominal lateral, femoral lateral and knee joint lateral surfaces (.Fig 1). Hair was absent on the above-mentioned skin affected areas. Lymph nodes weren't enlarged. No catarrhal signs. Data of skin and mucosa candidiasis affection were absent.

***Cardiovascular system*:** No complaints. Heart zona wasn›t visually changed. The heart tones were clear and rhythmic. The pulse rate was 80 *beats/min*. BP – 110/70 *mmHg*.

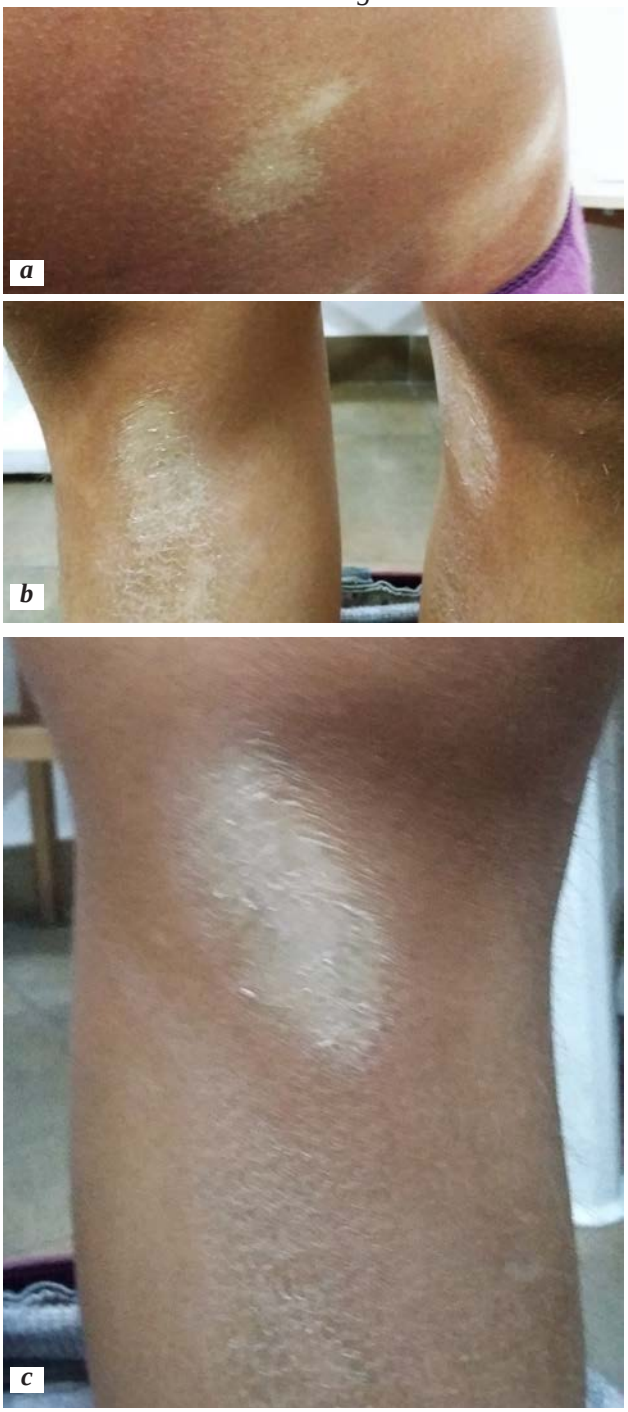

Figure 1. Skin affection in case of sclerodermia (hypopigmentation, skin induration). ***a*** *-abdominal lateral surface,* ***b*** *- femoral lateral surface,* ***c*** *- knee joint lateral surface.*

Respiratory system: No complaints. Vesicular respiration was carried out in all parts, no riles. Free nasal respiration.

Digestive system: Complaints of tenderness in abdominal area. Furred dry tongue. Abdomen wass tender on both superficial and deep palpation in all areas. The liver was at the costal arch edge, liver border was smooth, elastic, painless.

Urinary system: Enuresis, free urination. Tapping symptom was negative. Genital organs were formed by female type. Sexual status by Tanner- 2, mammal glands were developed Ma2, Ax2, P2, no menstruation.

On palpation the thyroid gland was slightly enlarged in volume of non-homogenous consistency, painless, movable of non-smooth surface.

Considering the complaints and clinical studies the diagnosis of 1st type diabetes mellitus was suggested.

The following laboratory studies were carried out to verify the diagnosis: blood and urine clinical analyses, blood biochemical analysis, blood hormonal studies with determination of adrenocorticotropic hormone and cortisol level, thyroid tropic hormone level, free thyroxin, insulin, C-peptide levels, as well as thyroid peroxidase antibodies, antibodies to the pancreas beta-cells and GAD (the enzyme, catalyzing the synthesis of aminobutirate from glutamate) and insulin, glycated hemoglobin level, glycemic profile. The study results revealed the increased level of the antibodies to the islet cells.

Blood general and biochemical analyses didn't reveal any pathologic changes. High levels of glycemia and glycated hemoglobin HbA1c amounting 10.2% (norm – 4-6%) were revealed. Glycosuria and ketonuria were revealed in general urinalysis.

Rheumatologist's consultation was carried out and the diagnosis of focal sclerodermia was confirmed. The diagnosis of the 1st type diabetes mellitus, proceeding typically as autoimmune diabetes type was made. The presence of antibodies to the islet cells and low indices of C-peptide on blood exactly proved the diagnosis diabetes mellitus of 1st type. Primary hypothyreoditis in decompensation stage against the autoimmune thyroiditis background was showed the TSH level increase (24.5 *mU/l*) and fT4 level decrease in blood (6.6 *pmol/l*), AT-TPO high level (480 *mU/l*) and characteristic changes in the ultrasound structure of the enlarged thyroid gland (volume 25.1 *ml*). Normal levels of blood adrenocorticotropic hormone (44 *pg/ml*) and blood cortisol (626.4 *nmol/l*) as well as normal potassium level (4.36 *mmol/l*) proved the absence of the chronic adrenal cortex failure.

Intensive rehydration and insulin therapy in insulin daily dose 30-34 *Un*, later gradually decreasing up to 16-18 *Un* daily under glycemia control was initiated. A dose of l-thyroxine up to 75 *mkg* in the morning was administered to compensate hypothyroidism. Energy increase and 3 *kg* weight gain was noticed by the patient in the conducted therapy process. Hormonal and biochemical indices as well as those of glycemia were normalized. The insulin daily dose decreased amounting up to 10 *Un* daily during 1 month due to the substitutional therapy for reaching normoglycemia.

The diagnosis of 1st type "Diabetes mellitus, manifestation, ketosis on admission" was made based on the anamnesis, clinical picture, the laboratory data and instrumental studies. Primary hypothyrosis was in decompensation stage as a result of autoimmune thyroiditis. Focal sclerodermia.

However, taking into account the manifestation of two endocrine glands autoimmune affection combination with organospecific non-endocrine disease of autoimmune type, focal sclerodermia in the girl, the presence of autoimmune polyglandular syndrome of the 2nd B type is not excluded.

Autoimmune polyglandular syndrome of 1st and 2nd A, B types were differentiated [*Myhre A. et al., 2001; Michels A, Eisenbarth G, 2009*]. Autoimmune polyglandular syndrome of 2nd type was characterized by endocrine gland affection with the development of primary hypocortisism, primary hypothyroiditis or thyrotoxicosis, diabetes mellitus of the 1-st type, primary hypogonadism, myasthenia and steatorhea. These manifestations were often accompanied by vitiligo, alopecia, pernicious anemia [*Betterle G, Zanchetta R, 2003; Sviridenko N et al., 2003*]. All the above mentioned diseases which occured in the combination of autoimmune polyglandular syndrome of 2nd type were mainly associated with HLA (haplotypes of HLA B8, Dw3, Dr3, Dr4 occur upconverted) [*Wallaschofski H et al., 2003; Soderbergh A, Myhre A et al., 2004*]. The syndrome occured sporadically in most cases. Family forms in various variants can be manifested in some generations.

The most frequent variant of autoimmune polyglandular syndrome of 2nd A type is Schmidt's syndrome, in which adrenal cortex and thyroid gland are affected with autoimmune process [*Betterle C et al., 2002*]. Main clinical manifestations of this syndrome are the symptoms of adrenal cortex chronic failure and hypothyroiditis. Antibodies to thyroid peroxidase and thyroglobulin are revealed in such patients. Autoimmune polyglandular syndrome of

2nd B type proceeds with 1st type diabetes mellitus (Carpenter syndrome) in 30% of patients. Antibodies to the islet cells of the pancreas are revealed in them. Autoimmune polyglandular syndrome of 2nd B type may be accompanied with the visual nerve atrophy, autoimmune thrombocytopenic purpura, sclerodermia, idiopathic diabetes insipidus with autoantibodies to vasopressin-producing cells, hypophysitis, isolated deficit of adrenocorticotropic hormone, pituitary tumor [*Betterle C, Zanchetta R, 2003*; *Ulinski T et al., 2006*].

Autoimmune polyglandular syndrome of 2nd type is generally manifested at mature age (reaching its peak at the age of 30) however, its occurrence in puberty is rather rare.

Autoimmune polyglandular syndrome of 2nd type components (adrenal cortex failure) join on average in some years [*Oelkers W, 1996*; *Ten S et al., 2001*].

The present clinical case peculiarities:

Early age of the disease manifestation, as well as short period of the syndrome component manifestation.

Simultaneous presence of three decompensated diseases – hypothyroiditis, 1st type diabetes mellitus and focal sclerodermia – promoted the development of the expressed clinical manifestation each of them.

Thus, it should be mentioned that autoimmune endocrinopathies develop not simultaneously, that's why it is necessary to remember the possibility of polyendocrine syndrome in one endocrine gland autoimmune affection and conduct targeted studies for earlier revelation of other endocrine glands affection.

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