Concurrent Parry-Romberg Syndrome and Systemic Lupus Erythematosus

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Parry-Romberg syndrome is a rare disorder characterized by progressive hemifacial atrophy of the skin, adipose tissue, muscle, cartilage, and underlying bony structures. Although various autoantibodies such as antinuclear antibodies (ANA), rheumatoid factor (RF), and anti-single-stranded DNA antibodies are found in patients with Parry-Romberg syndrome, coexistence with systemic lupus erythematosus is rare. We report a Parry-Romberg syndrome patient with positive ANA and presence of anti-double-stranded DNA antibodies who then developed systemic lupus erythematosus. We emphasized a thorough physical examination and periodic immunological evaluation in patients with Parry-Romberg syndrome. The presence of ANA or RF in a patient of Parry-Romberg syndrome carries the risk of developing systemic collagen-vascular disorders. (Dermatol Sinica 23: 148-153, 2005)

Key words: Linear scleroderma, Parry-Romberg syndrome, Progressive hemifacial atrophy, Systemic lupus erythematosus

Parry-Romberg徵候群是一種罕見疾病，其特徵是進行性半面皮膚萎縮，而影響範圍包括皮膚、脂肪組織、肌肉、軟骨和骨骼構造。雖然在Parry-Romberg徵候群的病患可發現各種自體抗體存在，其中包括antinuclear antibodies (ANA), rheumatoid factor (RF)及anti-single-stranded DNA antibodies，但同時合併紅斑性狼瘡的病例則很罕見。我們報告一例Parry-Romberg徵候群病患，其ANA和anti-double-stranded DNA antibodies呈陽性反應，之後合併發生紅斑性狼瘡。我們在此強調：在Parry-Romberg徵候群的病患，應做完整的理學檢查及定期的免疫學方面之檢查。因爲該類病患檢查有ANA或RF抗體存在時，追蹤發現有可能發展形成系統性免疫疾病。(中華皮誌 23: 148-153, 2005)
INTRODUCTION

Parry-Romberg syndrome (PRS) is a rare disorder. Various autoantibodies, such as antinuclear antibodies (ANA) and rheumatoid factor (RF), are found in patients with PRS, thus supporting an immunologic basis for this disorder. We describe a case of PRS in a patient who subsequently presented with systemic lupus erythematosus (SLE). A review of the literature demonstrates the rare coexistence of these two disorders.

CASE REPORT

An 11-year-old boy visited our dermatologic department in August 1998. The initial presentation was three hypopigmented, indurated plaques on the right temporal area, cheek, and chin that had existed for nearly 1 year (Fig. 1). The initial diagnosis was morphea. Skin biopsy from the right temporal area revealed dermal thickening with hypocellular and hyalinized collagen bundles. The skin appendages were decreased, and patchy lymphoplasmacytic infiltrate in the reticular dermis was noted. There was no evidence of panniculitis or follicular plugging (Fig. 2). The pathology was consistent with morphea. The initial laboratory study revealed the presence of a normal hemogram. The ANA test was positive, and exhibited a speckled, nucleolar pattern at a titer of 1:320. The anti-U1RNP antibody was negative. However, there were no other symptoms and signs of SLE, such as other skin rash, photosensitivity, arthralgia, or oral ulcer. Under the impression of localized scleroderma, a topical steroid was given with no improvement. The patient subsequently received oral penicillamine and intermittent subcutaneous steroid injections for treatment. There was no obvious improvement. However, less depigmentation after subcutaneous steroid injection was noted.

After 5 months, intermittent arthralgia of both knees and wrists developed. Serological profiles were reassessed in November 1999. The ANA was positive with a homogenous pattern at a titer of 1:320; the anti-double-stranded DNA antibody (anti-ds DNA Ab) was positive at a titer of 1:640. The anti-Sjogren syndrome-A antibody (SS-A) was also positive. The RF was negative. The patient noted precordial pain 1 month later. Pericarditis with pericardial effusion was diagnosed via 2D echocardiography.

In January 2000 the patient was admitted for eyelid and scrotal edema. The hemogram showed anemia (Hb: 8.6 g/dl) and lymphocytopenia (lymphocyte: 960/mm³). In addition, proteinuria (1449 mg/day) was noted. Lupus nephritis class V was proved by the renal biopsy.
Arthritis of both knees with tenderness and swelling was also found.

Furthermore, the patient fulfilled at least four of the 11 criteria for SLE. Steroid pulse therapy was given for SLE followed by 10 courses of immunosuppressive therapy with cyclophosphamide (Endoxan 750mg) combined with oral steroids (Prednisolone 45mg initial dose and tapered gradually) and hydroxychloroquine (Plaquenil 100mg twice a day). The signs and symptoms of SLE were under control.

The patient’s family history was non-contributory. The patient had no history of photosensitivity, oral ulcers, alopecia, neurologic symptoms, dysphagia, or Raynaud’s phenomenon.

According to the dermatologist’s follow-up, right sided hemifacial atrophy became more obvious as the patient grew. The skin indurations gradually resolved with mild to moderate fat atrophy and hypo- and hyperpigmentation of the overlying skin (Fig. 3).

The final diagnosis of concurrent PRS and SLE was made in Feb, 2002. There were no ophthalmologic, neurological or dental abnormalities. Computed tomography of the head was performed with no obvious brain lesion or bone abnormalities, but a decrease in the soft tissue of the right side of the face was noted. Unfortunately, the patient was never studied for Borrelia burgdorferi infection. Presently, the patient has undergone regular follow-up in the pediatric department for SLE.

**DISCUSSION**

Parry-Romberg syndrome is classically described as a progressive hemifacial atrophy of the skin, adipose tissue, muscle, cartilage, and underlying bony structures. Although the syndrome was first described by Parry in 1825, it was Romberg who detailed the clinical findings and called the disease “trophoneurosis of the face” in 1846. In 1871, Eulenberg applied the more descriptive term of “progressive facial hemiatrophy”.

**Fig. 2**
(A) Dermal thickening with hypocellular and hyalinized collagen bundles. The skin appendages decreased and patchy inflammatory cell infiltrate in the reticular dermis. (H&E, x100). (B) Patchy lymphoplasmacytic infiltrate in the reticular dermis. (H&E, 400X)

**Fig. 3**
The pictures were taken when the boy was 17 years old. (A) Right sided hemifacial atrophy. (B) Mild to moderate fat atrophy and hypo- and hyperpigmentation of the overlying skin.
Parry-Romberg syndrome usually develops in the first and early second decades of life. The idiopathic onset and cessation are entirely spontaneous. The natural history of the disorder often involves an active progressive phase (2 to 10 years) and subsequent stability.\(^3\) The distribution of PRS generally follows the pattern of sensory innervation of one or all of the three trigeminal nerve dermatomes. Frequently, extensions may include the entire side of the face. The disorder has a female to male incidence of 3:2.\(^3\) The atrophy involving the skin and underlying tissues is not preceded by indurations. Occasionally, the atrophy is not confluent, but instead is limited to the areas previously affected by indurations.\(^2, 4\) The overlying skin can be a normal skin color or pigmented, but it is usually freely movable. The extent and degree of the skin discoloration is highly variable, and may have no correlation with the atrophic changes of the osseous and soft tissue.\(^3\)

Major complications of PRS include: (1) neurological abnormalities (10%), including seizures, muscle weakness episodes, facial nerve palsy, migraine headache, and trigeminal neuralgia;\(^3, 5\) (2) ophthalmological abnormalities (10%-35%), including exophthalmos, ptosis, and uveitis;\(^3, 6\) and (3) oral abnormalities (41%), including dental abnormalities, malocclusion, and tongue changes.\(^7\) In the study conducted by Jablonska and Blaszczyk, among their 58 cases of linear scleroderma of the face and scalp, 21 showed transformation into PRS, and in 8 patients, linear scleroderma was present at other sites.\(^8\) We can learn from this report that the most frequent connective tissue disease associated with PRS is localized scleroderma.\(^8\) Although the issue of PRS differing from linear scleroderma is still debated, most investigators consider PRS an involutionary linear scleroderma or deep variant of linear scleroderma.\(^4, 5, 7, 9\)

In the literature, two different kinds of pathological findings of PRS have been reported. One pathological finding is lipoatrophy with mild subcutaneous fibrosis in the patient with non-indurated depressions; the other is marked dermal fibrosis and disappearance of appen-

dices in the patient with indurated lesions.\(^2, 10\)

The pathogenesis of progressive hemifacial atrophy is unknown. From an immunological point of view, the exact incidence of serologic abnormalities in linear scleroderma and PRS is unknown. According to the literature, ANA has been detected in the serum of 15% to 66.7% of patients with linear scleroderma and 57% of patients with PRS. RF could be detected positively in 41% of patients with linear scleroderma and in 36% of patients with PRS.\(^1, 2, 11\) To our knowledge, serological abnormalities including the presence of ANA, RF, and anti-single-stranded DNA antibody have been previously well-documented in patients with localized scleroderma, especially linear scleroderma and generalized morphea.\(^1, 11-12\) The presence of anti-ds DNA Ab may give further evidence of the presence of widespread immunological abnormalities in localized scleroderma and its variants.\(^13\)

Localized scleroderma (including linear scleroderma) could coexist with connective tissue diseases such as SLE.\(^14-19\) However, the case report of concurrent PRS and SLE is relatively rare, as evidenced by only 3 cases disclosed in the literature.\(^14, 17-18\) According to the literature, it seems that rashes, arthritis, and nephritis were the most frequent clinical manifestations in patients with linear scleroderma and SLE.\(^17\) As the data shown from the literature, 40% of patients with linear scleroderma who had both ANA and RF also had collagen-vascular disorders. The authors suggested that patients with linear scleroderma may be at risk for developing systemic collagen-vascular diseases.\(^1\)

The acquired progressive hemifacial atrophy of PRS distinguish it from congenital hemifacial microsomia (first and second branchial arch syndrome), Saethre-Chotzen syndrome, Seckel syndrome, and 13q syndrome. Partial lipodystrophy is included in the differential diagnosis, but it is usually bilateral and involves primarily adipose tissue.\(^3, 6\)

In our case, several problems were encountered. The initial presentation of PRS was morphea-like plaques when he was 10
years old. As the disease progressed, the skin indurations gradually resolved with mild to moderate fat atrophy and hypo- and hyperpigmentation of the overlying skin. As previously prescribed, it was compatible with occasional clinical manifestations of non-confluent atrophy limited to the areas previously affected by indurations.2, 4

The second problem encountered was found upon review of the clinical picture of PRS, as noted by Moore et al.20 The restrictive influence of the abnormal soft tissue envelope (in early onset younger than 5 years old) at the time of accelerated growth of the middle and lower face undoubtedly compounds any primary skeletal growth disturbance, manifesting as maxillary and mandibular hypoplasia with shift of the lower facial midline to the involved side. In contrast, late onset soft tissue changes may be associated with minor notching or ridging of the underlying frontal bone, but no major changes in facial skeletal base bones are recorded. The authors suggest that the late onset of the disease in the presenting case might have limited the influence of the abnormal skeletal structure.20 It is the only possible reason why only mild to moderate hemifacial atrophy was noted in this patient.

The third dilemma is the absence of anti-U1RNP makes the diagnosis of mixed connective tissue disease unlikely. However, it seems that the disease in this patient took a rare course: it started in childhood as PRS and evolved into typical SLE one year later. One might ask how many patients with SLE initially have, or manifested at any time, scleroderma-tous skin changes or coexistence with PRS. In an extensive review of clinical manifestations of SLE, no patient with scleroderma-tous changes has been described.16 There is only one reported case of a patient with lupus profundus suffering from severe facial disfiguration and PRS, who also fulfilled at least four of the 11 criteria for SLE. However, the skin pathology was consistent with lupus profundus.21 The skin pathology of our patient revealed dermal thickening with hyalinized collagen bundles. Although the specimen is not deep enough to show the whole subcutaneous fat area, no obvious lobular panniculitis was noted in this field. For this reason, it is still considered as an entity of scleroderma rather than lupus erythematosus panniculitis in our patient. The best way to understand the cause of facial hemiatrophy is to perform another skin biopsy deep enough to the subcutaneous fat area. However, the patient refused to receive skin biopsy again.

The fourth dilemma encountered in our case is the treatment of PRS and SLE. Firstly, SLE should be treated, and regularly follow the clinical course of PRS. After the active progressive phase passes, augmentation of the atrophic areas or surgical correction may be performed if facial deformity is obvious.3

In summary, we report the case of an 11-year-old boy with PRS preceding the onset of SLE by 1 year. From this case, we learn that it is important to perform a thorough physical examination and immunological evaluations in patients with linear scleroderma. Because linear scleroderma or PRS patients with ANA or RF are at risk for developing systemic collagen-vascular disorders, long-term observation with periodic re-evaluation is appropriate in these cases with positive ANA or RF.1

REFERENCES