Recovery from Bell Palsy after Transplantation of Peripheral Blood Mononuclear Cells and Platelet-Rich Plasma

Istvan Seffer, MD, PhD
Zoltan Nemeth, PhD

Summary: Peripheral blood mononuclear cells (PBMCs) are multipotent, and plasma contains growth factors involving tissue regeneration. We hypothesized that transplantation of PBMC-plasma will promote the recovery of paralyzed facial muscles in Bell palsy. This case report describes the effects of PBMC-plasma transplantations in a 27-year-old female patient with right side Bell palsy. On the affected side of the face, the treatment resulted in both morphological and functional recovery including voluntary facial movements. These findings suggest that PBMC-plasma has the capacity of facial muscle regeneration and provides a promising treatment strategy for patients suffering from Bell palsy or other neuromuscular disorders.

However, an expanded latency of the early monosynaptic (R1) of the blink reflex by right-sided stimulation of the face was recorded, whereas the latency of the late reflex response (R2) was normal at both sides. By left-sided stimulation, latency of R1 and R2 was normal ipsilaterally, but R2 was found to be expanded contralaterally.

Brainstem auditory evoked potential revealed normal peak and interpeak latencies without pathological signs. Based on these findings, abnormalities in trigemino-facial reflex at the right side were diagnosed.

From the age of 11 years, she was treated with therapeutic stimulus current treatments using periodical transcutaneous electric nerve stimulation (Corposano, KS-1/A1) and therapeutic active face exercises. These, however, did not improve her conditions.

At the age of 15 years, otorhinolaryngology examination was performed revealing intact outer ears and tympanic membranes at both sides. To assess cerebellar function, Barany test, Romberg test, Babinski-Weil test, finger-to-nose test, rebound test, and dysdiadochokinesia test were performed. These tests confirmed normal cerebellar functions.

Audiology examination did not detect reduction in hearing. In addition, audiometry revealed intact hearing at both sides. Electronystagmography test revealed no nystagmus. Further examinations confirmed abnormalities in central vestibular function and intact peripheral vestibular function.

In December 2013, the patient was admitted and examined in our clinic with symptoms as previously documented. Thus, with the permission of the patient,
autologous blood cell transplantation therapy was applied. The local Ethical Committee approved this therapy, and written informed consent was obtained before the therapy. Following that, she received repeated autologous suspension of peripheral blood mononuclear cell (PBMC)-platelet (PLT)-plasma transplantation 9 times in 1 year (Table 1).

**TECHNIQUE DESCRIPTION**

A total of 25 mL peripheral blood was harvested from the median cubital vein into 50 mL heparinized vacutainer tubes. Plasma of 20 mL blood was separated by centrifugation (10 minutes at 630 ×g). PBMCs of 5 mL blood were isolated using density gradient centrifugation as previously described by Nilsson et al. Briefly, 1:1 dilution of blood with Dulbecco’s Phosphate-Buffered Saline (Gibco, Invitrogen, Budapest, Hungary) was pelleted (20 minutes at 1,020 ×g) with Ficoll-Paque PREMIUM 1.077 g/mL density gradient media (GE Healthcare, CTS, Life Sciences, Budapest, Hungary). The interphase consisting of PBMCs was collected and washed 2 times with Dulbecco’s Phosphate-Buffered Saline. The resulting pellet was resuspended with 9.0 ± 0.1 mL of autologous plasma.

A total of 9.9 ± 0.1 mL of PBMC-PLT-plasma was locally injected in even proportions on the right side of the face in the areas of facial nerve (FN, CN VII) innervations. Injections were given subcutaneously and muscally approximately 1.2 mL to each region (temporal, orbicularis oculi, buccinator, levator anguli oris, orbicularis oris, zygomaticus major and minor, risorius, and levator labii superioris) using 3 mL syringes connected to 0.30 × 1/2 needle. This treatment was repeated 9 times within a year (Table 1).

**TREATMENT RESULTS**

Posttreatment anamnesis revealed significant improvement in the voluntary motion of the facial muscles. There was a remarkable improvement in facial contouring, and the facial asymmetry was significantly reduced (Fig. 1). Nasolabial fold and tear trough were noticeably developed on the right side (Fig. 1). Cheek augmentation was slightly reduced on the left side, whereas it emerged on the right side (Fig. 1). Contours of the asymmetrically drooping corner of left lips were slightly improved (Fig. 1). Following treatments, the patient was able to close her eyelid completely on left and by 80.7% on the right side (Figs. 2, 3). The drooping of angle of the mouth was remarkably reduced (42.2%) on the right side as compared with that of before treatment (Fig. 4). Taste sensation was maintained, and there was no pain in or behind the ear, and no numbness in the affected side of her face.

| No. | Treatments (wk) | PBMC Count/mL | PLT Count/mL | Total Cell Count/mL | Total Cell Count/Injection | Total Cell Count/Treatment |
|-----|----------------|---------------|--------------|---------------------|--------------------------|----------------------------|
| 1   | 1st            | 6.00 × 10⁵    | 4.50 × 10⁷   | 4.56 × 10⁷          | 5.64 × 10⁷                | 4.51 × 10⁸                 |
| 2   | 4th            | 1.20 × 10⁶    | 1.26 × 10⁸   | 1.27 × 10⁸          | 1.57 × 10⁸                | 1.26 × 10⁸                 |
| 3   | 8th            | 7.00 × 10⁵    | 1.06 × 10⁸   | 1.07 × 10⁸          | 1.32 × 10⁸                | 1.06 × 10⁸                 |
| 4   | 25th           | 2.60 × 10⁶    | 1.63 × 10⁶   | 1.66 × 10⁸          | 2.05 × 10⁸                | 1.64 × 10⁸                 |
| 5   | 29th           | 5.00 × 10⁶    | 8.30 × 10⁷   | 8.35 × 10⁷          | 1.03 × 10⁸                | 8.27 × 10⁷                 |
| 6   | 31st           | 5.00 × 10⁷    | 8.30 × 10⁷   | 8.35 × 10⁷          | 1.03 × 10⁸                | 8.27 × 10⁷                 |
| 7   | 50th           | 1.20 × 10⁵    | 1.58 × 10⁸   | 1.59 × 10⁸          | 1.97 × 10⁸                | 1.58 × 10⁸                 |
| 8   | 55th           | 1.34 × 10⁶    | 1.50 × 10⁸   | 1.51 × 10⁸          | 1.87 × 10⁸                | 1.50 × 10⁸                 |
| 9   | 65rd           | 6.30 × 10⁷    | 1.36 × 10⁹   | 1.37 × 10⁹          | 1.69 × 10⁹                | 1.35 × 10⁹                 |
| Mean| —              | 1.05 × 10⁸    | 1.17 × 10⁸   | 1.18 × 10⁹          | 1.45 × 10⁹                | 1.1 × 10⁹                  |
| SEM |                | 2.25 × 10⁵    | 3.34 × 10⁷   | 3.36 × 10⁷          | 4.68 × 10⁷                | 3.21 × 10⁷                 |

PBMC, peripheral blood mononuclear cell; SEM, standard error of mean.

---

**Fig. 1.** Development of asymmetry of the face after PBMCs and PLT-plasma therapy. Before treatment (A), after treatment (B). After treatment, symmetry of the face remarkably improved, the atrophied areas were significantly reduced, the right corner of the lips was significantly elevated, and a nasolabial fold appeared on the right side of the face.
CONCLUSIONS

According to the significant recovery that we observed after transplantation of autologous PBMCs and PLT-plasma therapy, this therapy has the potential to restore neuronal-muscular atrophy and provides a promising future strategy to cure facial atrophy.

ACKNOWLEDGMENTS

We would like to thank Kalman Wilhelm and Attila Schneider for their assistance in the treatments and Zoltan Szabo for performing measurements on the patient’s photographs.

Zoltan Nemeth, PhD
Seffer Clinic
Ujpesti Rakpart 3 I /1
Budapest
1137 Pest
Hungary
E-mail: seffer@seffer.hu
PATIENT CONSENT
The patient provided written consent for the use of her image.

REFERENCES
1. Roob G, Fazekas F, Hartung HP. Peripheral facial palsy: etiology, diagnosis and treatment. *Eur Neurol.* 1999;41:3–9.
2. Shafshak TS. The treatment of facial palsy from the point of view of physical and rehabilitation medicine. *Eura MedicoPhys.* 2006;42:41–47.
3. Watanabe T, Suzuki M. Equilibrium test findings in patients with Bell’s palsy. *Auris Nasus Larynx.* 2006;33:143–147.
4. Notermans NC, van Dijk GW, van der Graaf Y, et al. Measuring ataxia: quantification based on the standard neurological examination. *J Neurol Neurosurg Psychiatry.* 1994;57:22–26.
5. Miranda CS, Stefani CP, Morimoto MM, et al. Assessment of gait deviation on the Babinski-Weill test in healthy Brazilians. *Arq Neuropsiquiatr.* 2013;71:615–620.
6. Alusi SH, Glickman S, Patel N, et al. Target board test for the quantification of ataxia in tremulous patients. *Clin Rehabil.* 2003;17:140–149.
7. Kato I, Watanabe J, Nakamura T, et al. Electronystagmographic assessment of cerebellar lesions. *Auris Nasus Larynx.* 1986;13: S171–S180.
8. Sebben AD, Lichtenfels M, da Silva JL. Peripheral nerve regeneration: cell therapy and neurotrophic factors. *Rev Bras Ortop.* 2011;46:643–649.
9. Nilsson C, Aboud S, Karlén K, et al. Optimal blood mononuclear cell isolation procedures for gamma interferon enzyme-linked immunospot testing of healthy Swedish and Tanzanian subjects. *Clin Vaccine Immunol.* 2008;15:585–589.
10. Zhang M, Huang B. The multi-differentiation potential of peripheral blood mononuclear cells. *Stem Cell Res Ther.* 2012;3:48.