Lipofilling and Modified “Kligman’s formula” for the Treatment of Parry-Romberg Syndrome

Liapakis IE¹, Christopoulos A², Tzouganakis AC¹, and Paschalis EI³

¹Department of Plastic and Reconstructive Surgery, Hellenic Anticancer Institute, Greece
²Department of Plastic and Aesthetic, Monash Institute of Pharmaceutical Sciences, Greece
³Department of Ophthalmology, Harvard University, USA

Abstract
Parry-Romberg syndrome is a degenerative disease characterized by progressive hemifacial atrophy of the skin, muscle and bones of the forehead, eyes, mouth, nasolabial crease and the upper/lower maxilla. It causes skin hyperpigmentation and trigeminal neuralgia. The syndrome has higher prevalence in women between the ages of 5-15 and it stabilizes within 2-10 years. It results in significant facial deformity, which affects the patient’s self esteem and social appearance.

Aim of the study: We present a case of Parry-Romberg syndrome with facial deformity that was treated with lipofilling and bleaching of the skin using a modified “Kligman’s formula” cream.

Materials and Methods: A 21 years old female with left hemifacial atrophy was diagnosed with Parry-Romberg syndrome at age of 15, which has been stable for the last 2 years. The patient was treated with lipofilling of 20cc of fat in the left forehead, nose, nasolabial crease, cheek, and mental region. Treatment of skin hyperpigmentation performed for 1 month every night to eliminate the erythema, using a modified “Kligman’s formula” cream with added 5% ascorbic acid and applied gradually to the skin: the 1st week applied 1 hour before sleep, the 2nd week 2 hours before sleep, the 3rd week 3 hours before sleep and the 4th week all the night long. The day after and every day after the treatment, a hydration/sun care cream (with SPF over 30) applied to the skin in order to eliminate the irritation/dehydration of the skin.

Results: The appearance of the hemifacial atrophy and skin hyperpigmentation was significantly improved using lipofilling and the bleaching cream. We followed the patient 6 months after the procedure, since there is no evidence that more time is needed to evaluate the stability of the results. No complications occurred during and after the procedure.

Conclusion: Facial deformities derived from Parry-Romberg syndrome can be successfully treated with fat transfer and bleaching of the skin. More studies are required to demonstrate the efficacy of this procedure.

INTRODUCTION
Parry-Romberg syndrome is an acquired progressive hemifacial atrophy. It is a rare disorder (1/700,000), which affects mostly women. In the modern literature it first described by Parry and Romberg [1, 2], however, there evidence of its existence in ancient times (Figure 1). It affects the skin and subcutaneous tissue and, in some cases, extends to the muscles, cartilages or underlying bones [3]. Typically, it begins during the first two decades of life [4, 5] and progresses for 2-10 year during the active phase before stabilization, however, it has also been reported in older patients in their 5th or 6th decade of life [1, 6]. It is characterized by dermatologic, and, in rare cases, neurologic clinical changes on one side of the face, including trigeminal neuralgia, skin hyperpigmentation with mouth, eye, even hair involvement [4, 5, 7-10]. Parry-Romberg syndrome leads to scar-like skin changes, thinning of the skin and subcutaneous tissue...
with discoloration of the hair or alopecia areata, atrophy of the orbital, palpebral, zygomatic and masseter muscles. The final result is craniofacial asymmetry, affecting the self-esteem of the patient and their social acceptance [11, 12].

Several surgical techniques have been previously reported for the treatment of this condition. For mild cases with soft tissue involvement, fat/dermal grafts or dermal fillers including calcium hydroxyapatite, can be used to correct volume loss [13, 14]. For severe cases with asymmetry, it is advised to wait for stabilization of the condition and then proceed surgically to correct the asymmetry [14-16], with free flap transplantation, alloplastic implants, medial canthopexy or septrhinoplasty.

The aim of this case report is to present a mild case of Parry-Romberg syndrome using lipofilling and skin bleaching with a modified "Kligman's formula" cream.

MATERIALS AND METHODS

A 21 years old Caucasian female patient appeared at our clinic (OpsicClinical Plastic and Reconstructive Surgery) with left hemifacial atrophy. She was first diagnosed with Parry-Romberg syndrome when she was 15 years old and she has been stable for at least 2 years.

The patient was treated by lipofilling of a total of 20cc of fat at the left forehead, nose, nasolabial crease, cheek, and mental region (Figure 2). The adipose tissue used for the filing was harvested from the patient’s anterior abdominal wall. After local anesthesia was administered, the subdermal tissue lifted away from the underlying structures at the abdomen region by gently grasping the skin. Autologous fat collection was performed with rapid palindromic movement at the subcutaneous tissue of 10cc syringe 1mm in diameter with multiple holes, resulting in an atraumatic and bloodless collection of fat [17, 18]. Each 10 cc syringe was gently placed into a sterilized sleeve and centrifuged at 3000rpm for 2-3 min to collect the fat, which was separated into three layers: the top-layer, composed mainly of oil with triglycerides derived from the destroyed adipocytes; the middle-layer, composed of purified fat suitable for transplantation; and the bottom-layer, composed of serum and blood debris. The top layer of oil was removed and the bottom layer was drained. The refined fat cells were administered to the underlying tissues using a blunt tip cannula in 1.7 mms in diameter (Figure 3). The deposition of the fat was linear in small parts per passage in order to maximize cell survival.

Subsequently, skin hyperpigmentation was treated for one month with a cream containing 5% ascorbic acid in the original Kligman’s formula.

RESULTS

The hemifacial atrophy and the skin hyperpigmentation were significantly improved with no recurrence 6 months after the treatment (Figure 4).

DISCUSSION

Parry-Romberg syndrome is a progressive degenerative disease causing facial deformation, which may impact patient’s self esteem and social appearance. In mild cases, only the fat, skin and muscle may be involved, however, in more severe cases, ocular and/or neurologic manifestation may be present [19]. In younger patients, bony atrophy may require immediate intervention [20-22], but recent studies strongly suggest that treatment should be initiated only after disease stabilization [13-16]. If treatment begins too early, additional surgeries may be required [3] to accommodate disease progression, such as lipofilling, medial canthopexy or septrhinoplasty. The type of surgical reconstruction almost always depends on the severity of the deformity. In mild to moderate hypoplasia, lipofilling may be adequate, but in more severe cases, dermal fat grafts, silicone implants or adipofacial free flaps may be required in conjunction with skeletal support.

Currently, the use of fat transfer via liposuction was proposed as the "gold standard" for the correction of Parry-Romberg syndrome [24, 25]. The method was first described by Illouz et al. [26] and was popularized with the introduction of tumescent topical anesthesia by Klein et al [27]. However, Coleman et al.
[28] made the most critical modification, improving the overall success of the technique. He reported the use of a fat aspiration and re-application protocol, with careful aspiration and centrifugation [29, 30]. This method is particularly more efficacious [31] for treatment of the malar, cheek and chin region, but not as successful for treatment of the upper/lower lip and the temporal region. However, Matsumoto [32] and Yoshimura [3], described improved outcomes of cell survival, angiogenesis, and adipose tissue regeneration by enrichment of the aspirated fat cells with adipose-derived stem cells (ASCs). In our study, liposuction was carefully performed at the anterior abdominal wall and cells were purified with centrifugation. Only the middle band containing purified fat was selected for transfer, while the top and bottom bands were discarded. Application of these cells to the hemifacial atrophy was achieved at sequential administration of 20ccs of fat. The lipofilling was very careful, after aspiration with successive movements of the canula since there is evidence of severe complications even blindness after filler/fat application at the nose/forehead areas [34]. We followed the patient 6 months after the procedure, since there is no evidence that more time is needed to evaluate the survival of the fat [35, 36].

A secondary effect of Parry Romberg syndrome is skin hyperpigmentation. The etiology is not fully understood, however, combination treatments can improve the skin’s pigmentation [37]. For example, azelaic acid combined with 0.05% tretinoin or 15-20% glycolic acid can promptly depigment the skin [38]. Kojic acid 2% combined with hydroquinone 2% was shown to be superior to glycolic acid 10% and hydroquinone 2% [39]. The combination of hydroquinone 5%, tretinoin 0.1%, and desamethasone 0.1% in a hydrophilic ointment was first introduced by Dr. Albert Kligman as the “Kligman’s formula” in 1975 [40] and has been extensively used since for post-inflammatory hyperpigmentation (PIH), chloasma, melasma, age spots, scars and nevi of Ota or Huri [41]. Hydroquinone inhibits the conversion of dopa to melanin by blocking the activity of tyrosinase [42]. As suggested by Jimbow et al, hydroquinone interferes with DNA and RNA synthesis, degrades melanosomes and destroys melanocytes [42, 43]. In rare cases it can cause allergic reaction and contact dermatitis, [44-46] nail bleaching, and ochronosis-like pigmentation [47, 48]. Even though hydroquinone has been shown to cause animal toxicity [49], no complications have been reported in humans [50]. Alternative bleaching agents, such as kojic acid or azelaic acid, are useful but not as potent as hydroquinone [51, 52]. Tretinoin 0.05%-0.1% reduces pigmentation by inhibiting tyrosinase transcription and by interrupting melanin synthesis [53], but, in some cases, may cause erythema or increase pigmentation due to the irritation of the skin [54]. The tretinoin eliminates pigment and increases keratinocyte proliferation by preventing oxidation of hydroquinone, therefore it improves epidermal penetration. Furthermore, adding topical corticosteroids reduces the irritation of the other agents and inhibits melanin synthesis by decreasing cellular metabolism [55]. The addition of ascorbic acid to the original “Kligman’s formula” can increase the activity and efficacy of the hypopigmenting agents by improving the anti-oxidant effect and collagen stimulation (Figure 5, 6). In this study, skin hyperpigmentation was treated using 5% ascorbic acid into the "Kligman's formula". The treatment performed for 1 month every night (to eliminate the erythema) and applied gradually to the skin: the 1st week applied 1hour before sleep, the 2nd week 2hours before sleep, the 3rd week 3hours before sleep and the 4th week all the night long. The day after and every day after the treatment, a hydration/sun care cream (with SPF over 30) applied to the skin in order to eliminate the irritation/dehydration of the skin.

CONCLUSION

Parry-Romberg syndrome is a degenerative disease that leads to soft tissue atrophy as well as the skin hyperpigmentation. Surgical intervention is often required using fat transfer in conjunction with skin bleaching. We report a case of a patient treated with lipofilling and a modified cream which resulted to significant improvement and stable results for at least 6 months. Our results suggest that adding 5% ascorbic acid at the original “Kligman’s formula” may improve the skin bleaching, however, more studies are required to establish the power of the results.

REFERENCES


Liapakis et al. (2016)

Email: liapjyo@yahoo.com


