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Original article

Satoyoshi syndrome: A rare multisystemic disorder requiring systemic and symptomatic treatment

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Abstract

Satoyoshi syndrome is a rare multisystemic disorder with assumed autoimmune pathogenesis. Typical clinical features are progressive painful muscle spasms, alopecia, diarrhoea, and skeletal and endocrine abnormalities often resulting in early invalidism and death. Patients have been treated with immunoglobulins and glucocorticoids with varying outcome. We report on a 19-year-old German adolescent who has been successfully treated with a new combination of carbamazepine to reduce the severity and frequency of painful nocturnal muscle spasms, prednisolone, methotrexate and sex-steroids. Prednisolone treatment alone was not successful. After introduction of low-dose of methotrexate to the therapy the patient recovered from muscle spasms, alopecia and diarrhoea. Initiation of sex-steroid treatment resulted in pubertal development, regular menstrual cycles and improved quality of life.

Keywords: Satoyoshi syndrome; Muscular spasms; Alopecia; Amenorrhoea; Methotrexate; Carbamazepine

1. Introduction

Satoyoshi syndrome is a rare multisystemic disorder, first described by Satoyoshi and Yamada in 1967 [1]. It consists of progressive painful muscular spasms, diarrhoea, alopecia and endocrine abnormalities, e.g. amenorrhea [1–3]. Skeletal involvement includes epiphyseal and metaphyseal osteolytic lesions [4–6] thought to be due to repeated injuries to the growth plates, epiphyses and tendon attachments due to vigorous muscle spasms [6]. Less than 50 cases have been described worldwide [3].

We present a case of an adolescent female, focusing on hormonal abnormalities and a treatment combination with carbamazepine (CBZ), prednisolone, methotrexate (MTX) and hormonal replacement therapy. To our knowledge this successful treatment combination has not been reported so far.

2. Case report

A previously healthy athletic 14-year-old Caucasian girl was admitted to our hospital because of frequently recurring episodes of painful muscular spasms since the age of 12 years. Symptoms started initially in the small muscles of the hand, affecting other muscle groups, including abdominal wall muscles, tongue, thighs and masticatory muscles over the next 2 years. The painful spasms lasted 2–3 min and were triggered by exercise. Night sleep was disturbed.

Abbreviations: CBZ, carbamazepine; MTX, methotrexate; LH, luteinizing hormone; FSH, follicle-stimulating hormone; 17-OHP, 17-hydroxyprogesterone; P, pubic hair; B, breast stage; DHAS, dehydroepiandrosteronsulfate; CRH, corticotropin-releasing hormone; GnRH, gonadotropin-releasing hormone; ACTH, adrenocorticotropic hormone; HPG, hypothalamic–pituitary–gonadotrophic; IGF-(BP), insuline-like growth factor (binding protein); SD(S), standard deviation (score); BW, body weight; BMI, body mass index.

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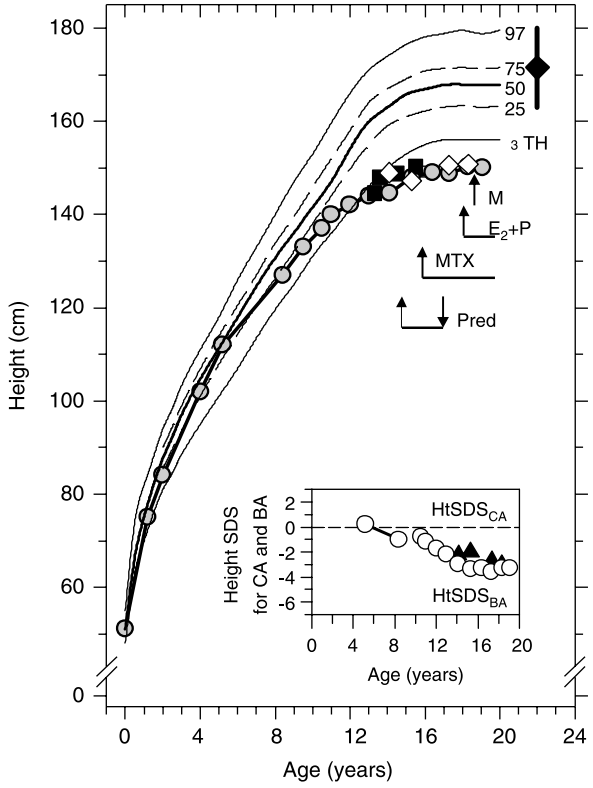

Fig. 1. Patient's growth chart. TH, target height; M, menarche; E_2, estrogen; P, progesterone; MTX, methotrexate; Pred, prednisolone; CA, chronological age; BA, bone age; ○, height; ■, bone age; ◇, predicted adult height; ○, height SDS for CA; ▲, height SDS for BA; ↑, therapy initiated; ↓, therapy discontinued.

In addition to the muscular symptoms her parents noticed that she had stopped growing and suffered from progressive hair loss.

Family history revealed healthy non-consanguineous German parents. Pregnancy and delivery were uneventful and postnatal development normal. She did not undergo puberty. Her twin siblings were healthy.

On admission at the age of 14.1 years, her height was 145.6 cm (−3.7 SD, growth chart, Fig. 1), body weight (BW) 35 kg (BMI: 16.3, BMI SDS: −1.2) with normal body proportions. Her hair was sparse and thin, eyebrows, eyelashes and body hair were present. Pubertal stage according to Tanner was P1, B3, no axillary hair, no menarche. Muscle spasms were frequently seen during the examination. Joints were neither swollen nor reddened and motility was not impaired. Vital signs and neurological examination were entirely normal. There was no weakness or atrophy of the upper or lower extremities.

3. Laboratory findings

Laboratory tests were normal for red and white blood count, serum electrolytes, liver enzymes, creatinine, C-reactive protein, alkaline phosphatase, clotting parameters, vitamins A and E, lactate and pyruvate, iron and copper metabolism. Serology for HIV and hepatitis B were negative.

Immunoglobulin levels revealed low IgG of 658 mg/dL (norm: 800–1800 mg/dL) and normal IgA (norm: 40–240 mg/dL) and IgM (norm: 50–200 mg/dL). CD4-positive lymphocytes were elevated to 52% (age-related normal range: 33–45%) and CD8-positive lymphocytes decreased to 17% (age-related normal range: 27–36%). Rheumatoid factors were negative. The unspecific antinuclear antibodies (ANA)-IIF were increased at 1:640, but no specific antibodies (AB) against anti-cytoplasmatic, mitochondrial, liver–kidney microsomes, smooth muscle, adrenal gland, thyroid, colon epithelial and ovarian tissue were detectable.

Basal and gonadotropin-releasing hormone (GnRH) stimulated luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels were increased to 5.6 and 11.3 IU/L (basal levels, normal values: LH, 0.7–4.7 IU/L; FSH, 3.9–7.0 IU/L) and 28.2 and 13.8 IU/L (stimulated levels, normal values: LH, 4.4–23.1 IU/L; FSH, 8.1–14.8 IU/L). Estradiol was low at 44.1 pmol/L (norm: 35–220 pmol/L). During insulin-induced hypoglycemia cortisol (667.7 nmol/L) and growth hormone (22.5 μg/L) rose normally. IGF-1 and IGF-BP-3 serum levels were normal for age and sex. Dehydroepiandrosteronsulfate (DHAS) was low (0.12 μmol/L, norm: 1.5–5.4 μmol/L). Basal and corticotrophin-releasing hormone (CRH) stimulated adrenocorticotropic hormone (ACTH) levels were normal. Other parameters, including plasma calcium, phosphate, parathyroid hormone, vitamin D3, thyroid hormone and 17-hydroxyprogesterone levels, were normal. Oral glucose tolerance test was normal.

Urinary excretion of amino and organic acids, cAMP, hydroxyproline, myoglobin were normal.

Chromosomal analysis revealed a female 46,XX karyotype. Using Southern blot analysis, myotonic dystrophy was ruled out by the lack of expansion of nucleic acids CTG on the myotonin-protein kinase gene on chromosome 19.

Gastroenterological function test (D-xylose challenge) and endoscopy of the oesophagus, stomach, duodenum and ileo-colon showed a mild intestinal malabsorption condition (D-xylose excretion in urine and faeces reduced) and small duodenal ulcerations.

Ultrasound examination of skeletal muscles, uterus and ovaries was normal.

Bone age, determined by X-ray of the left hand, was 13.3 years. Radiological investigation of the skeleton revealed osteolytic alterations commonly seen in Satoyoshi syndrome patients, which were located in the hands, pelvis, knees and proximal left fibula (see Fig. 2). Magnetic resonance scans confirmed deformities in the growth zone of both knees. Bone mineral density (Dexa-scan) was markedly decreased to −2.8 SD compared to age and sex-related normal values.