

Parry–Romberg syndrome

A global survey of 205 patients using the Internet

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Abstract—Parry–Romberg syndrome (PRS) is a rare neurocutaneous disorder characterized by progressive facial hemiatrophy. In this study, 205 patients with PRS were surveyed using the Internet. Estimates of the frequency of limb involvement (19%), epilepsy (11%), and other clinical and etiologic features were obtained. There was a wide range of age at onset and considerable diagnostic overlap with scleroderma “en coup de sabre.”

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Parry in 1825 and Romberg in 1846 described acquired progressive facial hemiatrophy variably affecting skin, fat, muscle, and bone. Hemiatrophy characteristically affects the maxillary region but may extend to the chin and forehead. Atrophy in the forehead appearing as a line is called scleroderma “en coup de sabre” and is often thought of as an overlapping condition.^{1,2} Neurologic symptoms, including epilepsy, migraine and facial pain, and brain lesions on CT and MRI,³ as well as eye (heterochromia, enophthalmos, uveitis), hair (depigmentation, alopecia), skin (hyperpigmentation, vitiligo), teeth, and jaw complications are also described. Hemiatrophy can also extend to involve the ipsilateral and, rarely, the contralateral arm, trunk, and leg.

Because of its rarity, the literature on Parry–Romberg syndrome (PRS) largely consists of case reports or small series. However, the Internet now offers the opportunity to extend knowledge about rare diseases.

Methods. The US-based “Romberg’s Connection” (<http://www.geocities.com/rombergs/>) is the only web site for persons with the disorder, attracting a mailing list of 258 patients with PRS and scleroderma en coup de sabre from 29 countries since 1996. The organizers of the web site contacted members of the mailing list and placed a prominent link to the study Web site (www.martis.freeserve.co.uk/Parry/), which hosted the online survey (questions available from the Web site). This inquired about basic features of the disease, frequency of complicating symptoms, investigations, and treatment. A supplementary survey on exacerbating factors,

etiologic factors, and treatment went online 2 months later. This included the Hospital Anxiety and Depression scale, a widely used measure of emotional distress in patients with physical illness.⁴ Hemiatrophy from birth may indicate hemifacial microsomia, a disorder of branchial arch derivatives, and so these patients were excluded from analysis. I also excluded two patients with whom I had contact previously. The study ran for 12 months.

Results. Two hundred fourteen people responded to the initial survey (table 1; see table E-1 on the Neurology Web site). Nine patients were excluded because of a history of facial hemiatrophy since birth (5 patients) or because of incomplete data (4 patients), leaving 205 patients for analysis (199 for supplementary questions). Twenty patients sent photographs, all of which were consistent with the diagnosis (figure). Table 1 shows the principal findings. Data were obtained from 24 countries (see figure E-1 on the Neurology Web site). Eighty percent of patients were women. In reply to the question “what is your ethnic origin?” white, Indian, black, Korean, and Japanese patients were all represented. The median age at onset was 10 years, with a range of 1 to 50 years. In most patients (71%), it began before age 15 years. Only 8% had an onset after age 25 years (see figure E-2 on the Neurology Web site). There was no left/right preponderance.

Two methods were used to estimate how commonly PRS overlaps with scleroderma en coup de sabre. First, 21% of the sample reported dual diagnoses from their doctor of scleroderma en coup de sabre and PRS/facial hemiatrophy. Second, using three pictures of scleroderma en coup de sabre and two of lower facial hemiatrophy on the Web site, 31% said they had a “line” and lower facial hemiatrophy. Despite obvious limitations, this does suggest that the conditions may overlap considerably.

With respect to possible etiologic factors, six (3%) respondents said there was someone in their family (only one

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Table 1 Parry-Romberg Syndrome—Clinical characteristics of 205 respondents*

Data	
Demographics	
Sex	165 Female, 40 Male
Age (median, range)	32 years (range 4–64)
Country of Origin*	USA (132), Australia (19), UK (13), Canada (12), others (29)*
Diagnosis	
Age of onset (median, range)	10 years (1–50) (Delay to diagnosis—4 years [0–41])
Diagnostic label†	45% Parry-Romberg disease/syndrome; 40% Romberg syndrome; 16% (progressive) facial hemiatrophy; 16% scleroderma “en coup de sabre” (5% isolated); 6% linear scleroderma (1% isolated)
Self rated severity	Very Severe (7%), severe (24%), moderate (36%), mild (23%), very mild (8%)
Location affected	
Face	100% (46% left, 52% right, 2% bilateral)
Forehead involvement	63%
with a line*	51%
Lower face	75% Cheek, 43% chin, 55% lips, 50% teeth/gums, 25% tongue
Arm, trunk, or leg	9% Arm (74% ipsilateral), 14% trunk (81% ipsilateral), 10% Leg (75% ipsilateral), 19% any involvement of arm, trunk, or leg
Other symptoms	
Epilepsy*	11% (4% described partial seizures)
Migraine/Facial Pain*	52% Migraine, 46% facial pain
Eye/Vision problems	46% (e.g. globe retraction, abrasions, uveitis), 17% history of uveitis
Jaw problems	35% jaw pain or difficulty opening or closing jaw
“Unusually Cold Hands”*	31%
Depression and Anxiety	46% anxious, 10% depressed (HAD score ≥ 8)
Autoimmune Disorders	Vitiligo (17%), thyroid problems (10%), systemic sclerosis (5%), inflammatory bowel disease (5%), rheumatoid arthritis (4%), ankylosing spondylitis (2%), lupus (SLE) (2%), and MS (0%)

* More data available on the *Neurology* Web site.

† More than one diagnostic label allowed.

subject with a first-degree relative) with facial asymmetry. None had been formally diagnosed, although orbital asymmetry had been confirmed medically in one. In two others, PRS was a plausible diagnosis. Respondents were asked to indicate whether they had ever had a range of autoimmune disorders as shown in table 1. Thyroid disorders were common (10%). An open-ended question about other



Figure. A 48-year-old woman with Parry Romberg syndrome. The facial hemiatrophy stops abruptly at the midline, forming a line on her chin and more faintly on her nose and forehead. Her symptoms began at age 9 years, and she was diagnosed at age 16 years.

medical disorders, a family history of medical problems, and ABO or rhesus blood types was unrevealing. Although 27% reported a childhood head injury, only 19 respondents (12%) reported injuries that they thought might be relevant to the onset of their condition. For example, “I was hit in the forehead (right side) by a ball and the symptoms appeared as the bruising went away.”

Of those patients who reported disease acceleration (26%), 68% were women who said that it worsened either during pregnancy or after childbirth. Nine women reported definite worsening during pregnancy, and eight reported worsening after delivery. Stress (26%) and surgery (8%) were also cited as accelerating factors. Although three patients reported antibodies to Lyme disease, none had symptoms of the disease.

The outcomes of various surgical treatments rated according to a simple scale are shown in table 2. Drug treatments were also used, notably steroids (7%), methotrexate (4%), penicillamine (2%), and azathioprine (1%), but there were insufficient numbers to assess benefit.

Discussion. Despite the limitations in Internet recruitment, this study gives, for the first time, a broad outline of the symptoms, complications, and response to treatment of a large group of patients with PRS. It

Table 2 Treatments and ratings of success (n = 199)

	% of respondents	Successful	Somewhat Successful	Unsuccessful
Any drug treatment	10%	—	—	—
Any surgical treatment	62%	—	—	—
Fat injections	39%	19%	53%	28%
Flap/pedicle procedure	19%	24%	55%	21%
Bone implant	11%	45%	41%	14%
Silicone injections	8%	13%	38%	50%

has raised the following points of interest. First, PRS is typically thought of as a disorder with a young age at onset. Although rare, later ages of onset (the oldest in this study was aged 50 years) do seem to occur. Second, the degree to which PRS overlaps with scleroderma en coup de sabre is controversial,¹ perhaps partly because, despite pathologic differences, the clinical reliability of distinguishing these conditions is modest.² The two methods in this study suggest an overlap of 20 to 30%, although the limitations of these methods must be emphasized. Third, possible disease acceleration during or immediately after pregnancy is a potentially novel finding. Fourth, the frequent reporting of “unusually cold hands” (in 31% of respondents) is limited by the lack of a control group but may be in keeping with underlying sympathetic dysfunction.⁵ Last, the majority of patients found some benefit from a variety of surgical procedures. The largest surgical series of PRS⁶ reports an excellent outcome in 35 to 72% of 78 patients using a flap procedure.

The pathophysiology of PRS remains unknown. Ablation of the superior cervical sympathetic ganglion in animals can replicate features of the disorder,⁵ and a range of evidence supports the idea that it may be an inflammatory autoimmune disorder.⁷ Pathologic studies of CNS involvement in PRS⁸ or scleroderma en coup de sabre⁷ are rare. There is little to support direct heritability from this study or others. Whatever causes PRS, there is compelling evidence that it has been around for at least 2,000 years.⁹

The Internet has obvious limitations for medical research. The respondents were a highly self-selected English-speaking group who had Internet access, were motivated to research their condition, probably younger than the general population, and were able to follow the online instructions. Those with severe neurologic disability may not have been able to take part. Disease or ascertainment bias could be responsible for the high proportion of female

patients and high levels of emotional distress seen. An additional drawback was the lack of diagnostic corroboration. PRS does at least have the advantage of being a clinically distinctive disorder, which is unlikely to be self-diagnosed. Moreover, the 20 patients who submitted photographs all appeared to have the condition.

The study demonstrates the possibility of using the Internet to study rare diseases. Despite major limitations, including ethical issues,¹⁰ the Internet may enable research in rare diseases, e.g., by collection of DNA, radiology, or randomized trials of treatment.

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