INTRODUCTION

Parry-Romberg syndrome is a progressive hemifacial atrophy of the skin and the subcutaneous tissue (Figure 1); in certain cases, muscles, cartilages, or bones may be involved. The syndrome is more commonly diagnosed in females in their early 20s and progresses over a 2-10 years period. However, sometimes it can be diagnosed as late as 40 or 60 years of age. It is characterized by thinning of the skin and the subcutaneous tissue and may be accompanied by hyperpigmentation, alopecia areata, hair color changes, involvement of the mimetic muscles underneath, and trigeminal neuralgia.

The treatment depends on the severity of the symptoms; for mild cases, fat/dermal grafts or fillers including hyaluronic acid and calcium hydroxyapatite may be used. For more severe cases, intervention is delayed until symptoms are stable. Several invasive procedures have been proposed such as, free flap transfer, canthopexy, septo-rhinoplasty, or implantation of alloplastic materials.

In this study, we present the management of two Parry-Romberg syndrome cases using fat transfer and skin bleaching using a modified "Kligman's formula."
induced Tumescent anesthesia to minimize pain and bleeding at the anterior abdomen. We then used a multiple holes’ cannula (1 mm diameter) with 10 cc luer lock syringes to harvest the fat. We centrifuged the fat at 3000 rpm for 3 minutes to separate the fat into three layers. The top and lower layer which contained destroyed adipocytes, oil, triglycerides, serum, and blood were removed and the refined fat of the middle layer was administered using a 1 cc syringe with a blunt tip cannula (in 1.7 mms diameter) to the area of deformity (Figure 2). Fat deposition was linear, in small portions per passage, in order to maximize cell survival (Figures 3 and 4). The skin hyperpigmentation was addressed using the modified “Kligman’s formula” with 5% ascorbic acid.

The second patient was a 42-year-old Caucasian female with right hemifacial atrophy. She was first diagnosed at age of 39 years with continuous progression of the disease. She was treated by 80 cc of fat transfer to her right temporal region, cheek, lower eyelid, and nasolabial crease (Figures 5 and 6). The fat was harvested from the anterior abdomen under Tumescent anesthesia and centrifuged for 3 minutes at 3000 rpm and was administered to the right face using similar cannula (Figures 2 and 5). A second session of fat transfer of 50 cc was required to optimize the results. In addition, biopsies were taken from the atrophic area in both procedures to establish diagnosis.

3 | RESULTS

In the first patient, both the hemifacial atrophy and the skin hyperpigmentation remarkably improved with stable results for at least 6 months postop (Figure 4).

In the second patient (Figure 7), two fat transfer sessions were needed but no skin bleaching treatment was required. Interestingly, in the pathology report there was no evidence of atrophy of the dermis and subcutaneous fat, but there was evidence of epidermal atrophy, papillary dermal fibrosis, and mild peri-adnexal, with lymphocytic-perivascular infiltration (Figure 8). Biopsies were taken 12 months after the last fat transfer to establish the diagnosis (Figure 9). Histopathologic findings showed that the epidermal atrophy was stable, as well as the mild atrophy/paucity of the appendageal structures. In addition, the findings included thickening of the collagen bundles, mild peri-adnexal with lymphocytic-perivascular dermal infiltration, and impressive thickening of the trabeculae subdividing of the subcutaneous fat (probably due to the lipofiling). To our knowledge, this is the first histopathologic report of a Parry-Romberg syndrome patient.

4 | DISCUSSION

Parry-Romberg syndrome is typically a superficial condition however, muscle or bony involvement with eye and trigeminal nerve complications have been reported. Surgical reconstruction is often required to help skeleton and ocular growth once the symptoms are stable. Fat transfer, dermal grafts, and medpore/silicone implants can be used with free flaps, canthoplasty, or rhinoplasty in more complicated cases.

Currently, liposuction and lipofiling are the “gold standard” for the treatment of Parry-Romberg syndrome. Liposuction was first described by Illouz and then was popularized by Klein with “Tumescent” anesthesia. However, Coleman introduced lipofilling technique with gentle liposuction and centrifugation of the fat, thereby increasing the survival rate of the transferred fat cells.

**Figure 1**: “Fayum” probably with Parry-Romberg syndrome from 70bC at Egypt

**Figure 2**: Cannulas used for liposuction (upper) and lipofiling (lower) to the face
Previous reports have shown only 40%-70% of fat cells survive when transferred to the face. In order to further improve fat cells survival, Matsumoto and Yoshimura enriched aspirated fat cells with adipose-derived stem cells (ASCs), and described adipose tissue regeneration and angiogenesis.

In our study, we performed liposuction of the anterior abdomen wall, we centrifuged the fat, and isolated the middle layer containing pure fat cells for subsequent lipofiling. The top and bottom layers were discarded. Purified fat was transferred in both cases with repeated injections. In order to prevent severe complications, we took special care to ensure that the injections were as atraumatic as possible. Hence, a cannula with diameter larger than the recipient vessels was used blindness after filler induction around the nose, forehead, and temporal region. The patients were followed for at least 6 months after lipofiling, which is adequate to assess fat survival.

We also added 5% vitamin C to the original “Kligman’s formula” in order to manage skin hyperpigmentation. “Kligman’s formula” is
the gold standard for the treatment of melasma. It contains hydroquinone 5%, tretinoin 0.1%, and dexamethasone 0.1%.\textsuperscript{34} It has been extensively used for the treatment of postinflammatory hyperpigmentation (PIH), chloasma, age spots, scars, and nevi of Ota or Huri alone or with laser therapy\textsuperscript{35–37}. Hydroquinone inhibits the conversion of dopa to melanin. Jimbow et al.\textsuperscript{38} proved that it degrades melanosomes and destroys melanocytes. Although there are no known risks, allergic reactions and ochronosis-like pigmentation have been reported.\textsuperscript{39}

The disorder is characterized by progressive darkening of the skin and degeneration of collagen and elastic fibers. The degeneration is followed by ochronotic deposits consisting of crescent-shaped, ocher-colored fibers in the dermis. The condition is difficult to treat, but it can respond to topical steroids, bimatoprost treatment, and peeling. Other whitening agents like kojic acid and azelaic acid\textsuperscript{40} are not as effective as hydroquinone and may cause complications (Table 1). Er:YAG and Q-switch\textsuperscript{34} lasers can provide short term improvement however, they may cause prolonged erythema which requires in average 6 months to resolve.

Tretinoin inhibits tyrosinase transcription, increases proliferation of keratinocytes, and interrupts melanin synthesis\textsuperscript{41} but may
cause erythema and skin irritation as well.\textsuperscript{42} It has to be combined with hydroquinone to improve skin penetration. The addition of hydrocortisone to the formula eliminates skin irritation and decreases melanin synthesis.\textsuperscript{43,44} However, the use of hydrocortisone should be limited to 3-4 months to prevent skin atrophy, telangiectasia, and extreme sensitivity to sun exposure.

Vitamin C (L-ascorbic acid) increases the bleaching activity of the formula as it blocks the oxidative chain reaction from tyrosine/dihydroxyphenylalanine (DOPA) to melanin\textsuperscript{45} and stimulates collagen synthesis.\textsuperscript{46}

In our study, the modified formula was gradually applied to minimize skin irritation for 1-month period. During the first week, it was applied for 1 hour on the skin. On the second week it was applied for 2 hours, on the third week for 3 hours, and on the forth week for overnight. Hydration and sun care cream were used for moisturization and sun protection. Strict sun avoidance along with broad-spectrum sunscreen were recommended to prevent relapse. The proposed bleaching treatment required 3-4 months for stable results.\textsuperscript{43}

### 5 | CONCLUSION

Lipofilling and bleaching of the skin with the proposed modified Kligman’s formula significantly improves Parry-Romberg syndrome. However, more studies are needed to establish the safety and efficacy of the results.

### ORCID

Ioannis E. Liapakis \(\text{http://orcid.org/0000-0001-7568-2323}\)

Eleftherios I. Paschalis \(\text{https://orcid.org/0000-0002-4544-4452}\)

### REFERENCES


---

**TABLE 1** Bleaching agents used for the treatment of hyperpigmentation and possible complications

<table>
<thead>
<tr>
<th>Bleaching agents</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azelaic acid with 0.05% tretinoin (38)</td>
<td>No complications</td>
</tr>
<tr>
<td>Azelaic acid with 15%-20% glycolic acid (38)</td>
<td>No complications</td>
</tr>
<tr>
<td>Kojic acid 2% in combination with hydroquinone 2%</td>
<td>No complications</td>
</tr>
<tr>
<td>Glycolic acid 10% with hydroquinone 2% (39)</td>
<td>No complications</td>
</tr>
<tr>
<td>“Kligman’s formula” (hydroquinone 4% with tretinoin 0.1% and dexamethasone 1% in a hydrophilic ointment)</td>
<td>Allergic reactions, contact dermatitis, nail bleaching, and ochronosis-like pigmentation</td>
</tr>
<tr>
<td>Tretinoin 0.05%-0.1% (53)</td>
<td>Erythema or increase the pigmentation due to skin irritation</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>No complications</td>
</tr>
</tbody>
</table>