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Endocrinological disorders in haematological diseases

Endocrinological disorders in haematological diseases present a serious problem in clinical practice, especially for haematologists and internists. Pathology of haematopoeitic system and disorders in the function of endocrine glands are diagnosed in some of the patients seen at haematology clinic and hospitalized in haematological and medical wards. This study presents main endocrinological problems that a haematologist or an internist dealing with haematological diseases may face in their medical practice.

CHANGES IN BLOOD CELL COUNT OBSERVED IN ENDOCRINOPATHY

In the course of hypothyreosis the co-existence of normocytic anaemia, microcytic anaemia, Addison-Biermer anaemia (8.5% of cases), and haemolytic anaemia has been found. The occurrence of anaemia is usually the result of several factors: the impairment of the bone marrow function due to the decrease in oxygen consumption, reduced iron absorption due to the absence of hydrochloric acid, heavy menstrual flows, changes in red blood cells resulting from the decreased potassium content and increased sodium content, anti-thyroid antibodies found in blood serum and an intrinsic factor. These anaemias are usually moderate and they subside after the treatment of hypothyreosis. Apart from that the bleeding time is longer due to the impairment of activity of the blood coagulation factor VIII. As a result there is a tendency to ecchymosis and haemorrhage.

In hyperthyreosis other diseases are observed: leukopenia, granulocytopenia, increased percentage of lymphocytes and monocytes. There may be also a moderate hypochromic anaemia, and, sporadically, thrombocytopenia and anaemia due to autoaggression. In hyperthyreosis the spleen is palpable below the costal arch in 10% of cases, and lymph nodes are enlarged. Leukopenia diagnosed before the treatment for hyperthyreosis is started, is not a contraindication for the administration of thyreostatics, but a strict haematological supervision is required in the course of therapy.

Conditions occurring with the excess of cortisol (Cushing syndrome, Cushing disease) are characterized by leukocytosis, decreased number of eosinophils and lymphocytes, and also a secondary polycythemia may be found (4). These changes result from the effect of the excessive amount of suprarenal steroids.

In the course of hypofunction of the adrenal cortex lymphocytosis and eosinophilia are found in about one third of all cases, and normochromic anaemia is also observed (5).

GRANULOCYTOPENIA AND AGRANULOCYTOSIS FOLLOWING THE ADMINISTRATION OF ANTITHYROID DRUGS

When the patients suffering from hyperthyreosis are treated with derivatives of thiamasol and thiouracyl, complications are observed in 2 to 4% of cases, mainly granulocytopenia and thrombocytopenia. A single decrease in the granulocyte content in peripheral blood less than 1,000 in

mm^3 requires a frequent determination of leukocytosis with a blood smear. If granulocytopenia persists, the drug should be withdrawn. The drug that is a derivative of thiamasol must not be changed for other antithyroid drugs, which is a derivative of thiouracil. When antithyroid agents are withdrawn, the granulocyte level in the blood usually returns to normal level.

Agranulocytosis in the course of treatment with anti-thyroid drugs is a serious complication that may result in death. It occurs in about 0.2% of patients treated with derivatives of thiamasol and thiouracyl, independently of a dose, form of drug and duration of administration (usually in the first three months, and sometimes after many months of treatment). A patient should be informed about the compulsory periodical blood cell count and necessity to see a doctor immediately when the following symptoms occur: sore throat, temperature, ulceration of the mouth, pneumonia. After the recovery from agranulocytosis the patients with hyperthyreosis are treated with beta adrenolytics and lithium carbonate until radical treatment is undertaken.

ADDISON-BIERMER DISEASE AND (POLYGLANDULAR AUTOIMMUNE DISEASE – PGA)

PGA may be subdivided into PGA1, PGA2, PGA3 depending on the diseases that are involved. Co-existence of disorders in the function of endocrine glands and Addison-Biermer disease are found in PGA2 and PGA3 but not in PGA1.

PGA2 is found mainly in middle-aged females and is characterized by hypofunction of adrenal glands and thyroid gland (due to Hashimoto disease), and diabetes mellitus, celiac disease, albinism, patchy baldness, glomerulitis, primary biliary cirrhosis. Megaloblastic anaemia occurs later than endocrinological disorders. Patients with diagnosed PGA2 should be frequently tested for Addison--Biermer disease.

In patients with diagnosed PGA3 no pathology of adrenal cortex is observed, and Addison-Biermer anaemia occurs in young age prior to endocrinological diseases. Patients with diagnosed Addison-Biermer anaemia should be monitored to look out for endocrinological diseases, especially for thyroid gland and diabetes.

ENDOCRINE DISORDERS IN THE COURSE OF TREATMENT OF HAEMATOLOGICAL DISEASES

Glycocorticosterides administered in many haematological diseases may cause post-steroid diabetes because of antagonistic effect against insulin. It usually occurs in individuals with impaired glucose tolerance.

Rapid withdrawal of corticosteroids or diminishing the dose in patients with atrophy of adrenal cortex following long-lasting corticotherapy may result in severe acute adrenocortical insufficiency. In the course of multiple myeloma, as a result of disorders in hemostasis, haemorrhagic necrosis and severe failure of adrenal cortex may occur.

The most common complication following radiotherapy (52%) used in the treatment of Hodgkin's disease is hypothyreosis, which may occur even many years after the treatment.

Interferon alpha used in hematology in about 6% of cases results in the disorders of the function of the thyroid gland (1, 2). Hypothyreosis is found in 62% of patients with the thyroid dysfunction, and in the remaining cases asymptomatic thyroiditis and hyperthyreosis (Graves-Basedow's disease, toxic inflammation) occur. These disorders may occur both in the course of treatment with interferon and after the treatment is completed, and in 50% they subside when the therapy is discontinued.

When the treatment with interferon alpha is planned, it is recommended to determine TSH and free thyroxine, and also to test the concentration of a-TPO and a-TG. In the course of treatment and half a year after the treatment is completed, the determination of thyroid hormones should be repeated. If

hyperthyreosis is diagnosed, it is recommended to discontinue the treatment with interferon alpha and perform a test for iodine uptake in the thyroid gland. A low or inhibited iodine uptake in the thyroid gland is indicative of asymptomatic or toxic thyroiditis, and it is the indication for the administration of beta-adrenolytics and possibly corticoids. A normal or increased iodine uptake indicates Graves-Basedow's disease. In the majority of patients small doses of thyreostatics are sufficient in the treatment.

Hypothyreosis detected in the course of treatment with interferon alpha requires the administration of L-thyroxine. Interferon alpha should not be withdrawn. Hypothyreosis due to interferon alpha is a permanent condition and requires hormonal substitution for life. Patients treated with gamma-interferon may develop diabetes connected with the appearance of antibodies against beta cell antigens.

In the course of treatment with vincristine and cyclophosphamide Schwartz-Bartter syndrome may occur, which is characterized by the increased secretion of vasopresin, water retention and hyponatraemia from dilution. Clinical symptoms are not characteristic: there may be nausea, vomiting, lack of appetite, hyperexcitability, changes in personality, dementia and myospasms. Laboratory tests may reveal hyponatraemia, hypomolality of plasma, micturition of condensed urine, normal or increased concentration of vasopressin in blood plasma (in other forms of hyponatraemia the concentration of vasopressin in blood plasma is indeterminable). Schwartz-Bartter syndrome may result in the death of the patient.

THYROID LYMPHOMA

Thyroid lymphoma is an interdisciplinary haematological and endocrinological disease. Lymphoma originates from lymphocytes B, and constitutes 1–5% of malignancies in the thyroid gland and 2.5% of all lymphomas (2). A diagnosed hyperthyreosis is caused by the destructive effect of neoplasm on the tissue of the gland and the release of thyroxine into the bloodstream. The risk factor in primary thyroid lymphoma is Hashimoto disease (about 0.5% of cases of Hashimoto disease develops into lymphoma), therefore some authors claim that in every case of Hashimoto disease a biopsy of the thyroid gland should be performed (7). On the physical a hard non-encysted tumour that infiltrates the neighbouring organs is palpable. Differentiation between thyroid lymphoma and Hashimoto disease may be difficult, therefore immunocytochemical reactions are used for this purpose.

The extensive knowledge of co-existence of endocrinological and haematological disorders among haematologists, endocrinologists and internists may contribute to better diagnostic and therapeutic procedures.

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SUMMARY

Endocrinological disorders in haematological diseases present a serious problem in clinical practice, especially for haematologists and internists. Pathology of haematopoietic system and disorders in the function of endocrine glands are diagnosed in some of the patients seen at haematology clinic and hospitalized in haematological and medical wards. The study presents changes in morphology of blood observed in endocrinopathy, granulocytopenia and agranulocytosis following the administration of antithyroid drugs, co-existence of Addison-Biermer disease and disorders in the function of endocrine glands, endocrine disorders in the course of treatment of hematological diseases and thyroid lymphoma.

Zaburzenia endokrynologiczne w chorobach hematologicznych

Zaburzenia endokrynologiczne w chorobach hematologicznych stanowią niemały problem w praktyce klinicznej, szczególnie dla lekarzy hematologów i internistów. U części pacjentów zgłaszających się do poradni hematologicznych, hospitalizowanych w oddziałach hematologicznych lub internistycznych, stwierdza się zarówno patologię układu krwiotwórczego, jak i zaburzenia funkcjonowania gruczołów wydzielania wewnętrznego. W pracy przedstawiono zmiany w obrazie morfologicznym krwi, obserwowane w endokrynopatiach, granulocytopenię i agranulocytozę po stosowaniu leków przeciwtarczycowych, współistnienie choroby Addisona-Biermera i zaburzeń czynności gruczołów wydzielania wewnętrznego, zaburzenia endokrynne w trakcie leczenia chorób hematologicznych, chłoniaka tarczycy.