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Case Report

Late-onset Parry-Romberg Syndrome with atypical neurological manifestations: A case report ☆,☆☆

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ABSTRACT

Parry-Romberg Syndrome (PRS) is a rare neurocutaneous disorder characterized by gradual facial hemiatrophy. We present a case study of a 64-year-old woman with late-onset PRS and linear scleroderma. The patient exhibited atypical PRS symptoms including leg numbness, hyper-reflexia, trigeminal neuralgia, and severe headaches. Diagnostic evaluations revealed chronic left-sided cerebral infarction, microhemorrhages, and nerve involvement. Treatment options for PRS are limited and aim to manage symptoms. This case highlights the diagnostic challenges of late-onset PRS, emphasizing interdisciplinary approach. Further research and improved therapies are essential for better patient outcomes.

Introduction

Parry-Romberg Syndrome (PRS), also known as progressive facial hemiatrophy, is a rare neurocutaneous disorder characterized by progressive atrophy of soft tissues on one side of the face [1]. PRS was first described by Parry (1825) and Rhomberg (1846). PRS typically involves unilateral facial changes, although rare bilateral cases have been documented [2]. Progressive facial tissue atrophy leads to functional impairments and significant cosmetic concerns, greatly impacting patient quality of life [3].

Onset is usually in childhood or adolescence. PRS predominantly affects the skin, subcutaneous fat, muscles, and bones

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on the involved side [4]. In this report we present a patient with late-onset PRS with written informed consent. The exact pathogenesis of PRS remains unknown. Etiology appears multifactorial with proposed origins including trauma, infection, vascular malformation, autoimmunity, fat metabolism abnormalities, and sympathetic dysfunction [5]. Some PRS cases demonstrate central nervous system (CNS) involvement with neurological manifestations like focal epilepsy, migraine, and the presence of unilateral brain lesions on the same side as the facial atrophy [6]. Characteristic neuroimaging findings can include intracranial calcifications on CT and white matter hyperintensities on MRI [7].

This case report aims to provide a detailed analysis of a 64-year-old woman diagnosed with late-onset PRS by focusing on the clinical presentation, diagnostic evaluation, treatment options, and outcomes. By examining the specific features of this case and comparing them with the existing literature, we aim to contribute to the growing body of knowledge on PRS, facilitating accurate diagnosis, optimal management strategies, and improved patient outcomes.

Clinical presentation

The patient is a 64-year-old woman with a history of linear scleroderma, migraine headaches, and left facial hemiatrophy presenting with worsening neurological symptoms. The patient's symptoms began in her late teens with episodic migraine headaches characterized by auras, nausea, and pain requiring medications for relief. She also had a long-standing history of left leg numbness described as nonradiating, constant, and mild to moderate in intensity with no alleviating factors. This had been present since 2020.

More recently, the patient developed worsening left-sided headaches of increasing severity as well as new-onset trigeminal neuralgia affecting the left side of her face. She described a throbbing, pressure-like pain in the left facial region. Physical exam showed signs of left facial hemiatrophy which is a hallmark of PRS and distinguishes it from other facial asymmetry conditions [8], but no other cranial nerve deficits. There was hyper-reflexia of the right extremities and decreased sensation to light touch, vibration, and proprioception in the left lower extremity.

Diagnostic workup

Lab studies

The patient underwent a comprehensive laboratory evaluation including complete blood count (CBC), comprehensive metabolic panel (CMP), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and creatine kinase (CK). All results were within normal limits and did not indicate any significant abnormalities.

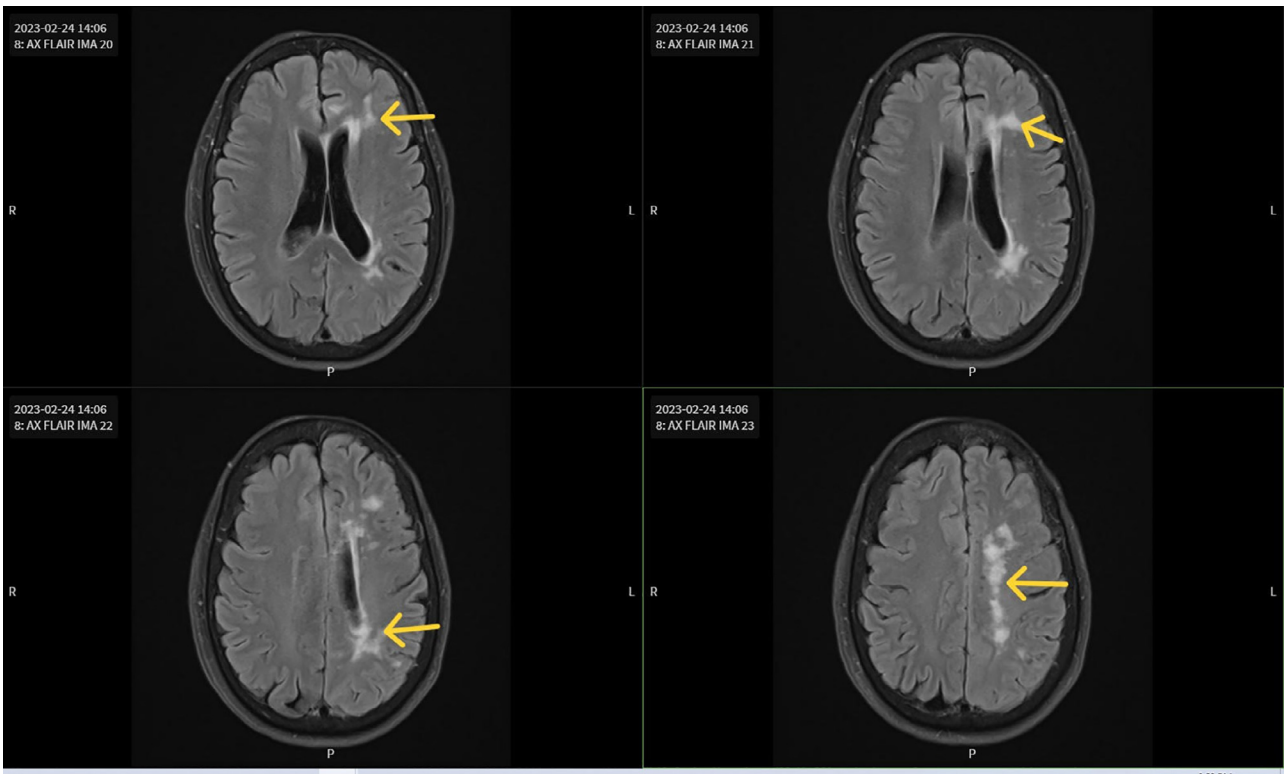

Fig. 1. – 64-year-old female with PRS. FINDINGS: Axial FLAIR MRI shows increased T2 signal within the left frontal white matter. TECHNIQUE: MRI performed at 1.5T with 5 mm slice thickness. Axial FLAIR: TR 6000 ms, TE 120 ms.

Neuroimaging

Initial brain magnetic resonance imaging (MRI), in July 2022, demonstrated a chronic left-sided watershed infarction between the middle cerebral artery (MCA) and anterior cerebral artery (ACA) territories, accompanied by punctate foci of old hemorrhage, indicating possible small vessel disease. MRA was relatively unremarkable.

Due to worsening headaches, the patient underwent a follow-up brain MRI on February 24, 2023, which included T1-weighted, T2-weighted, FLAIR, SWI, and postcontrast T1-weighted sequences. The MRI revealed asymmetric T2/FLAIR hyperintensities in the left frontal and left parieto-occipital white matter regions, particularly in the left frontal subcortical white matter lesions involving the anterior cerebral artery/middle cerebral artery watershed zone. Additional lesions were centered in the parasagittal area, and subtle T2/FLAIR hyperintensity was observed in the left temporal lobe (Fig. 1). Susceptibility weighted imaging (SWI) demonstrated numerous chronic microhemorrhages clustered within the left cerebral hemisphere, particularly in the left frontal, parietal, and occipital lobes which appeared as punctate foci without evidence of blooming or associated calcification on CT. Additional left hemispheric changes showed mild volume loss with ex vacuo dilation of the left lateral ventricle. Reduced sulcation over the left frontoparietal convexity was evident. Left eye enophthalmos, increased facial soft tissue and bony changes were compatible with the patient's history of left-sided Romberg syndrome status post facial reconstruction (Fig. 2).

MRI of the cervical spine (C-spine) was obtained to assess for hyperreflexia. This MRI revealed central disc bulges at the C4-C5 and C5-C6 levels that could potentially contribute to radiculopathy. Additionally, thoracic and lumbar spine MRIs were conducted in response to the patient's complaint of left leg numbness. No acute abnormalities were detected in these scans, ruling out spinal cord pathology as a cause of the symptoms.

To further assess the left leg numbness and evaluate for peripheral nerve issues, an MRI of the tibia and fibula was ordered. This MRI revealed hyperintensity and enlargement of the tibial nerve.

Neurophysiological testing

An electroencephalogram (EEG) was obtained to assess the patient's headaches and exclude the possibility of seizure activity. EEG results showed a normal routine EEG; however, there was a suggestion of asymmetry in the amplitude of the posterior dominant rhythm. This could imply potential cortical involvement or functional asymmetry in the brain's electrical activity. Lastly, an EMG/NCS (electromyography and nerve conduction study) was conducted to rule out any peripheral neuropathy. The EMG/NCS confirmed the presence of left sciatic neuropathy, indicating this as the likely cause of the left leg numbness symptoms.

Despite an extensive diagnostic workup, the underlying cause of the peripheral nerve pathology remains unclear. However, the critical diagnostic features including left hemispheric small vessel disease, peripheral nerve injury, and autoimmune abnormalities point towards PRS as the likely unifying diagnosis explaining this patient's constellation of neurological signs and symptoms. Further research into the complex pathogenic mechanisms, especially the autoimmune processes, is warranted to fully elucidate the disease mechanisms underlying this challenging syndrome.

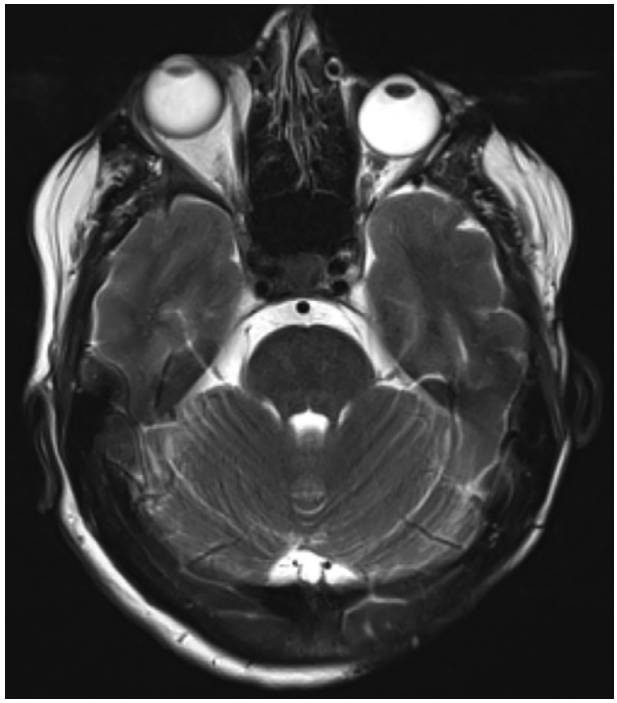

Fig. 2 – 64-year-old female with PRS. FINDINGS: Axial T2 MRI shows showing left enophthalmos, increase in superficial fatty tissues, and left greater than right facial region due to postoperative changes. Atrophic left masseter muscle. Decrease in extracalvarial fat overlying the left hemicranium, greater overlying anterolateral left frontal lobe. Partially seen left parotid atrophy. TECHNIQUE: Axial T2 MRI at 1.5T, TR 5000 ms, TE 80 ms, 5 mm thickness.

Differential diagnosis

Given the complexity and overlapping features of various neurocutaneous disorders, it is important to consider differential diagnoses when evaluating a patient with PRS-like symptoms. Rasmussen encephalitis, atrophoderma of Pasini-Pierini, and other causes of progressive facial hemiatrophy should be considered in the differential diagnosis. Rasmussen encephalitis is a progressive inflammatory disorder of the brain that predominantly affects 1 hemisphere and may present with neurological deficits, including hemiparesis and seizures [9]. Atrophoderma of Pasini-Pierini is a distinct skin condition characterized by depressed, hyperpigmented lesions, often with a cribriform appearance, that typically affects the trunk and extremities [10]. However, careful evaluation of the clinical presentation, imaging findings, and associated features in the

present case helped rule out these differential diagnoses. The overall features supported a diagnosis of PRS.

Treatment and outcome

PRS management focuses on symptoms and complications. Due to the rarity of PRS, limited knowledge exists regarding the effectiveness of commonly used treatments [11]. Different therapeutic outcomes have been observed with the use of medications such as methotrexate, cytoxan, and other immunosuppressive drugs; however, no treatment has been proved to halt PRS progression [12]. This patient was not on any disease-modifying medications for her linear scleroderma or PRS. Her migraines were managed with propranolol and acetaminophen. While immunosuppressants like methotrexate have been tried for similar conditions, no agents have shown clear efficacy in PRS [11]. Neuromuscular consultation was recommended for leg symptoms, which could be attributed to peripheral nerve involvement. No interventions were pursued for the patient's numbness and hyperreflexia of the legs. Further follow-up will be important to determine the impact of specialist input on this patient's symptoms and disease course. As more atypical PRS cases receive comprehensive evaluation and collaborative management, knowledge of optimal therapies will evolve.

Parry-Romberg Syndrome most common features.

Clinical features	Imaging findings	Treatment	Prognosis
Facial hemiatrophy	Ipsilateral cerebral atrophy	Symptomatic control	Variable
Neurologic manifestations (Headaches, Seizures…)	White matter lesions	Immunosuppressants	Stabilization after 2-20 y
Skin, fat, muscle, bone atrophy on affected side	Microhemorrhages	Plastic surgery	Spontaneous recovery unlikely
	Skull hemiatrophy	No definitive cure	

Discussion

Parry-Romberg syndrome (PRS) is more common in women, with a female-to-male ratio of 3:2 [13]. Incidence ranges from 0.3 to 2.5 cases per 100,000 population annually [14]. Despite reports of late-onset PRS, onset is typically in the first decade of life with slow progression over 2-20 years before stabilization [5,15]. Various hypotheses have been proposed to explain the pathogenesis of this condition. The exact cause of PRS remains unclear, but several theories have been proposed, including vascular abnormalities, autoimmunity, neural abnormalities, and genetic predisposition [16]. The vascular hypothesis suggests that aberrant blood flow and ischemic events play a significant role in the pathogenesis of PRS, which is supported by findings of watershed infarctions and microhemorrhages in brain imaging studies [17].

In PRS, the progressive atrophy primarily affects the subcutaneous fat, later involving the muscles and bones on one side of the face. If the disease onset occurs during puberty, there is a possibility of bone and cartilage involvement [15]. The areas most commonly affected include the cheek, eye socket, mouth corner, and forehead. Although initially localized, atrophy can extend to the opposite side.

Epilepsy and headache are prevalent symptoms in cases of linear scleroderma affecting the head and face and involving the nervous system [18]. In the majority of patients with PRS, headache episodes typically occur after the onset of progressive hemifacial atrophy. A recent study reported that the average age of onset for PRS was 14.2 years, while the average age of onset for headaches was 20 years [19]. Interestingly, these symptoms have sometimes manifested prior to the onset of skin changes by several months or even years, as observed in our patient who experienced migraines starting in her late teens. Furthermore, our patient exhibited symptoms of hypoesthesia and poor discrimination, which can be associated with PRS [20].

CT and MRI detect intracranial abnormalities in PRS, including atrophy, white matter lesions, calcification, meningeal changes and skull atrophy [21,22]. These are often ipsilateral to skin lesions but can be contralateral. In our case, MRI revealed a chronic left-sided watershed infarction between the middle cerebral artery (MCA) and anterior cerebral artery (ACA) territories, accompanied by punctate foci of old hemorrhage, suggestive of potential small vessel disease. Notably, magnetic resonance angiography (MRA) of the brain did not identify any significant abnormalities, except for a right hemispheric atrophy and subcentimeter foci of low signal intensity in the left frontoparietal region.

Diagnosis of linear scleroderma of the head and face primarily relies on the identification of skin changes, while central nervous system involvement is rare [8]. Neuroimaging findings lack specificity. However, combining CT and multimodal MRI enhances accuracy through detailed cutaneous and CNS assessment.

Conclusion

This case of late-onset PRS with atypical neurological findings expands the known clinical spectrum of this rare disorder. Despite comprehensive diagnostics showing chronic microvascular and peripheral neuropathic changes, treatment options remain limited without disease elucidation. Detailed documentation of heterogeneous manifestations is imperative to understand pathogenesis, guide management, and advance therapies. This report highlights considering atypical PRS presentations, utilizing multimodal diagnostics, and investigating cases to improve patient care.

Ethical approval

Given the nature of the article, a case report, no ethical approval was required.

Author contribution

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Patient consent

Complete written informed consent was obtained from the patient for the publication of this study and accompanying images.

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