

# Parry-Romberg syndrome

## *Physical, clinical, and imaging features*

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### ABSTRACT

ضمور نصف الوجه التدرجي المعروف أيضاً باسم متلازمة Parry-Romberg (ضمور نصف الوجه المترقي) هو مكتسب، واضطراب تدريجي بطيء، تحدث أكثر لدى النساء، مما يؤثر في المقام الأول على جانب واحد من الوجه، وتتميز بضمور جانب واحد، وفقدان الجلد والأنسجة تحت الجلد في الوجه والعضلات، والعظام. تدخلت العين والأعصاب أمر شائع. المسببات المحتملة غير واضحة ودون أي علاج معروف. نبلغ عن حالة نادرة من متلازمة Parry-Romberg مع الميزات التقليدية. نناقش المظاهر السريرية، والنتائج الإشعاعية والتصويرية، والتشخيص التفريقي، وخيارات العلاج المتاحة في هذا التقرير.

Progressive hemifacial atrophy also known as Parry-Romberg syndrome is an acquired, slowly progressive disorder, occurring more in women, primarily affecting one side of the face, mainly characterized by unilateral atrophy, and loss of skin and subcutaneous tissues of face, muscles, and bones. Ocular and neurologic involvements are common. The possible etiology is unclear without any known cure. We report a rare case of Parry-Romberg syndrome with classical features. The clinical features, radiological imaging findings, differential diagnosis, and available treatment options are discussed in this report.

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Parry-Romberg syndrome (PRS), also named as progressive hemifacial atrophy is an acquired, sporadic neurocutaneous disorder that is mainly characterized by unilateral self-limited atrophy and loss

of skin and subcutaneous tissue of the face.<sup>1-5</sup> It was first reported by Parry, and then elaborated as a syndrome by Romberg.<sup>6,7</sup> It is a slowly progressive disorder, occurring more in women, primarily affecting one side of the face, including skin, subcutaneous tissue, muscles, cartilage, and bones.<sup>1-4,6</sup> The onset of this syndrome generally occurs in the first and second decades of life with skin changes resembling scleroderma, which is usually accompanied by this neurological effects of PRS, including seizures, migraine, trigeminal neuralgia and darkening of skin; partial seizures are the most common neurologic complication.<sup>2-4,8</sup> Ocular involvement is common, and the most frequent manifestation is enophthalmos.<sup>2-5,9</sup> Its origin is unclear without any known cure. Several possible causes have been postulated (encephalitis, trauma, scleroderma, vasculitis, migraine, infections, genetic and hereditary factors, autoimmunity, and so forth) but a multifactorial pathogenesis may be the first etiology.<sup>1-5,9</sup> Possible neuroimaging findings of PRS in CT and MR imaging are; atrophy of skin and subcutaneous tissue of face, intracranial calcifications, cerebral atrophy, deep and subcortical white matter lesions, encephalomalacia, hydrocephalus, meningeal, and leptomeningeal enhancement, aneurysms, cortical thickening and dysgenesis, infarctions in the corpus callosum, and so forth.<sup>1,5,10</sup> We describe a rare case of PRS with classical features, associated with alopecia, hyperpigmentation around the left globe and eyebrows, and unilateral asymmetric loss of subcutaneous fat in left lower leg. Our objective in presenting this particular case is to highlight the classical neurologic, skin and ocular findings of PRS with addition of subcutaneous fat loss in long extremities.

**Case Report.** A 48-year-old female with complaints of prominence of left forehead and asymmetric

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left-sided hemifacial atrophy, alopecia, asymmetric thinning of left lower leg, without any history of trauma, presented to the Dermatology Department of our hospital. She also had slight skin pigmentation over the left eyebrow and the left palpebral conjunctiva. Her symptoms started around 6 years ago with mild hemifacial atrophy on the left forehead, and progressed slowly with alopecia. The asymmetric thinning of her left lower leg had started around one year before. No facial motor and sensory deficits were noted physically with normal tongue movements, without any enophthalmus or ptosis of the left upper eyelid. Her neurologic and fundus examinations were both normal with normal psychomotor attitudes. The right face appeared completely normal. On physical examination, the left-sided facial and forehead asymmetry was detected mainly due to subcutaneous fatty loss with prominent bony ridges on the left forehead and left maxillary region. Intra and extraoral examination revealed normal physical yields without any atrophy of chewing muscles and/or tongue. Paranasal sinus x-ray examination also presented a normal frontal and maxillary sinus on the left side. There was asymmetric prominent subcutaneous fat and tissue loss in the left cruris region on inspection (Figures 1A & 1B, Figures 2A & 2B). She had several normal brain CT scans and electromyographic approaches during the first 6 years. Following consultation, she was admitted as inpatient admission to the Surgery Department, then referred to Egerad private medical imaging center for brain MRI. The brain MRI revealed asymmetric, prominent fatty loss in the dural and galeal parts of the left frontal region. No cortex or deep white matter involvement, including white matter hyperintensities-cortical atrophy was indicated (Figures 3A-C).

Laboratory results for a complete blood count and biochemistry revealed hemoglobin: 13.58 [normal value (NV): 12-16 g/dl], hematocrit: 41.3 [NV: 37-50 g/dl], mean corpuscular volume: 90.2 [NV: 80-99 g/dl], mean corpuscular hemoglobin 28.5 [NV: 33-37 g/dl], white blood count (4700 / $\mu$ lt [NV: 4800-10800/ $\mu$ lt], C-reactive protein 2.23 mg/dL [NV: 0-10 mg/dL], sedimentation 38/hour [NV: 0-20/hour], and mild thrombocytosis (430.000 g/dl) were indicated. Prothrombin time, and activated partial thromboplastin time were normal with negative hepatitis B surface antigen, anti hepatitis B surface antibodies, hepatitis C virus, and human immunodeficiency virus. The triiodothyronine - thyroxine - thyroid stimulating hormone levels were within normal range. Urine analysis was normal, CSF analysis showed mildly elevated protein (16 mg/dL; NV: 0-10 mg/dL), normal glucose and no pleocytosis. In the differential diagnosis, scleroderma or connective tissue disorders were considered, however, she had negative HLA-B27 with normal glucose and electrolyte levels in serum blood. Based on the clinical findings and history, a diagnosis of Parry-Romberg syndrome was made. Alloplastic aesthetic surgery with autologous fat injection to the atrophied left forehead was suggested to our patient by a plastic surgeon, but due to financial difficulties, she declined any surgical management. The treatment plan excluding the surgical management of our patient was physical and clinical follow-up in our research hospital; the follow up included physical rehabilitation including sports and exercise, use of a chin mask, and/or analgesic use.

**Discussion.** Parry-Romberg syndrome is an uncommon; rare pathology of poorly understood



**Figure 1** - An image showing: A) general physical appearance of the patient; and B) left sided facial hemiatrophy and left forehead prominence with bony ridges.

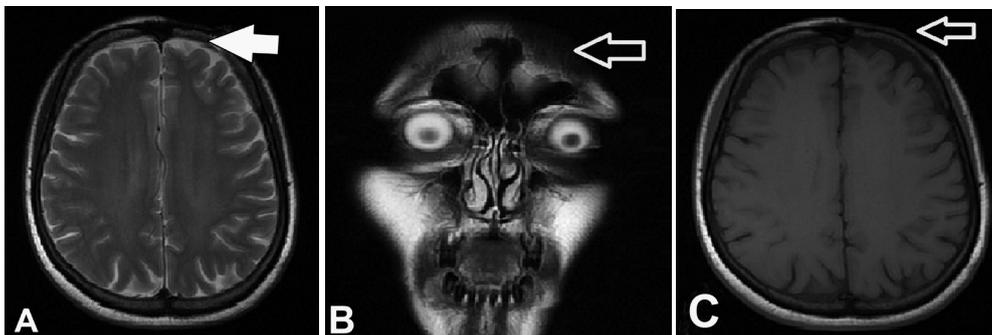
etiology. It is characterized by a slow progressive unilateral atrophy of the face, including skin-soft tissue, muscles and bones, which were present in our case.<sup>1-5,9</sup> The extension of the atrophy is frequently limited to one side of the face, and ipsilateral facial involvement is rare (10-20% of cases were reported bilaterally).<sup>2-5,8,9</sup> The early hemifacial asymmetry progresses over years to extreme loss of subcutaneous tissues, resulting in a sunken and wrinkled face on one side.<sup>5,8,9</sup> The incidence of PRS is not well-established, the average onset of disease is around 10 years of age; however, onset can be found as late as 40-50 years in some patients;<sup>8-10</sup> our patient was a 48-year-old female. The severity of PRS with late onset, including facial atrophy-asymmetry, neurological and ocular findings and so forth, may be less than PRS in younger ages, probably due to the complete development of craniofacial and nervous structures.<sup>5,8-10</sup> To date around 150 cases of PRS had been reported in the literature.<sup>1-10</sup> This syndrome is more prevalent in females without any precise geographical distribution. It mostly manifests on the left side of the face, and can occur in any members of the same family.<sup>1-5,8</sup> Characteristically, hemifacial atrophy is usually self-limited and stabilizes in most of the patients after 5-10

years duration.<sup>8-10</sup> Guerrerosantos et al<sup>10</sup> classified PRS into 4 types: Type 1 and 2 involve a decrease in the facial soft tissue, type 3 and 4 also involve thinning of soft tissue, as well as bone and cartilage atrophy. Type 1 is the mildest form, and type 4 is the most severe, and most serious form.<sup>10</sup> Our patient is considered to be type 3 due to thinning of the subcutaneous soft tissue in the left face and cruris region.

Electromyography, blink reflex, and trigeminal evoked potential abnormalities may indicate false implications through the brain stem as the etiology of the disease, and hyperactivity of the brain stem sympathetic centers, which may be caused by autoimmune processes, may lead to the cutaneous and subcutaneous atrophy in PRS.<sup>1,5,10</sup> Clinically, dry and hyperpigmented skin may be the first sign, also present in our patient, and in some cases, a demarcated line between normal and abnormal skin can be seen, known as the en coup de sabre that means “cut of the sword”, can also be shown in a localized form of scleroderma.<sup>1-3</sup> Ocular involvement is common, such as progressive enophthalmos, pseudoptosis, uveitis, pupillary disturbances, heterochromia, and restrictive strabismus. The most frequent ophthalmic manifestation



**Figure 2** - An image of the patient showing: A) asymmetric fatty loss and thinning of left lower leg; and B) non-homogenous alopecia.



**Figure 3** - An image showing: A) fatty loss of the scalp and galeal subcutaneous fatty tissue of the left frontal area, seen in T2 weighted (W) axial image; B) tissue loss of the scalp of the left frontal region, presented in T2W coronal image; and C) calvarial fat and soft tissue loss in left frontal side, shown in T1W axial image.

is enophthalmos due to loss of fat around the affected orbit, which was not observed in our patient.<sup>2-5,9</sup> Alopecia and thinning of the ear due to fat atrophy on the involved side are also frequent signs; alopecia was present in our case.<sup>1,9,10</sup>

Neurological complications of PRS are trigeminal neuralgia, facial paresthesia, migraine, and seizures. Epilepsy, especially contralateral epilepsy may also occur occasionally,<sup>5,10</sup> however, except for headache, other findings were not found in our patient. Atrophy of the tongue on the affected side, deviation of the mouth and nose to the affected side, atrophy of the upper lip leading to an exposition of teeth, small teeth with short roots on the involved side are the other important features of PRS, which were absent in our patient.<sup>8-10</sup> Although the pathophysiology of this disease is not well known, some authors have proposed that the primary cause is neurologic disturbance of fat metabolism, resulting from a trophic malformation of the cervical sympathetic nervous system.<sup>5,9,10</sup> Parry-Romberg syndrome may have strong correlation with autoimmune disorders, endocrine, and hereditary disturbances, scleroderma, and Rasmussen encephalitis.<sup>1,5,10</sup> Neuroimaging findings of PRS may be intracranial calcifications, cerebral and cerebellar atrophy, deep white matter lesions, encephalomalacia, heterogeneous meningeal enhancement and so forth.<sup>5,10</sup> The brain MR imaging of our patient showed asymmetric, prominent fatty loss in the dura and galea of the left frontal side without any deep white matter and cortical involvement of the cerebrum and cerebellum. There is no curative therapy for PRS and treatment options are limited, symptomatic treatment including pain relief, anticonvulsant drugs, and reconstructive surgery are the main management modalities; steroid and immunosuppressive therapy have also been tried in some cases.<sup>3,10</sup> Surgical treatment is usually based on the reposition of fat on the atrophied side, autogenous fat and cartilage grafts, silicon injections and prostheses, bovine collagen and inorganic implants are the alternatives of aesthetic surgical correction of fatty atrophy.<sup>3,9,10</sup>

Our case had left face asymmetry with slight left facial hemiatrophy, a prominent left forehead with bony ridges due to subcutaneous fatty tissue loss, slight pigmentation over the left eyebrow and conjunctiva, and alopecia, which are the classical features of PRS in previous reports.<sup>1-10</sup> She had normal neurologic and ocular findings, with normal psychomotor functions, and brain MRI revealed an asymmetric fatty loss in the left frontal side without any cortex or deep white matter involvement. She also had subcutaneous fatty loss in the left lower leg, resulting in an asymmetric thinning of the left cruris, which on literature review, is a previously unknown feature of PRS.<sup>1-10</sup>

Due to the non-existence of a precise cure, affected patients should be managed by a multidisciplinary team of physicians, surgeons, dentists, and psychologists to alleviate all possible difficulties related to PRS. Fat and dermis grafts are the most appropriate for type 1 and 2 PRS, whereas panfacial volumization with autologous fat-cartilage and bone graft-galeal flap injection is an excellent tool for replacing volume and restoring contour to the aging face in type 3 and 4 PRS.<sup>3,10</sup> Alloplastic aesthetic surgical implantation with lipoinjection was suggested for our patient, but she declined.

In conclusion, PRS is a rare disease that manifests with facial hemiatrophy and subcutaneous fatty loss on the affected side; its pathophysiology remains unknown. No definite curative treatment exists for PRS, and the most widely available treatment approach is based upon plastic aesthetic surgery.

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