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A CLINICAL CASE OF WEBER-CHRISTIAN DISEASE

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A clinical case of elderly female patient diagnosed with Weber-Christian disease developed on the background of long standing chronic autoimmune thyroiditis with impaired function of the thyroid gland (hypothyroidism) and unstable hormonal status, after surgery (hysterectomy, oophorectomy).

KEY WORDS: Panniculitis, Weber-Christian Disease, autoimmune thyroiditis

КЛІНІЧНИЙ ВИПАДОК ХВОРОБИ ВЕБЕРА-КРІСЧЕНА

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Клінічний випадок хвороби Вебера-Крісчен у пацієнтки похилого віку, яка розвинулася на фоні тривало протікаючого хронічного автоімунного тиреоїдиту з порушеною функцією щитовидної залози (гіпотиреоз) та нестабільного гормонального статусу після хірургічного втручання (гістеректомія, оваріектомія).

КЛЮЧОВІ СЛОВА: панікуліт, хвороба Вебера-Крісчена, автоімунний тиреоїдит

КЛИНИЧЕСКИЙ СЛУЧАЙ БОЛЕЗНИ ВЕБЕРА-КРИСЧЕНА

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Клинический случай болезни Вебера-Крисчена у пациентки пожилого возраста, которая развилась на фоне длительно протекающего хронического аутоимунного тиреоидита с нарушенной функцией щитовидной железы (гипотиреоз) и нестабильного гормонального статуса после хирургического вмешательства (гистеректомия, овариектомия).

КЛЮЧЕВЫЕ СЛОВА: панникулит, болезнь Вебера-Крисчена, аутоимунный тиреоидит

INTRODUCTION

Weber-Christian disease (idiopathic lobular nonsuppurative panniculitis) is a rare systemic disease of the connective tissue from group of panniculitis. The incidence and prevalence of Weber-Christian disease is unknown. Less than 200 cases have been reported so far [1]. Currently there is no single concept of the etiology and pathogenesis of this disease. Presumably immune-pathological nature of the disease plays a role with such provoking factors as injury, surgery, disorders of fat metabolism and the endocrine system, liver and pancreas [1–3]. Weber-Christian disease (WCD) is characterized by the acute (subacute) appearance of erythematous, edematous, and tender subcutaneous nodules 2 cm in diameter and more in the upper and lower extremities, trunk and face. Individual nodules usually resolve over a 2-week period, leaving an atrophic depressed scar.

Depending on the form of the nodules there are 3 main clinical forms of WCD [4]:

1. Nodular – lesions are isolated from each other, do not coalesce, clearly demarcated from the surrounding tissue with normal skin color to bright pink color;
2. Plaque – nodules are merged in a dense lumpy conglomerate, color over it varies from pink to bluish-purple;
3. Infiltrative – fluctuations in the area of separate lesions or conglomerates with red, purple or bluish-purple color.

In addition to specific changes in the skin and subcutaneous fat, Weber-Christian disease

appear next to non-specific symptoms, such as myalgia, arthralgia, high or low-grade fever, weight loss, which often complicates the diagnostics of this disease and increases the rate of referral frequency to various specialists [5].

Laboratory data of patients with WCD are non-specific and include increased ESR, leukocytosis or leucopenia and eosinophilia. Biopsy of lesions usually reveal presence of edema, foci of necrosis of fat lobules, cell infiltration with lymphocytes, plasma cells, histyocytes playing a role in histological confirmation of the diagnosis[4].

There is no specific treatment for Weber-Christian disease. Therapeutic responses have been reported with the use of corticosteroids, hydroxychloroquin, azathioprine, thalidomide, cyclophosphamide, tetracycline, cyclosporin and mycophenolate mofetil [4, 6–7].

Prognosis of WCD widely varies. Significant morbidity and mortality may occur in patients with inflammation involving visceral organs and poor response to therapy.

OUR CASE

Female patient of 57 years-old presented with complaints on a burning sensation and tightness of the skin in the area of the anterior abdominal wall, loin, hips; pain in the cervical, thoracic, lumbar regions of spine, joints of wrists, feet, knees with the mechanical rhythm of pain and morning stiffness for about 15 minutes, «crepitus» in the joints during movement and restriction of its motion; torso muscle pain. Also complains were of recurrent headaches of diffuse nature, dizziness, fatigue, general weakness, periodical chest pain without irradiation provoked by stress, relieved in rest; hearing loss. Patient was concerned about progressive memory loss, periodical chills, feeling of a lump in the throat, difficulty in swallowing.

Anamnesis of the disease. From early childhood, the patient had acquired skin defects (extensive scarring), presumably due to past infectious lesions of the skin in the early neonatal period (in the age of 4 days). However, in 2008 after surgery for uterine leiomyoma, the patient began to notice the appearance of a feeling of skin tightness in the area of these lesions, muscle aches, joint pain, aching, diffuse abdominal pain, periodical increase of temperature up to 37, 2 C°. Patient didn't seek for medical care because of these complaints, considering these symptoms as signs of «violations of the thyroid gland function» (since 1987 had chronic autoimmune thyroiditis, hypothyroidism, takes L-thyroxine) and «hormonal changes» after the operation. Since 2012 the patient's condition began to deteriorate progressively – the feeling of skin tightness has intensified, appeared painful nodules with bluish-purple staining of the skin with fluctuation over it in the area of the front wall of the abdomen, loin, hips; memory worsened significantly, appeared pain in the area of thyroid gland projection, dizziness. The patient referred to the endocrinologist, neurologist, dermatologist and was sent for consultation to the genetic center, where Werner syndrome was suspected; but subsequently there were found no conclusive data indicating the presence of Werner syndrome due to the criteria by International Registry of Werner's syndrome group [8]. In 2013, she was consulted by rheumatologist and directed to the rheumatology department, where she was diagnosed with idiopathic recurrent lobular nonsuppurative panniculitis (Weber-Christian disease); she was treated with corticosteroids and NSAIDs with positive dynamics of her state – decreased temperature, diminished pain and skin changes. Subsequently, the patient is held annually examinations and treatment in a specialized rheumatological department.

Anamnesis of life. Patient is not working; denies smoking, alcohol abuse. She had surgical menopause since 2008 – hysterectomy, oophorectomy due to leiomyoma of uterus. According to the patient 30 years ago she was first diagnosed with chronic autoimmune thyroiditis, hypothyroidism; constantly takes L-thyroxin (75–100 mg). First was diagnosed with high blood pressure 7 years ago, constantly takes antihypertensive drugs (lisinopril). From postponed illnesses: chronic bilateral sensoneural hearing loss 3d–4th degree (since 2002); median tunnel syndrome of the left arm (surgical treatment in 2002, 2014); ischemic stroke in the basin of the left middle cerebral artery with right-sided hemiparesis (16.07.2015); encephalopathy of mixed origin (hypertensive, atherosclerotic, dyshormonal), retinal angiopathy of both eyes of hypertensive type, open-angle glaucoma of both eyes 1a degree (2016); right upper jaw granulomas in the area of 14, 16, 17 teeth (surgical treatment in 2016);

Objective examination. General condition of the patient is satisfactory, clear consciousness, posture is active. Patient is oriented in place, time, herself. Height – 162 cm, weight – 76 kg, BMI = 29 kg/m^2. Skin: pale with areas of vitiligo; slightly dry, skin turgor preserved; on the front of the abdominal wall – skin hypotrophy with elements of scarring and slight cyanosis; in the right thigh – skin scarring with purple-bluish coloration, slightly painful on palpation. Visible mucous membranes are clean, moist; subcutaneous adipose tissue is developed moderately, distributed symmetrically. Musculoskeletal system: the outline of small joints of the hands, wrist, knee, ankle, foot joints is smoothed. There are solitary Heberden's nodes in the distal interphalangeal joints (DIP) and Bouchard's nodes in the proximal interphalangeal joints (PIP) of the hands; in the 1st metatarsophalangeal joints (MTP) joints of the feet – signs of exostosis. On palpation joints are painless, with crepitus on motion. Thyroid gland is not enlarged. Lungs: resonance percussion sound on percussion, vesicular breathing over the lungs fields on auscultation, RR-19/'. Heart borders on percussion are extended to the left on 1 cm, heart tones on auscultation are rhythmic, clear with HR 72 bpm. BP *sin* 158/100 mm Hg, *dext* 160/102 mm Hg, radial pulse is synchronous, rhythmic at 72 bpm. Abdomen: abdomen is soft, painless on superficial and deep palpation in all regions. Liver at the costal margin, painless; spleen is not palpable. Pasternatskiy sign is negative on both sides. Urination is free, painless.

The results of current patient's investigations: full blood count: leucocytosis: 9,5*10^9/L, increased ESR: 20 mm/h, eosinophilia: 7 %; urinalysis, fasting plasma glucose, lipid profile, thyroid function tests – all parameters within the normal range; electrolytes: decreased ionized Ca – 1,0mmol/l; serological tests: positive ANA (antinuclear antibodies), positive anti-dsDNA (anti-double stranded DNA) with titer of 40U/ml. Anti-ENA (anti-extractable nuclear antigen), anti-JO-1, Anti-chromatin, anti-Scl70, anti-centromere antibodies were negative.

X-ray of wrists: asymmetric narrowing of the interarticular space; subchondral sclerosis, presence of small (fine) sybchondral cysts, signs of osteoporosis, soft tissue enlargement; x-ray of left foot: asymmetric narrowing of the interarticular space; subhondral sclerosis, presence of small (fine) sybchondral cysts, osteophytes, deformity in the area of PIP, DIP joints; MRI of spine – polysegmental vertebral osteochondrosis, spondylarthritis, spondylosis, disc protrusions at the level L3–L4, L5–S1; densitometry of forearm – mineral density in distal region is decreased, osteopenia, T-score: – 1,8; densitometry of spine – mineral density of L1, L2, L3, L4 is decreased – significant osteopenia, total T score: – 2,4.

Ultrasonography of thyroid gland: total volume: 10 cm^3; isthmus: 6 cm^3; diffuse-focal pathological changes of thyroid gland.

ECG: sinus rhythm with HR – 74, horizontal position of electric axis of the heart, non-specific ST-T changes in left ventricular posterior wall; ECOCG: sclerotic changes in the walls of the aorta, signs of left ventricular hypertrophy.

Biopsy of skin: patient refused to do biopsy.

Diagnosis: Main: Reccurent lobular nonsuppurative panniculitis (Weber-Christian disease), chronic course, activity of 1-st., with primary subcutaneous fat tissue lesion (infiltrative form). Primary polyosteoarthritis with lesions of small joints of wrists, wrist, ankle, knee, small joints of the feet. Spondyloarthritis. Insufficiency of the joint function I degree, Ro I. Osteopenia.

Concomitant diagnosis: Chronic auto-immune thyroiditis, diffuse-nodular form. Hypothyroidism, severe form, compensatory stage. Osteochondrosis with a lesion of the lumbo-sacral spine. Polysegmetal unstable form. Instability of the vertebral-motor segments of L3–L4, L4–L5, L5–S1, herniated intervertebral disks of L4–L5, L5–S1. Arterial hypertension stage III (ischemic stroke 2015), grade 2. Retinal angiopathy of both eyes of hypertensive type, open-angle glaucoma of both eyes 1a degree. Ischemic heart disease. Atherosclerotic cardiosclerosis. CHF, stage IIa, with preserved left ventricular pump function (EF – 62 %), III FC (NYHA). CV Risk 4. Overweight (BMI – 29kg/m^2).

Recommendations and treatment. Recommendations were to maintain healthy lifestyle, decrease sodium intake, lipid lowering diet, aerobic non strenuous exercises. Recommended drugs were: hydroxychloroquine (plakvinil) 0.2 g 2 time per day for a long time; meloxicam 15 mg per day – 10 days, and in the subsequent course of no more than 10 days in the event of pain; glucosamine sulfate 1500 mg per day for 3 months, after 6 months a second

course may be given; osteogenon (combined formulation with calcium and phosphorus) 2 tab twice daily for 6 months under the control of serum calcium and phosphorus; pantoprazole, 40 mg once daily for 7 days; L-thyroxin 100 mg per day under control of thyroid hormones; bisoprolol 5 mg in the morning, lisinopril 10mg in the evening under blood pressure control; aspirin 75 mg once daily continuously. Also the patient was recommended to repeat densitometry after 6 months, autoantibodies after 3 months; repeat visit to rheumatologist, endocrinologist, neurologist after 3 months.

DISCUSSION

Weber-Christian disease in our patient developed on the background of long standing chronic autoimmune thyroiditis with impaired function of the thyroid gland (hypothyroidism). The hormonal status of the patient showed significant fluctuations over years despite of *thyroid* hormone *replacement therapy* (Figure 1, 2).

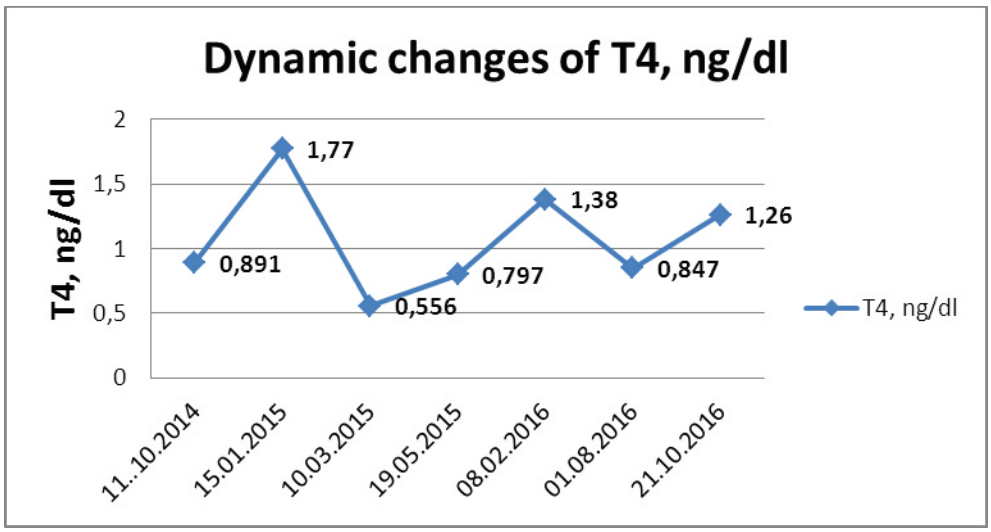

Fig. 1. Dynamic changes of T4 in period of 2014-2016 years; T4 – L-thyroxin, ng/dl.

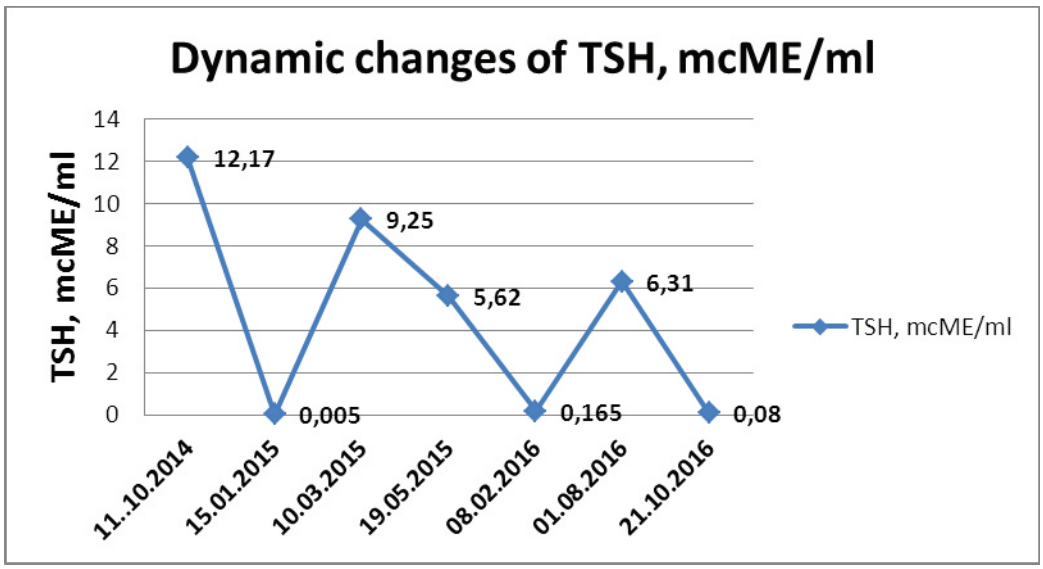

Fig. 2. Dynamic changes of TSH in period of 2014-2016 years; TSH-thyroid-stimulating hormone, mcME/ml.

Although the causes and pathogenesis of Weber-Christian disease are not yet established and are the subject of discussion, a number of studies demonstrate the existence of a linkage of WCD to autoimmune diseases. There are reported cases of Weber-Christian disease associated with autoimmune chronic hepatitis [8], glomerulonephritis [9], diabetes mellitus [8], rheumatologic diseases such as rheumatoid arthritis [7] and vasculitis [10], as well as an increase in antibody titers such as ANA [10–12], anti-dsDNA [8, 13], as well as in our patient, and also ACA [14, 15], which may indicate the participation of immune mechanisms in the development of this disease. Studies highlight surgical interventions, hypothermia, infections, endocrine diseases as possible risk factors in the development of WCD [1–3, 5, 16]. The clinical manifestations of Weber-Christian disease in our patient occurred after surgery (hysterectomy, oophorectomy), which was probably a trigger factor in this case.

Despite the fact that the patient refused to perform biopsy and histological data was not obtained, the clinical picture of the disease, compliance with the criteria of the Ukrainian association of rheumatologists [4], as well as the positive effect of treatment with corticosteroids and hydroxyquinolone allowed diagnosis of Weber-Christian disease in our patient.

CONCLUSIONS

Weber-Christian disease still remains a medical mystery with unknown causes and mechanisms of its occurrence. This clinical case is an observation that supports the immune theory of the development of this disease and is an illustration of the fact that the key factors for the early diagnosis of rare diseases such as WCD are a careful history taking, attentive and accurate approach to the patient, as well as a systematic analysis of laboratory and instrumental surveys.

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