Case Report

Three Cases of Recurrent Generalized Muscle Spasms in China

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Three cases of recurrent generalized muscle spasms were reported. All three cases are of Chinese descent and show some typical features of recurrent painful muscle cramps, alopecia, diarrhea and abnormalities of bone and endocrine systems. Recurrent generalized muscle spasms or Satoyoshi's disease is recognized as an entity of the disease not only in Japan but also in China. The result that one of the three cases is associated with myasthenia gravis might suggest an immunological abnormality as a mechanism of the disease.

Key Words: Muscle cramp, Alopecia, Diarrhea, Myasthenia gravis, Bone deformity, Mucosal atrophy, Reduced IgG

Eijiro Satoyoshi first described a syndrome of progressive muscle spasms, alopecia, diarrhea and retarded growth in 1963.¹⁾ Since then, over about twenty years, twenty cases (17 Japanese, 1 Chinese, 1 English and 1 Dutch) have been reported in the literature.

In this communication we present three cases of Chinese descent, showing some typical features of recurrent painful muscle spasms in isolated muscle or groups of muscles, associated with abnormalities of multi-systems, which included bone, gastrointestinal and endocrine systems, and an autoimmunological defect. In one of our cases the disease is associated with myasthenia gravis.

CASE REPORTS

Case 1 — A 17-year-old girl was admitted to our hospital in August 1982. Her chief complaint was recurrent generalized painful muscle spasms that had been experienced for four years. Birth and early development were normal until age 13. She developed severe painful cramps for the first time in right calf muscle in the summer of 1978. Several days later, the same occurred in the

left calf muscle. After that, the frequency of muscle cramps gradually increased day-by-day. The attack spread to almost the whole muscles of the legs, abdomen and arms. These cramps were usually limited to individual muscle, or a portion thereof. About one year later, intermittent painful cramps developed throughout the whole body. One year prior to her admission, due to severe pain in muscles, including unilateral or bilateral temporal and masseter muscles, she bit her tongue. The painful muscle spasms were precipitated by other factors which included exposure to cold, fatigue and emotional stress. Relief was usually obtained after mild massage. There was no loss of consciousness or urinary or fecal incontinence during attacks. Diarrhea and frequent defecation soon developed and were intermittently persistent. They occurred after spasms for a half year. After diarrhea appeared, she began to lose hair and eyebrows. The menarche had not appeared. Her growth and development were delayed after the illness.

Her past and family history were unremarkable.

General examination — She was of short stature (154 cm) and weighed 36 kg. Her face

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was anemic. Vital signs were normal. Her hair and eyebrows were thin. There was little axillary hair. Pubic hair was absent. Breasts were undeveloped. Heart and lungs were normal. The span of the extremities was proportional to the trunk height. There were no marked deformities of her major joints, which included both wrists and ankles, and there was no pes planus. Gynecological consultation was requested because of amenorrhea and it revealed only hypoplasia of the uterus (vestigial uterus).

Neurological examination — She was alert. Her intelligence was normal. The sensory system was intact. There was generalized slight muscle wasting. Slight winging of the scapulae was noted. Muscle strength in upper and lower limbs was normal and muscle tone was somewhat lower than normal. The deep tendon reflexes in lower limbs were sluggish, but those in upper limbs were normal. The planter responses were flexor.

Laboratory Data — Routine studies on blood, urine, stool and CSF were unremarkable other than slight microcytic anemia (Hgb. 11.8 gm) with a normal white blood count and differentials. Serum potassium was 4.89 mEq/L, sodium 138 mEq/L, calcium 8.6 mg%, and phosphorus 3.7 mg%. Urinary excretion of calcium and phosphorus during a 24-hour period were 4.0 to 5.4 mg% and 38 mg%, respectively. Serum GPT, LDH and CPK were normal. T_3 and T_4 were 190 ng/ml and 55 ng/ml, respectively. Blood creatine and creatinine were 3.6 mg% and 2.6 mg%, respectively. Repeated determination of fasting blood sugar revealed a range of 79.2 mg% to 81 mg%. An oral glucose tolerance test with 100 gm of glucose was performed and it revealed a relatively flat curve with a peak of blood sugar of up to 128.6 mg% one and half hours after the meal. Two hours after the meal, blood sugar was 104.8 mg% (Fig. 1).

Blood lactate was measured prior to and after ischemic exercise. The lactate content of the blood after ischemic exercise was five times that before. A radioimmunoassay showed myoglobin of less than 50 ng% (normally less than 80 ng%).

X-ray films of the chest and skull were normal. X-ray films of both knees showed clearing and widening of the epiphyseal line and a lower density

Fig. 1. Oral glucose tolerance test.

Fig. 2.

area in the proximal portion of the right fibula (Fig. 2).

EMG was performed with concentric needle electrodes in the right temporal, deltoid and abductor pollicis muscles. All the insertional activity was prolonged and showed multi-phasic fasciculations at rest. During voluntary contraction, the interference pattern was well developed, its amplitude being 0.4 to 1.5 mV. The conduction

velocity of the right tibial nerve was 33.9 m/s, with an amplitude of 11 mV. The latency of the right ankle to abductor hallucis muscle was 4.7 m/s with an amplitude of 5 mV.

EEG and ECG were both normal.

During hospitalization, carbamazepine, phenobarbital, quinine sulfate and chlorpromazine were given, but they were not effective for the spasms. The patient was discharged and followed-up for 2 years.

Case 2 — A 20-year-old male worker was admitted to our hospital with the chief complaints of loss of hair for 3 years and recurrent painful muscle spasms for 2 years. His parents and six siblings were in good health. There was no family history of neurological diseases. Birth, early and juvenile development were all normal. At the age of 17, he started to gradually lose his hair, eyebrows and eyelashes. One year later, he developed painful muscle cramps, which involved the muscles of the limbs and trunk. These cramps occurred in discrete groups of muscles and the location was uncertain. The painful muscle spasms were precipitated by some factors including exposure to cold, physical effort and emotional stimulation. The spasms were sufficiently intense to produce displacement and fixation of the limbs. During sustained contraction, the muscle became board-like to the touch and bulged prominently. Relief was best obtained by mild massage. He had experienced no diarrhea or frequent defecation.

Examination — His stature (160 cm) and weight (55 kg) were moderate. Vital signs were normal. There were no cataracts in both eyes. His hair was very delicate. Eyebrows, eyelashes, beard, axillary hair and pubic hair were all absent. Heart and lungs were normal. The cranial nerves and sensory system were intact. The general musculature was relatively well-developed, but the temporal muscle was thinner. Muscle strength and tone were within normal limits. During voluntary contraction, the muscles became board-like to palpation, and bulged prominently. There were no deformities of joints and no pes planus. Urological consultation revealed no abnormalities of the testicles.

Laboratory Data — Routine studies on blood,

urine and stool were normal. Serum potassium was 4.37 mEq/L, sodium 136 mEq/L, calcium 10 mg%, and phosphorus 4.87 mg%. Serum GPT, LDH and CPK were within normal limits. Repeated determination of fasting blood sugar revealed a range of 100 to 125 mg%. An oral glucose tolerance test with 100 gm of glucose revealed a relatively normal curve (Fig. 1).

Barium-meal fluoroscopy of the gastrointestinal tract was normal except that the mobility of the small intestine was slightly lagging.

Case 3 — A 16-year-old girl was admitted to our hospital on Sept. 1983, complaining of loss of hair, painful muscle cramps for 7 years, and easy fatigability and ptosis of the eyelids for 3 years. Her birth and development were normal. At age 9, painful muscle cramps began in her calf, hand and foot muscles, which were precipitated by voluntary effort. She gradually developed deformities of both knees. She had no history of diarrhea. At age 15, muscle spasms decreased for no obvious reason, meanwhile she began to develop easy fatigability, ptosis of both upper lids and felt diplopia. These symptoms usually appeared in the evening and disappeared on sleeping. Then she was referred to some hospitals and a diagnosis of myasthenia gravis was made on the basis of a positive neostigmine test. The menarche appeared at age 16, but after only 2 times there was no subsequent menstruation. Her family history was unremarkable.

On examination, she was short-statured (138 cm) and weighed 34 kg (Fig. 3). There was frontal baldness, no axillary or pubic hair and the eyebrows were scanty (Fig. 4). Liver and spleen were not palpable. There was hypoplasia of the mammary glands and uterus, and bilaterally short legs with deformities of the knee joints (Fig. 5). Neurological examination was normal except for bilateral ptosis of eyelids.

Laboratory studies — Routine blood analysis was normal. The oral glucose tolerance test curve was flat (Fig. 1). EMG was consistent with myasthenia gravis. On muscle biopsy, nuclei of muscle cells were found to be increased in number and muscle showed a diffuse reduction of fiber diameter with infiltration of lymphocytes. X-ray film of the knee joints demonstrated widening

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

of the epiphyseal line (Fig. 6). On fibrogastroscopy, mucosal atrophy of the stomach and duodenum were observed. A fungoid lesion of 0.3 mm diameter was seen on the mucosal surface of the stomach.

From the above results a diagnosis of Satoyoshi's disease complicating myasthenia gravis was made. She was treated with neostigmine and Chinese traditional medicine and 8 months after discharge her condition was still stable.

DISCUSSION

In the literature, twenty cases of a peculiar syndrome of "recurrent generalized muscle spasms" have been reported, all in Japan^{2,3} ex-

cept for a case each from England³) and Holland⁴), since the first report by Satoyoshi et al. in 1963. Our cases of this syndrome are reported in this paper. It is concluded that "recurrent generalized muscle spasms" or Satoyoshi's disease occurs as a clinical entity not only in Japan but also in China. In this connection, it should be noted that one of the two cases reported by Satoyoshi was a Chinese²).

These cases consist of two female and one male. Their ages of onset were 13, 17 and 9 years, respectively. The first symptoms in cases 2 and 3 were alopecia which tended to be alopecia universalis. Case 1 also showed alopecia, although her symptom of onset was muscle spasms.

Diarrhea was not the first symptom in our cases. It was noted only in Case 1, and was slight and of short duration. The 2 female patients suffered from amenorrhea. Gynecological examination revealed only hypoplasia of the uterus. All of the three cases showed retarded growth. In brief, the characteristics of the clinical pictures of these cases were consistent with the syndrome of recurrent generalized muscle spasms (Table 1).

In laboratory studies, although only Case 3 showed severe deformities of both knees, X-ray films of both knee joints in Case 1 and 3 showed widening of the epiphyseal lines. Oral glucose tolerance tests demonstrated a relatively flat curve in all of the three cases. Blood lactate

Table 1. The clinical pictures of Satoyoshi's disease in 23 cases

Case No.	1	2	3	4	5	6	7	8	9	10	11
Sex	F	M	F	F	F	F	M	F	F	M	M
Age at onset	9	9	13	13	10	15	7	11	8	9	8
First symptom	S	SA	SD	SA	SA	S	A	S	SA	SA	SA
Severity of spasms	+++	+++	++	++	++	++	+++	++	+++	++	++
Diarrhea (severity)	++	+	+++	—	—	+	+	±	++	++	—
Age at onset	12	9	14			16	16		10	9	
Alpecia (severity)	+	+++	++	+++	+++	+++	+++	±	+++	+++	±
Age at onset	10	10	14	17	10	16	7	8	8	9	8
Amenorrhea (severity)	+		+	+	+	+		±	+		
Age at onset			14	14		17		16			
Deformity of joints	+++	+++	±	—	—	++	+++	+	+++	+++	±
Age at onset	11	13				13	10		14		
Growth retardation	+++	+++	—	±	±	+	+++	—	+++	+++	—
Age at death	27		29	19	15					19	
Complication	—	—	—	SLE	—	—	Trauma	Tb	Nephritis	—	—

(1) Nos. 1 to 19 (Satoyoshi, E., et al.). No. 2 is a Chinese.
(2) No. 20 (Keyser).
(3) Nos. 21 to 23 (This series).

after determined ischemic exercise was within normal range, and there was no other evidence of glycogen storage disease. So, it seemed that not McArdle's disease.

On fibrogastroscopy, a fungoid lesion in addition to mucosal atrophy of the stomach and duodenum was found in Case 3, and pathological studies showed no cystic polyps but only an inflammatory change.

To date, the etiology of this syndrome has remained unknown. Satoyoshi suggested that chronic malabsorption was a prime cause since his autopsied patients demonstrated marked changes of the gastrointestinal tract. In our cases, however, the changes of the gastrointestinal tract were unremarkable, although barium-meal examination of the whole digestine tract was performed in

Cases 2 and 3, and fibrogastroscopy was performed in Case 3 and in another case suspected of having this syndrome.

A case of this syndrome with a reduced IgG content in serum was reported elsewhere.⁵⁾ The authors considered that the case showed a marked reduction in IgG content in serum which is usually seen in myotonic dystrophy. The syndrome of "recurrent generalized muscle cramps" and myotonic dystrophy share the same features such as hair loss, amenorrhea and abnormal carbohydrate metabolism. Such conditions may suggest that some relationship might exist between these two diseases etiologically and pathogenetically. Unfortunately, examination of immunoglobulins in serum was not performed in our series. In another case who mimicked this syndrome, the albumin, α_1 -, α_2 -, β - and γ -globulin, IgG, IgA and IgM contents in serum were all within normal limits.

It is suggested that there is a relationship with

12	13	14	15	16	17	18	19	20	21	22	23
F	F	F	F	F	F	M	F	N	F	N	F
15	10	11	12	14	12	15	19	10	13	17	9
SA	S	SA	SA		S		A	S	S	A	A
++	++	++	+	++	+++	++	+	+++	++	+++	++
±	+	-	-	++	-	-	+	++	+	-	-
	23						21	11	13		
+++	+	++	+++	+++	+	++	+++	+	+++	+++	+++
10	18	11	16	14	12	12	21	11	13	18	9
+	+		+	+	+				+		+
16	16		16	16	18				13		16
-	-	+++	±	-	-	-	-	-	±	-	+++
		12									
-	+	+	+	-	-	-	-	+	+++	±	+++
-	Tb	-	-	-	-	-	MG				MG

some autoimmune defects. Case 3 in this series presented both recurrent generalized muscle cramps and myasthenia gravis. At present, as far as we know, this might be the second reported case in the literature.⁶⁾ These two diseases share the same features too, which can be associated with autoimmune disease somehow. This phenomenon lead us to suggest that a relationship with immune defects may exist between the two disease entities etiologically, but the exact role of the autoimmune mechanism is still unclear, so this problem deserves further studies in the future.

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