Clinical Features of Chronic Inflammatory Demyelinating Polyneuropathy With Autoimmune Hepatitis

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Abstract

Chronic inflammatory demyelinating polyneuropathy (CIDP) with autoimmune hepatitis is rare in clinical practice. Here we present a case to describe the relevant clinical features and provide case data for the diagnosis and treatment of the disease. The diagnosis was supported by medical history, physical examination, laboratory and imaging examination, nerve conduction velocity and cerebrospinal fluid examination. The combined disease was identified by autoimmune antibodies and ultrasonography. Combined with the patient’s history of chronic progression, clinical manifestations of peripheral nerve damage, cerebrospinal fluid showing protein-cell separation and nerve conduction velocity showing decreased amplitude and conduction velocity, CIDP was confirmed. Combined with the patient’s examination result of abdominal bulging, color Doppler ultrasound examination showed cirrhosis, positive (+) anti-liver/kidney microsomal type 1 antibody (anti-LKM-1), considering combination of autoimmune hepatitis type II (AIH-II). The clinical symptoms of both were significantly improved by hormone therapy. CIDP is clinically uncommon in elderly male patients, and it is also rare to have AIH-II. But according to the typical pathogenesis, clinical manifestations, detailed physical examination, laboratory and imaging examination, and neuro-immunological data, clinical diagnosis can be made. Pathological data are needed to confirm the diagnosis. Both have poor natural prognosis. However, the use of hormone therapy according to its pathogenesis can effectively alleviate clinical symptoms and prevent progression.

Keywords: CIDP; Autoimmune hepatitis; LKM-1; Cerebrospinal fluid; Cirrhosis

Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP)

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Case Report

History

A 67-year-old man with previous physical fitness, presented with numbness and weakness of limbs without obvious induction 2 years ago which gradually aggravated. At present, the holding was not tight, the walking was unstable, and there was a feeling of stepping on the cotton, accompanied by constipation, no fever and night sweats. After treatment in the local hospital, the patient’s symptoms did not improve significantly. In order to seek further treatment, the patient came to our hospital, and the outpatient department received orthopedics. After symptomatic treatment, the patient did not improve significantly and was transferred to the department of neurology after consultation.

Methods

Physical examination

Physical examination was conducted on the patient, including vital signs, skin and mucous membrane, heart, lung, abdomen and limbs. Nervous system was examined including brain higher function, cranial nerve, movement, sensation, deep and shallow reflex, pathological sign, ataxia movement and meningeal stimulation sign.

Laboratory examination

Examination was conducted in the laboratory of our hospital, including blood routine examination, erythrocyte sedimentation rate, vitamin, liver and kidney function, blood glucose, blood lipid, coagulation function, B-type natriuretic peptide (BNP), autoimmunity antibody, tumor marker, tuberculosis antibody, hepatitis marker and thyroid function.

CSF examination

After informed consent of the patient and family members, the patient was placed on the bed with the curved side, hands clasped the knee, local anesthesia was performed with lidocaine, and the needle was punctured at L3-4. CSF examinations included color, transparency, protein characterization, sugar characterization, cell count and classification, protein quantification, chloride, sugar, lactate dehydrogenase (LDH), high-sensitivity C-reactive protein (hsCRP) and adenosine deaminase (ADA). After the operation, the puncture needle was pulled out and fixed with a sterile gauze block. Pillow was removed and patient lied flat for 6 h.

Electromyography and color Doppler ultrasonography

In response to the patient’s numbness and weakness in the limbs, the nerve conduction velocity and electromyography of the extremities were performed by a highly trained technician in the neurological function room of our hospital. For the abdominal distension of the patient, abdominal color Doppler ultrasonography was performed by a highly trained technician in the color Doppler room of our hospital.

Treatment and follow-up

After informed consent of the patient and family members, patient was given prednisone 500 mg/day, intravenous infusion, for three consecutive days and then directly oral prednisone 1 mg/kg/day, maintained for 1 month. Patient returned to the hospital for follow-up visit, and the dose was adjusted according to the changes of the condition. At the time of follow-up, blood routine examination, liver and kidney function, nerve conduction velocity of the extremities and abdominal color Doppler ultrasound were performed.

Results

Physical examination results

On physical examination, temperature was 37 °C, pulse was 65 beats/min, respiratory rate was 20 times/min, and blood pressure was 126/79 mm Hg. Patient was conscious, had unclear speech, and was helped into the ward. He was cooperative in physical examination. There was no yellow staining and bleeding point on the skin and mucous membranes of the whole body, the skin was dark, and there were no enlargement of superficial lymph nodes, middle trachea, and no enlargement of thyroid gland. Symmetrical chest without deformity, steady breathing, clear breathing sounds in both lungs, no dry and wet rales were heard. The heart boundary was not large, and the heart rate was 65 beats/min. The heart rhythm was regular. No pathological murmurs were heard in the auscultation area of each valve. There were abdominal distention, no tenderness and rebound pain. The hard liver could be touched by a horizontal finger under the right costal margin, and the spleen was not touched under the costal margin. The Murphy’s sign was negative. There was no tapping pain in the kidney area, muscle atrophy in the limbs, and mild edema in both lower limbs. Nervous system examination showed muscle strength of extremities of proximal level 4 and distal level 3. Pain, temperature, touch, vibration, positional sensation and sputum reflex disappeared. Pathological signs were negative, and meningeal irritation was negative.

Laboratory examination results

Blood routine showed white blood cell (WBC) of 1.91 G/L, red blood cell (RBC) of 3.67 T/L, Hb of 92 g/L, hematocrit (HCT) of 0.301, mean corpuscular hemoglobin (MCH) 306 g/L, red cell distribution width (RDW) of 17.3%, platelets (PLT) of 115 G/L and platelet distribution width (PDW) of 11.6%. Blood
the abdominal swelling was reduced. After 1 month of dis-
movement was more sensitive, the skin was whitened gradually and
limbs was restored, the gait was normal, the superficial sensa-
tion extended by more than 50% from the upper limit of the
normal value. The conduction velocity and amplitude of the
demyelination, decreased amplitude and decreased conduction
velocity. After glucocorticoid treatment, the patient’s symp-
toms were significantly improved, according to which clinical
diagnosis could be performed, and a nerve biopsy was required
to confirm the diagnosis.

This patient had multiple muscle weakness and peripheral
nerve demyelination, which needed to be differentiated from
multifocal motor neuropathy (MMN), but the unsupported
points were: the patient had hypoesthesia and increased pro-
tein, and the hormone treatment effect was good [12]. The pe-
ripheral nerve damage of this patient was predominant, which
needed to be differentiated from recurrent Guillain-Barre syn-
drome (GBS), but the unsupported points were: long course
of disease, no history of precursor infection, no combination
of facial nerve paralysis and respiratory muscle paralysis [13].
The patient had peripheral demyelinating lesions, cirrhosis,
hypothyroidism and dark skin. POEMS syndrome was also
considered, but the patient’s M protein was negative [14]. The
patient had decreased peripheral nerve depth and superficial
sensation, which needed to be differentiated from paraneoplas-
tic neuropathy. However, the patient’s repeated examination
showed no tumor, and the tumor markers were negative. The
nerve biopsy was effective, which was not consistent with the
disease [15].

The etiology of CIDP is unclear, and immunotherapy is
effective, suggesting that the disease has immune-mediated
pathogenesis. Prednisone is currently the preferred drug for
drug therapy. The clinical symptoms of the patient improved
significantly after hormone therapy, suggesting that immune
factors were involved in the pathogenesis. However, the com-

Imaging examination results

Cardiac color ultrasound showed degenerative aortic valve
with mild to moderate incomplete closure, a small amount of
regurgitation in the bicuspid and tricuspid valves, low limit of
normal cardiac function, and a small amount of pericardial ef-
fusion. Ejection fraction value was 50%. Chest X-ray showed
left costal diaphragm angle blunt, a small amount of pleural effusion? Pleural thickening? In magnetic resonance imaging
(MRI) of the thoracic vertebra, the thoracic vertebrae signal
showed a slight uneven reduction, and the blood system dis-
ease was to be discharged. Thoracic disc degeneration was
shown. Color ultrasound indicated cirrhosis, pelvic effusion,
and abdominal wall swelling.

CSF examination results

CSF pressure was 120 mm H2O. CSF routine showed trans-
parent, no clot, Pandy test positive, total number of cells 0,
colorless. CSF biochemistry showed proline of 0.92 g/L, Cl
of 121.1 mmol/L, glutamic acid of 2.03 mmol/L, LDH of 33,
hsCRP of 0.9 mg/L and erythrocyte sedimentation rate (ESR) of
26 mm/h; anti-LKM-1 was positive (+), and the remaining was
negative. Bone marrow puncture results showed leukopenia.

Nerve conduction velocity examination results

Lower extremity motor nerve conduction showed distal la-
tency extended by more than 50% from the upper limit of the
normal value, motor nerve conduction velocity decreased by
more than 30% from the lower limit of the normal value, and F
wave latency extended by more than 20% from the upper limit
of the normal value. The conduction velocity and amplitude of
sensory nerve in lower limbs decreased, suggesting that there
was demyelinating lesion in the peripheral nerve and the pe-
ripheral nerve was generally damaged.

Treatment and follow-up results

After hormone treatment, the muscle strength of both lower
limbs was restored, the gait was normal, the superficial sensa-
tion was more sensitive, the skin was whitened gradually and
the abdominal swelling was reduced. After 1 month of dis-
charge, the patient returned to the hospital: the skin was white
as normal, the abdominal distension disappeared, the muscle
tension of the limbs was normal and the shallow feeling was
basically normal. The blood routine showed that the anemia
was better than before, and the liver color Doppler showed im-
provement of cirrhosis without pelvic fluid.

Discussion

Diagnosis criteria of CIDP include symptom progression over
8 weeks, chronic progression or remission-recurrence. The
clinical manifestations are limb weakness of different degrees,
most of which are symmetrical, and a few are asymmetric.
Both proximal and distal limbs can be involved, and the ten-
don reflex of limbs is reduced or disappeared, accompanied
by deep and shallow paresthesia. CSF examination shows
protein-cell separation. The results of electrophysiological ex-
amination show that nerve conduction velocity is slowed, con-
duction block or abnormal waveform dispersion. Peripheral
neuropathy caused by other reasons is excluded from nerve
biopsy; corticosteroid therapy is effective [1, 4, 11]. The pa-
tient had a 2-year history of chronic progression and relapsing
remission. Symptoms mainly manifested as dysarthria, numb-
ness of limbs, muscle atrophy, low muscle tone, sputum reflex
disappeared, decreased acupuncture sensation like gloves and
socks, and sphincter dysfunction. CSF showed increased pro-
tein and protein-cell separation. Nerve examination showed
demyelination, decreased amplitude and decreased conduction
velocity. After glucocorticoid treatment, the patient’s symp-
toms were significantly improved, according to which clinical
diagnosis could be performed, and a nerve biopsy was required
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pathogenesis. Prednisone is currently the preferred drug for
drug therapy. The clinical symptoms of the patient improved
significantly after hormone therapy, suggesting that immune
factors were involved in the pathogenesis. However, the com-

biochemistry showed normal electrolytes, liver function, renal
function, blood lipids, blood sugar; albumin (Alb) was 35.5
g/L. Tumor markers, central nervous system specific protein
S100β, serum ferritin, alpha-fetoprotein, TB-spot, tuberculosis
antibody-IgG, tuberculosis antibody-IgM, human immuno-
 deficiency virus (HIV), hepatitis B virus (HBV), hepatitis C
virus (HCV), TP-PA, urine routine and coagulation function
were normal. Thyroid function showed thyroid-stimulating
hormone (TSH) of 13.258 mU/L, FT3 of 2.51 pmol/L, VB12
of 195.76 pg/mL and erythrocyte sedimentation rate (ESR) of
26 mm/h; anti-LKM-1 was positive (+), and the remaining was
negative. Bone marrow puncture results showed leukopenia.
mon onset age of this disease is 40 - 60 years [1]. The patient could be classified as a late-onset case. In patients with severe disease, intravenous immunoglobulin (IVIG) or plasma exchange therapy can be performed first. IVIG therapy is suitable for patients with severe neurological impairment and rapid progression. IVIG therapy is ineffective for patients with CIDP who have sensory impairment as their primary manifestation. Patients with chronic progressive and recurrent CIDP with demyelinating but axonal denatation respond well to plasma exchange. The vast majority of patients respond effectively to one of these three methods (first-line treatment). If all three methods are ineffective, immunosuppressive agents can be used as second-line drugs, such as azathioprine, cyclosporine, cyclophosphamide, etc. In addition to drug treatment, adjuvant treatment of large doses of B vitamins and nutritional support, functional exercise, etc., can promote limb rehabilitation and reduce complications [3, 4, 16]. Although the patient had severe motor sensory nerve injury at the time of admission, after informing the patient and his families of the indications and contraindication of the three treatment methods, they decided to use hormone shock therapy after discussion. Immunoglobulin or plasma exchange therapy was not used, but the patient’s condition recovered well, suggesting that hormone therapy is sensitive and effective for CIDP.

The patient’s abdomen bulged, bloating was obvious and the hard liver could be reached under the right costal margin, which was difficult to explain by CIDP. Color ultrasound showed cirrhosis, pelvic effusion and abdominal wall swelling, and positive (+) anti-LKM-1, in accordance with AIH-II type [6, 17, 18]. LKM-1 is commonly found in AIH or chronic hepatitis C. The patient was excluded from chronic hepatitis C and AIH could be considered. The disease is most common in women, with a ratio of male to female of 1:4, and there are two peak ages of onset at 10 - 30 years and above 40 years [6, 7]. It is a rare case of an elderly man.

The patient needed to be differentiated from primary biliary cirrhosis in terms of clinical symptoms and laboratory tests, but the patient was an elderly man with no weakness, jaundice or pruritus. Liver function examination showed that alkaline phosphatase and gamma-glutamyl transpeptidase were normal; serum anti-mitochondrial antibody M2-specific antibody was negative and could be identified. However, the shortcoming was that there was no pathological examination. In addition, it needs to be differentiated from primary sclerosing cholangitis, chronic viral hepatitis, alcoholic steatohepatitis and drug-induced liver damage [19, 20].

The clinical features of AIH are increased serum aspartate transaminase, hypergamma-globulinemia and positive autoantibodies. Severe cases can progress rapidly to cirrhosis and liver failure. Studies have shown that patients with severe AIH have a survival rate of 50% at 3 years without treatment and 10% at 5 years. After treatment, the patient’s 20-year survival rate reached 80%, and the life expectancy is not significantly different from that of normal healthy people matched by gender and age. Absolute indications for treatment include serum aspartate transaminase (AST) ≥ 10 times the upper limit of normal, or serum AST ≥ 5 times the upper limit of normal, and γ-globulin ≥ 2 times the upper limit of normal; histological examination showed bridging necrosis or multi-lobular necrosis [6, 21, 22]. The patient’s liver function was normal and no histological examination was performed. However, this patient had relative indications: fatigue, joint pain, jaundice and other symptoms, abnormal serum AST and gamma-globulin levels, which were lower than the absolute criteria. Color ultrasound indicated cirrhosis, and treatment was needed to relieve the symptoms.

The main purpose of AIH treatment is to relieve symptoms, improve liver function and pathological tissue abnormalities, and slow down the progression to liver fibrosis. Glucocorticoid alone or in combination with azathioprine is currently the standard treatment for AIH. This patient had a relative indication of treatment, and because of the combination with CIDP, the preferred treatment for both was hormones. Due to the critical condition, hormone shock therapy and long-term maintenance therapy were adopted. The patient’s cirrhosis was improved and the treatment was effective, which supported the diagnosis of AIH-II type.

This case has some highlights and shortcomings. This patient was an elderly man, with late-onset CIDP, with typical peripheral nerve damage in CIDP. At the same time, the disease was combined with AIH-II, which is rare in epidemics, considering the pathogenesis is immune-mediated. The patient had nervous system, digestive system, circulatory system and skin damage. After hormone therapy, he achieved significant improvement, which is the highlight of this case. However, this case is a single-sample clinical case and lacks large sample support. In addition, this case lacked neurological data, no segmental demyelination changes, no reduction in myelinated nerve fibers, insignificant inflammatory response, demyelination and remyelination and other pathological evidence.

Conclusions

CIDP is uncommon in clinical practice, and it should be considered when there is chronic progression and remission of recurrence, mainly manifested as disarticulation, numbness and weakness of limbs, muscular atrophy, low muscle tension, disappearance of tendon reflex, hypocausia of gloves and socks, and sphincter dysfunction. The nerve conduction velocity and CSF examination should be improved in time for clinical diagnosis. A neuropathological examination is also needed for the diagnosis. When combined with abdominal distension and liver damage, AIH should also be considered. Timely treatment can relieve symptoms, improve liver function and pathological tissue abnormalities, and slow the progression to liver fibrosis.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Informed Consent

At the time of the retrospective analysis carried out here, we no longer had access to the patient.

Author Contributions

YB, YYD, RA and DYZX: data collection; YB, YYD and XDL: data analysis; YB and YYD: manuscript preparation; YB and GJL: reviewing of manuscript.

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