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CASE REPORT

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Progressive facial hemiatrophy complicated by sclerodactyly, Raynaud's phenomenon, anti-ribonucleoprotein antibody, and trigeminal nerve disturbance

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Abstract A Japanese woman was diagnosed as having progressive facial hemiatrophy when she was 26 years old. After 30 years, Raynaud's phenomenon and sclerodactyly suddenly appeared; at the same time, positive rheumatoid factor and anti-ribonucleoprotein (anti-RNP) antibody were noted on serological examinations. When she was 60 years old, trigeminal nerve disturbance also appeared. The associations between progressive facial hemiatrophy, systemic scleroderma, and trigeminal nerve disturbance are interesting and should be discussed.

Key words Anti-ribonucleoprotein (anti-RNP) antibody · Progressive facial hemiatrophy · Raynaud's phenomenon · Sclerodactyly · Trigeminal nerve disturbance

Introduction

Progressive facial hemiatrophy or Parry–Romberg syndrome is a rare disease of unknown etiology.[1,2] However, this rare disease is sometimes complicated by various connective tissue diseases.[3–16] We have been following up a female patient for 40 years who had been diagnosed as having progressive facial hemiatrophy when she was 26 years old, which was later complicated by sclerodactyly, Raynaud's phenomenon, anti-ribonucleoprotein (anti-RNP) antibody, and trigeminal nerve disturbance. Here, we report the case of this patient and discuss the associations between progressive facial hemiatrophy, systemic scleroderma, and trigeminal nerve disturbance.

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Case report

A 26-year-old Japanese woman noticed left-sided facial atrophy in 1962. She visited a dermatologist, and was diagnosed as having "sclerodermie en coup de sabre" by skin biopsy. She visited the department of neurology of our hospital at the age of 28, and was clinically diagnosed as having progressive facial hemiatrophy or Parry–Romberg syndrome. She received oral anabolic steroid therapy, and the progression of facial atrophy was stopped for a few years. At the age of 37 she stopped visiting our hospital. However, when she was 40 years old, right-sided facial atrophy appeared, so she visited our hospital again. At that time, her erythrocyte sedimentation rate (ESR) was normal and rheumatoid factor and anti-nuclear antibody were negative. She received topical steroid ointment therapy, and the progression of facial atrophy stopped again for the next few years. Her condition remained stable for more than 10 years.

In the autumn of 1992, when she was 56 years old, she suddenly suffered from Raynaud's phenomenon, sclerodactyly, and arthralgia of bilateral wrists and fingers. She was introduced to the Department of Rheumatology by a neurologist. Physical examination revealed bilateral facial atrophy with enophthalmos, which was dominant on the left side (Fig. 1). Sclerodactyly was noted in both hands, but no proximal scleroderma and digital pitting scars were noted. The joints of her fingers and wrists were symmetrically swollen and painful; however, no destructive changes of bones and cartilage were observed on roentgenograms. Her respiratory sounds and chest X-rays were normal. She did not complain of swallowing disturbance. No neurological abnormalities were found. As shown in Table 1, no abnormal findings were detected through routine laboratory tests, including hematology, blood chemistry, and urinalysis. However, serological examinations revealed a high ESR (34 mm in the first hour) and marked hypergammaglobulinemia. Her serum immunoglobulin G level was 3609 mg/dl. The anti-nuclear antibody (ANA), anti-RNP antibody, and rheumatoid factor were positive. Her ANA showed a

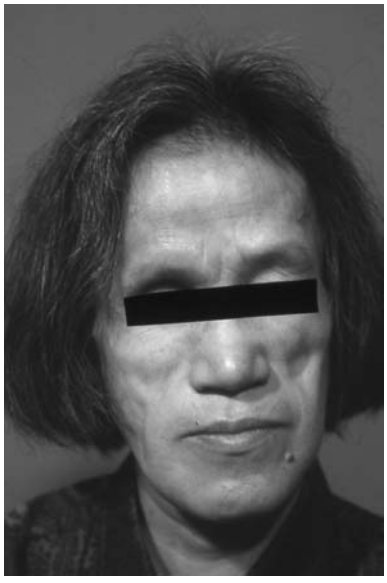

Fig. 1. Portrait photograph of the face of the patient. Marked bilateral facial atrophy was observed

Table 1. Laboratory findings

Hematology	
WBC	7100/μl
Hemoglobin	12.8 g/dl
Platelet	25.2×10^4/μl
Blood chemistry	
Total protein	8.7 g/dl
Albumin	3.8 g/dl
AST	24 IU/l
ALT	15 IU/l
γGTP	45 IU/l
BUN	11 mg/dl
Creatinine	0.8 mg/dl
Na	140 mEq/l
K	3.8 mEq/l
Cl	103 mEq/l
CK	81 IU/l
Serology	
CRP	<0.3 mg/dl
ESR	34 mm/h
IgA	462 mg/dl
IgG	3609 mg/dl
IgM	181 mg/dl
Rheumatoid factor	36 IU
Anti-nuclear antibody	2560× (speckled)
Anti-SS-A antibody	(−)
Anti-SS-B antibody	(−)
Anti-Scl-70 antibody	(−)
Anti-centromere antibody	(−)
Anti-U1-RNP antibody	(+)
Anti-Sm antibody	(−)
Anti-Jo-1 antibody	(−)
Urinalysis	
Protein	(−)
Occult blood	(−)
Casts	(−)

WBC, white blood cells; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γGTP, gamma-glutamyltranspeptidase; BUN, blood urea nitrogen; CK, creatine phosphokinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Ig, immunoglobulin

speckled pattern and its titer was high (2560-fold). Anti-SS-A, anti-SS-B, anti-Scl-70, anti-centromere, anti-Sm, and anti-Jo-1 antibodies were all negative. She was treated with a low dose of prednisolone (10 mg/day), and her arthralgia was immediately improved. Prednisolone dose was tapered to 5 mg/day. Raynaud's phenomenon was markedly improved by the oral administration of prostacycline derivatives.

Sclerosis of the skin had not progressed until she was 60 years old, at which time she suffered from right-sided facial and oral dysesthesia. The distribution of dysesthesia was consistent with the lesion of the second branch of the right trigeminal nerve. Computed tomography of the brain did not disclose any intracranial abnormalities besides the marked atrophy of subcutaneous tissue. The dysesthesia was improved by treatment with a low dose of carbamazepine (100 mg/day). She has now been visiting our hospital regularly for almost 40 years.

Discussion

Progressive facial hemiatrophy or Parry–Romberg syndrome is a rare disease characterized by slowly progressive atrophy of one side of the face, caused by the loss of subcutaneous fat and connective tissues. Owing to its remarkable physical features and various complications, many neurologists, dermatologists, ophthalmologists, and plastic surgeons have paid considerable attention to this unique disease. However, the etiology of progressive facial hemiatrophy remains controversial. The neurogenic theory had been proposed by Archambault[1] and Wartenberg,[2] who have published extensive and representative reviews of progressive facial hemiatrophy in the first half of the twentieth century. They emphasized that progressive facial atrophy is caused by imbalance in the autonomic nervous system, that is, the hyperstimulation of the sympathetic nerve causes the loss of subcutaneous fat and connective tissues, which leads to facial atrophy. This sympathetic nerve theory was later supported by experiment in rats.[17] Indeed, certain patients with progressive facial hemiatrophy exhibit symptoms of sympathetic nerves such as Horner's syndrome. Moreover, a recent detailed study has revealed frequent involvement of the central nervous system in progressive facial atrophy.[18,19] However, our patient did not exhibit neurological symptoms other than trigeminal nerve disturbance, which occurred many years after facial hemiatrophy had appeared, and no intracranial abnormalities were revealed by computed tomography.

On the other hand, progressive facial hemiatrophy is often complicated by various connective tissue diseases. In such complications, the coexistence of progressive facial hemiatrophy and localized scleroderma was most frequently reported.[3–9] The coexistence of progressive facial hemiatrophy and systemic scleroderma was also reported.[10,11] The close association between progressive facial hemiatrophy and scleroderma was supported by results of biochemical analyses of collagen and glycosaminoglycans

of the skin from patients with progressive facial hemiatrophy.[20] Dermatan sulfate/hyaluronic acid ratios were elevated in skin from patients with progressive facial hemiatrophy, which was consistent with findings in patients with morphea or systemic scleroderma. Moreover, other connective tissue diseases, such as rheumatoid arthritis,[10,12] systemic lupus erythematosus,[10,13,14] lupus profundus,[15] and cutaneous vasculitis,[16] were reported to be complicated by progressive facial hemiatrophy. Thus, certain cases of progressive facial hemiatrophy seem to have close associations with connective tissue diseases.

Our case was initially diagnosed as "sclerodermie en coup de sabre," which is a subtype of linear scleroderma, by skin biopsy. Thus, the facial atrophy in our patient seems to be closely related to scleroderma, although the association and difference between progressive facial atrophy and sclerodermie en coup de sabre should be delineated more clearly.[18,19] This viewpoint is strongly supported by the fact that our patient later presented sclerodactyly, Raynaud's phenomenon, and positive anti-RNP antibody, which suggested systemic scleroderma. The exact diagnosis of our patient might be difficult. Mixed connective tissue disease might be taken into consideration from the viewpoint of positive anti-RNP antibody. However, our patient showed no clinical symptoms suggesting systemic lupus erythematosus or polymyositis, so the diagnosis of a limited type of systemic scleroderma with positive anti-RNP antibody might be most appropriate.

Lastly, our patient also exhibited trigeminal nerve disturbance. Trigeminal nerve disturbance is sometimes observed in both progressive facial hemiatrophy[21] and systemic scleroderma.[22] The etiology of trigeminal nerve disturbance might be explained by the mechanical compression of the nerve in subcutaneous tissues, because the facial atrophy in our patient was extremely severe. However, autoimmune mechanisms such as angitis could not be excluded. Unfortunately, the detailed mechanism of trigeminal nerve disturbance was not disclosed, because our patient refused further examinations such as nerve biopsy. However, it should be noted that the anti-RNP antibody is associated with neurological manifestations in systemic scleroderma,[22] and that the anti-RNP antibody was positive in our patient.

In conclusion, we encountered a rare case of progressive facial hemiatrophy, later complicated by Raynaud's phenomenon, sclerodactyly, anti-RNP antibody, and trigeminal nerve disturbance. All physical and serological symptoms could be regarded as components or complications of scleroderma. Thus, patients with progressive facial hemiatrophy should also be examined serologically and carefully followed up for complications through connective tissue diseases, particularly scleroderma.

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