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A Rare Case Report of Stiff-Person Syndrome Analogous to Adult-Onset Still's Disease

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Keywords: Stiff-person syndronme, adult-onset Still’s diseases, rash, hyperpyrexia

Abstract: Objective: To clarify the diagnosis of stiff-person syndrome (SPS), distinguish adult-onset Still's diseases (AOSD), and give reasonable treatment. Methods: Laboratory tests of serum and cerebrospinal fluid, rigorous neurological examination and electromyography were performed, while Clonazepam, hormone, gamma globulin, nutritional nerve and symptomatic support treatment were given to the disease. Results: Symptoms of the disease were completely resolved, including no return of fever or rash, no obvious abnormalities on neurological examination, and normal laboratory tests and electromyography. Conclusion: The symptoms of SPS with hyperpyrexia and rash overlap with AOSD, which is easily to be misdiagnosed. Timely and systematic treatment of the disease has a good prognosis, but the risk of recurrence is also high. Clinicians should strengthen the understanding of the disease and carefully choose a reasonable treatment plan.

1. Introduction

Stiff-person syndronme (SPS) is a rare autoimmune disease of the central nervous system. Clinically, it is mainly manifested as progressive axial muscle tonicity, seizures, painful muscle spasms, seizures induced by emotional and motor stimuli, positive anti-GAD antibodies in serum and cerebrospinal fluid. Electromyography is characterized by the activity of active and antagonistic muscle motor units in the quiet state [1-3]. Adult-onset Still's disease (AOSD) is characterized by fever, rash and arthralgia, which is also an autoimmune disease and rare in clinic. Its symptoms overlap with those of SPS with hyperpyrexia and rash, which is easy to be misdiagnosed. A case of atypical SPS with rash was admitted to Jining First People's Hospital in September 2017. The report is as follows:

2. Case Report

The patient surnamed Wang, male, 39 years old, was admitted to hospital on September 18, 2017 due to "limb weakness for half a month, abdominal and lower limb stiffness and tightness for 10 days". Half a month before admission, the fever was 40℃, and there was weakness in both lower limbs, manifested as walking instability, left leg was obvious, and sometimes the feeling of tipping. After taking cold medicine, the body temperature dropped to normal, but the weakness in left lower limbs gradually worsened, and occasionally the upper limbs were unstable. Ten days before

admission, the patient had muscle stiffness in both lower extremities, muscle tightness in both lower extremities and abdominal muscles, and the stiffness was more obvious when he extended his legs. The symptoms were not improved during sleep, and he occasionally had involuntary shaking of his limbs, lasting 10 minutes each time. Double upper limb lift difficulty, can be flexible use of chopsticks, with intermittent laryngeal tightness, laryngeal sound, gasp, palpitation, sweating, irritable, lasting several minutes each time. Two days before admission, the patient had weakness in chewing, choking in drinking water, slurred speech, and weight loss of 4kg since onset. On general physical examination, rash of varying size (history 1 month), nodules, scratches, and scabs were observed on the extremities and right abdomen. Neurological examination: Except for superficial hypoesthesia below the bilateral eye fissure and above the neck. The right nasolabial fold was shallow, the muscle tension of both lower extremities was increased, the muscle strength of the left lower extremities was grade 5-, the tendon reflexes of the extremities were hyperactive, the tendon reflexes of both upper extremities (+++), the tendon reflexes of both lower extremities (++++), patellar clonus and ankle clonus were present. Bilateral Babinskin sign (+), bilateral Chaddock sign (+). The neck was soft, bilateral Kerning sign (+), and the rest of the neurological examination was normal. Auxiliary examination at admission: Lumbar MRI showed degeneration and L2-S1 disc herniation on September 15, 2017. Admission diagnosis: Weakness and stiffness of limbs pending investigation, SPS; Rash to be investigated; Lumbar disc herniation.

Diagnosis and treatment process: after admission, the relevant examination results, blood routine, coagulation 5 items, a function 7 items, syphilis, AIDS showed no obvious abnormalities; Biochemical whole item showed slightly high blood lipid, other normal; Tumor markers: neuronal isoenolase and carcinoembryonic antigen were slightly higher; Urine routine showed urinary protein (+), and no other abnormalities were found. MR of craniocerebral + cervical + thoracic vertebrae: possible osteoma of the middle occipital bone, inflammation of the left ethmoid sinus, soft tissue thickening in the posterior part of the nasopharyngeal crest, cervical 3-7 disc herniation, thoracic degeneration, no signs of nerve root compression.

At about 05:12 on the fourth day of admission, the patient suddenly felt throat tightness after emotional agitation, laryngeal ringing, wheezing, cyanosis, shortness of breath, involuntary shaking of limbs, obvious lower limbs, feeling dark, transient loss of consciousness, and head injury. There were skin rash and bleeding on the top of the head on physical examination, and no obvious changes in the nervous system on physical examination. Oxygen was given, and no craniocerebral hematoma or fracture was found on urgent brain CT examination. The neurosurgery department had urgent consultation. The wound was disinfected and bandaged, dressing was changed every other day, and TAT was injected intramuscular. The patient had multiple skin rashes and muscle rigidity all over his body. After consultation in an infectious disease hospital, the patient did not meet the characteristics of tetanus and rabies. Varicella virus was considered as the characteristic of skin rash, and ganciclovir was added for antiviral. Preliminary clinical considerations: SPS?

On the 6th day of admission, neurological physical examination showed high muscle tension in both upper limbs, remaining the same as before. The rash was broken, and the secretion of the rash was collected for culture and drug sensitivity. The diagnosis was considered SPS, and diazepam injection was given. The symptoms were improved.

On the 7th day, fever reappeared with the highest body temperature of 38.3°C. Blood routine showed white blood cells 19.9×10^9/L, neutrophils 16.53×10^9/L, monocytes 1.19×10^9/L, neutrophils 82%, and procalcitonin 0.12ng/ml. Chest CT: bronchitis, right upper lobe emphysema, right lobe hypodensity. The enhanced magnetic resonance imaging of brain showed no obvious abnormality. Still thinking about SPS? Giving Clonazepam 1mg orally, twice a day.

On the 8th day, the patient's walking instability, muscle rigidity improved, skin rash improved, but sleep increased, the family requested to be transferred to a higher hospital for further treatment.

2017.9.26 Admitted to department of neurology, Shandong Provincial Hospital. Neurological physical examination: speech was not clear and fluent, limb muscle strength was grade 5, muscle strength of both upper limbs was normal, muscle tension of both lower limbs was increased, tendon reflex (+++), suspicious positive Babinski sign on the left side, soft neck, no resistance, meningeal irritation sign (-). Admission diagnosis: SPS? Diagnosis and treatment process: c-reactive protein 17.54mg/L, erythrocyte sedimentation rate 28mm/h, hepatitis b surface antibody, core antibody, e antibody (+), blood TORCH: hsv-igm (+), giant cell and rubella virus-igg (+). Electromyography (EMG): No obvious abnormalities were observed in sensory and motor transmission of the detected nerves. The occurrence rate and latency of F-wave of the detected nerves were normal. A small number of single action potentials were observed in the resting state of bilateral rectus abdominis muscles, especially in the right rectus abdominis muscles, and no obvious abnormalities were observed in the other muscles. Cerebrospinal fluid routine: CSF red, cloudy, nucleated cell count 42×10^6 /L, monocytes 17×10^6 /L, multiple nuclear cells 25×10^6 /L, red blood cells 37×10^6 /L, Pan's test 1+, cerebrospinal fluid biochemistry: Glucose 4.87mmol/L, protein 1.17g/L, cerebrospinal fluid microbial: negative. Tumor syndrome-related antibodies (anti-GAD, Amphiphysin IgG) were negative. Other examinations were normal. Clonazepam, hormone, propyl ball, nutritional nerve and symptomatic support were given, and the patient was discharged. Discharge diagnosis: SPS. After 3 months of follow-up, the patient's symptoms disappeared completely. The final diagnosis was SPS.

3. Discussion

Both SPS and adult AOSD belong to autoimmune diseases, and their pathogenesis is unknown. The diagnosis is made by excluding other diseases in clinical practice. It is difficult to distinguish SPS with fever and rash from atypical AOSD, and the reasonable diagnosis and treatment early or late is related to the prognosis of patients.

SPS is a functional immune disease in neurology department, which belongs to a paraneoplastic syndrome [4]. There were specific laboratory index, including glutamic acid decarboxylase Antibodies to Aciddecarboxylase (GAD), Amphiphysin (a 128-protein located in the presynaptic membrane of neurons) and gephyrin(a cell solute protein selectively clustered in the postsynaptic membrane of inhibitory synapses) [5], mental stimulation, like emotional irritability or body feeling stimulation and sudden hearing can induce muscle rigidity and muscle spasm, often accompanied by autonomic nerve function disorder, intelligence and sensory system are not involved. SPS usually develops occultively, only presenting as episodic myalgia in the early stage, and postural abnormalities characterized by increased flexor and extensor tension, decreased voluntary movement, muscle hypertrophy and lordosis can be seen on physical examination. The symptoms mostly start from the trunk muscles, then gradually extend to the proximal muscles, and finally accumulate in the distal muscles [6]. Patients may also experience muscle spasms caused by emotional upset, fright (induced by tactile, auditory, and visual stimuli), or sudden contraction of adjacent muscles [7]. At this point, it should be distinguished from tetanus. In this case, the patient had multiple skin rash and muscle rigidity, no masseter spasm or rigidity, no trismus, motor unit potential appeared on EMG, and intravenous diazepam could improve the symptoms [8]. After consultation in the infectious disease hospital, it did not meet the characteristics of tetanus and rabies, so it was excluded. SPS is an autoimmune disease, which can coexist with other immune diseases clinically. It is not difficult to understand that the atypical SPS with fever and rash can be confused with AOSD.

Adult-onset still's disease (AOSD) is a rare systemic inflammatory disease involving multiple factors, which belongs to rheumatology and immunology department [9]. The incidence was (0. 16 ~

0. 40) /100 000, with a prevalence of (1-34) /1 million, mostly among young people [10]. The age of onset showed two peaks: 15-25 years old and 36-46 years old [11]. There is no specific diagnostic index and unified diagnostic criteria. Clinically, the syndrome is characterized by high fever, rash, joint pain and elevated white blood cell. The clinical manifestations are complex and diverse, and the symptoms are not typical. In adults with SPS, the rash is transient. It usually appears in the evening with fever and disappears after the fever in the morning. The limbs and trunk are more common, and some patients are accompanied by pruritus and fever. Most of them involve joints, manifested as joint pain, severe may have systemic pain, liver, spleen, lymph node enlargement, no specific laboratory indicators. Many times repeatedly detection ability after ruling out other diseases diagnosis [12], and the risk of recurrence is also high [13].

In this case, the patient had a high fever (40 ℃), a rash, and severe systemic symptoms, similar to AOSD, but with a high fever for half a month, the rash preceded the fever and was nontransient, characterized by generalized muscle spasms and not governed by volitic activity, such as "wooden people". A negative syphilis test would rule out neurosyphilis. Early application of benzodiazepines can significantly improve symptoms [14], which does not support AOSD. Electromyography of this patient showed no obvious abnormalities in the sensory and motor transmission of the detected nerves, the occurrence rate and latency of F-wave of the detected nerves were normal, and a small number of single action potentials could be seen in the resting state of bilateral rectus abdominis muscle, especially in the right rectus abdominis muscle, while no obvious abnormalities were observed in the other muscles. Tumor syndrome-related antibodies (anti-GAD, Amphiphysin antibody IgG) were negative, which did not completely coincide with the theory of rigid man syndrome. However, clonazepam, hormone (methylprednisolone shock therapy, progressively reduced dose to 60mg/d then reduced one tablet every two weeks), human immunoglobulin, nutritional nerve and symptomatic support therapy showed definite efficacy. After 3 months of follow-up, the patient's symptoms completely disappeared, and there was muscle rigidity in the whole process, which supports the diagnosis of SPS.

4. Conclusion

Both SPS and AOSD are autoimmune diseases, hormone, gamma globulin and other immunosuppressive therapy are effective, clinical rare, many times repeatedly detection ability after ruling out other diseases diagnosis, reports followed up for a few years later diagnosed with rheumatoid arthritis and systemic lupus erythematosus neurosyphilis or lymphoma, etc., It is impossible to determine the outcome of the disease or the initial misdiagnosis. In conclusion, the prognosis of timely systematic treatment is good, but the risk of recurrence is also high. Clinicians should strengthen the understanding of this disease and carefully choose a reasonable treatment plan.

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