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Longitudinal Single Case Report: Intravenous Therapeutic Plasma Secretome Therapy in a Parkinson's Patient with Vascular Comorbidities

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ABSTRAK

Background: Parkinson's disease is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons, resulting in a complex combination of motor and non-motor symptoms. Conventional therapies such as levodopa are primarily symptomatic and often lead to long-term complications, highlighting the need for alternative approaches capable of modifying disease progression. **Objective:** This case report aims to evaluate the short-term clinical effects of a single session of cell rejuvenation therapy using Hematopoietic Stem Cell (HSC)-based Therapeutic Plasma Secretome (TPS) in a Parkinson's patient with vascular comorbidities. **Methodology:** A 71-year-old male diagnosed with Parkinson's disease and a history of mild stroke received TPS therapy via intravenous infusion at a dose of 1 million cells/kg body weight, prepared at a BPOM-certified facility. Functional evaluation was conducted longitudinally using the UPDRS-8 scale over a four-week period. **Results:** The UPDRS-8 score improved from 8 to 6, accompanied by clinical improvements including increased walking speed, resolution of tremors, and enhanced independence in daily activities. No significant adverse effects were observed during the monitoring period. **Conclusion:** These preliminary findings support the potential of HSC-based TPS as a safe and promising non-invasive therapy for improving motor function in Parkinson's patients. However, as a single case report lacking a control group and with a limited observation period, the results cannot yet be generalized. Further research through controlled clinical trials, long-term monitoring, and the development of reliable biomarkers is necessary to verify the efficacy and safety of this therapy.

INTRODUCTION

Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder worldwide after Alzheimer's disease. It is characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta and disruption of motor circuitry in the midbrain. The cardinal symptoms of PD include resting tremor, bradykinesia, muscle rigidity, and postural instability. These motor symptoms are frequently accompanied by non-motor manifestations such as autonomic dysfunction, sleep disturbances, and cognitive impairment. Globally, PD affects approximately 1% of individuals over the age of 60. In Indonesia, the reported prevalence of PD is 7 per 1,000 elderly individuals, a figure projected to rise in tandem with the nation's aging population trend. Consequently, the economic and social burden of this disease is expected to increase substantially in the coming decades.

Conventional pharmacological therapy, particularly levodopa, can offer significant symptomatic relief of motor symptoms. However, such treatment is purely symptomatic and does not

alter the course of disease progression. Long-term use is often associated with complications such as motor fluctuations and dyskinesia, which make clinical management increasingly complex (Armstrong & Okun, 2020). These limitations underscore the need for innovative therapeutic approaches that not only alleviate symptoms but also have the potential to modify the underlying pathogenesis of PD.

Several preclinical studies have demonstrated that administration of secretome or exosomes derived from stem cells—such as mesenchymal stem cells (MSCs)—can enhance neuroplasticity and support the survival of residual dopaminergic neurons. The primary mechanisms include reduction of oxidative stress, inhibition of α-synuclein aggregation, and improvement of mitochondrial function—three processes central to the pathogenesis of PD (Ankrum et al., 2023; Martinez-Morales et al., 2023). Although these initial findings are promising, most of the data originate from animal models and in vitro studies, with limited clinical reports in humans. Therefore, systematically documented case reports play a valuable role in bridging the gap between preclinical evidence and real-world clinical applications, particularly in developing countries such as Indonesia.

Therapeutic Plasma Secretome (TPS) offers an advantage as a non-invasive therapy that can be administered either systemically or intranasally. Animal model studies have shown significant improvements in motor symptoms and reductions in neurogenic inflammation following TPS administration. This approach also circumvents major challenges associated with direct cell therapies, such as risks of immunogenicity and tumorigenesis, along with complex regulatory and ethical issues concerning the use of living human cells. Nevertheless, standardized protocols, efficacy parameters, and long-term safety profiles of TPS require further development and validation (Martinez-Morales et al., 2023; Ankrum et al., 2023).

In this context, the documentation of individual cases demonstrating clinical benefits from TPS holds potential to provide preliminary data supporting broader research exploration. The objective of this case report is to evaluate the clinical outcomes of a single TPS intervention session in a male patient diagnosed with PD. The primary focus is to measure changes in motor function and daily living activities using the Unified Parkinson's Disease Rating Scale – Part 8 (UPDRS-8) longitudinally. This study also aims to explore the possible impact of TPS on broader functional domains, such as social participation and physical activity, particularly in patients with vascular comorbidities. The main hypothesis is that TPS can yield short-term improvements in motor symptoms and enhance patient independence without causing significant adverse effects.

CASE PRESENTATION

The patient was a 71-year-old male with a history of minor stroke in 2006 and an ischemic stroke in May 2024. Since June 2024, he began exhibiting classic features of Parkinson's disease, progressing gradually with symptoms including bradykinesia, rigidity in the right lower limb, and intermittent tremors, particularly evident during febrile episodes. These complaints significantly impacted his daily activities such as eating, dressing, and walking, thereby lowering his overall quality of life. Additionally, the patient experienced difficulty with fine motor tasks such as thumb-to-finger tapping, further suggesting an underlying progressive neurological disorder.

Table 1. Patient Clinical Profile and Therapeutic Plan

Parameter	Description
Age	71 years old
Sex	Male
Medical History	Minor stroke (2006), ischemic stroke (May 2024)
Onset of Parkinson's Symptoms	June 2024
Key Symptoms	Bradykinesia, right lower limb rigidity, intermittent tremors
Impaired Daily Activities	Difficulty eating, dressing, walking; impaired fine motor coordination

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Pre-therapy UPDRS-8 Score	8 (moderate functional impairment)
Type of Therapy	Therapeutic Plasma Secretome (TPS)
Therapy Source	Hematopoietic Stem Cell (HSC), BPOM-certified facility
Dosage	1 million cells/kg body weight, administered intravenously
Mechanism of Action	Secretome fraction: neurotrophic, anti-inflammatory, and immunomodulatory factors
Therapy Objective	Enhance neural microenvironment and support functional regeneration
Ethics and Consent	Written informed consent; compliant with the Declaration of Helsinki

As part of the initial clinical evaluation, the patient's functional status was assessed using the Unified Parkinson's Disease Rating Scale – Part 8 (UPDRS-8), which focuses on motor functions in daily living. The pre-treatment UPDRS-8 score was recorded at 8, indicating moderate functional impairment. Given the patient's clinical condition, vascular history, and progressive symptoms, a single session of regenerative therapy using Therapeutic Plasma Secretome (TPS) was administered as a stem cell-based intervention.

The TPS was derived from hematopoietic stem cells (HSC), processed in a facility certified by the National Agency of Drug and Food Control (BPOM). The dose was 1 million cells per kilogram of body weight, prepared by isolating the secretome fraction rich in paracrine factors such as neurotrophic agents, anti-inflammatory mediators, and immunomodulators. The therapy was administered intravenously to ensure systemic distribution, aiming to improve the neural microenvironment, reduce neurogenic inflammation, and support neuroregeneration. Throughout the procedure and post-intervention period, the patient was monitored by a medical team in a neurorehabilitation clinic. Ethical approval was secured, and all procedures were conducted in accordance with the principles of the Declaration of Helsinki. Prior to the intervention, the patient and his family received a detailed explanation of the therapy's mechanism, potential benefits, and associated risks. Written informed consent was obtained.

The patient's clinical progress was monitored periodically over a four-week period following therapy. On the third day post-treatment, the patient reported no new complaints and demonstrated an improvement in gait speed. He was able to participate in a community birthday celebration at a local school, indicating a return to social participation and improved confidence in engaging in outdoor activities. By the seventh day, he continued to report no complaints and noted gradual improvement in his physical condition. He began planning to initiate light physical exercise using a stationary bicycle, reflecting positive motivation for continued self-rehabilitation.

On the 14th and 28th days post-treatment, the patient reported no recurrence of tremors, which had previously occurred during febrile illness. Furthermore, he was able to independently hold a spoon and plate while eating and walked at a faster pace compared to his pre-therapy condition. These changes reflect recovery of fine motor function and improvement in daily activities, particularly in mobility and independence.

Functional status was evaluated systematically using the UPDRS-8 instrument. Before therapy, the patient scored 8, with specific complaints including slow thumb-finger tapping, tremors during illness, slow gait, rigidity in the right leg, and short steps. This score indicated a moderate level of impairment in daily motor function. A follow-up evaluation at four weeks post-treatment revealed a reduced UPDRS-8 score of 6. This two-point improvement was considered clinically meaningful, correlating with enhanced ability to perform functional activities independently. The outcome was supported by direct observations, including the disappearance of tremors, improved finger dexterity, increased social participation, and independent eating ability. Thus, the decrease in UPDRS-8 score not

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only provides quantitative validation of clinical improvement but also supports the possibility of a true therapeutic effect from the stem cell-based intervention.

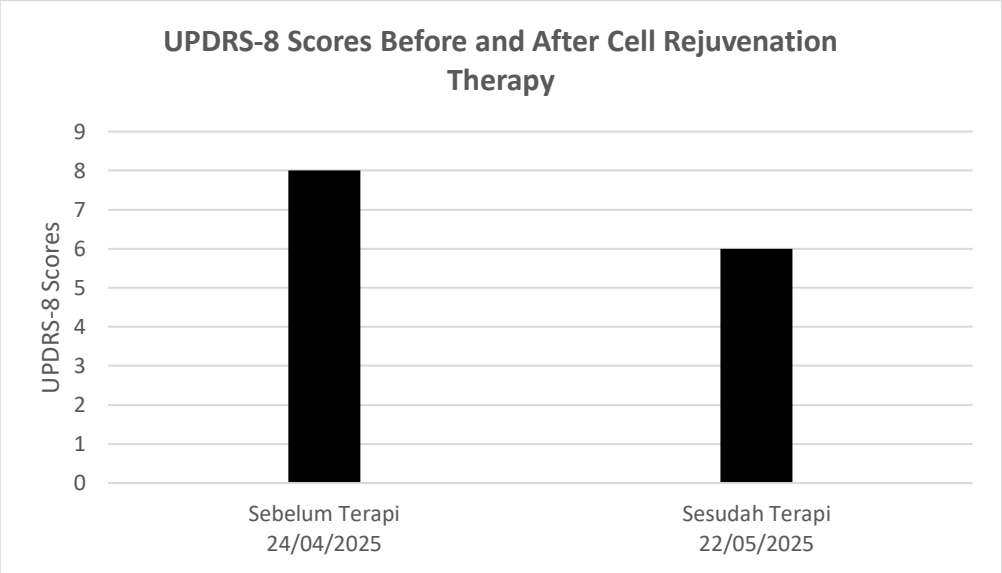

Figure 1. Graph of UPDRS-8 score changes before and after therapy, showing a reduction from a score of 8 to 6 within four weeks post-therapy.

Overall, this case presentation demonstrates a positive clinical response to a single session of HSC-derived TPS, both subjectively (daily clinical observation) and objectively (decrease in UPDRS-8 score). The observed improvement occurred within less than one month after the intervention, providing a strong initial basis for considering TPS as a potential option in managing Parkinson's symptoms in elderly patients with a history of vascular disease.

DISCUSSION

The clinical outcomes observed in this patient indicate a measurable improvement in Parkinson's symptoms within a relatively short period following a single session of hematopoietic stem cell (HSC)-based cell rejuvenation therapy. The reduction in UPDRS-8 score from 8 to 6 over four weeks signals a positive enhancement in motor function, particularly in daily living activities such as independent eating and unassisted walking. This effect aligns with experimental findings that mesenchymal stem cells (MSCs) mediate neuroprotective effects through the release of trophic factors such as brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF), and by reducing oxidative stress and inflammation, both of which contribute to neurodegeneration in Parkinson's disease (Jang et al., 2020). Furthermore, intravenous administration of MSCs allows for systemic effects that promote neural tissue recovery without the need for invasive procedures—a notable advantage over intracranial cell transplantation strategies.

Recent literature highlights the growing role of regenerative therapy in Parkinson's treatment, particularly given the limitations of long-term use of levodopa and dopamine agonists. For instance, Cha et al. (2023) noted that stem cell therapies derived from human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) offer long-term therapeutic potential that surpasses conventional symptomatic approaches.

A study by Tabar et al. (2025) reported that transplantation of human embryonic-derived dopaminergic progenitors into the striatum of Parkinson's patients resulted in a significant reduction of 23 points in the MDS-UPDRS Part III score after 18 months, with no major neurological complications. Similarly, Sawamoto et al. (2025) demonstrated an average improvement of 9.5 points over 24 months following intracranial transplantation of iPSC-derived progenitors. While these approaches have shown impressive results, the TPS therapy administered in our case presents advantages in accessibility, safety, and practicality, as it can be delivered via intravenous infusion without surgical intervention. A meta-

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analysis by Wang et al. (2023) also reported that homogenized stem cell therapies provided significant benefits for motor function and daily activities in Parkinson's patients during "off" periods, although the outcomes varied depending on cell type and transplant site.

Beyond clinical efficacy, it is important to consider the mechanistic differences between TPS and cell transplantation. TPS primarily leverages the paracrine effects of stem cells—namely, the secretion of exosomes and anti-inflammatory factors that enhance the neuronal microenvironment—rather than direct structural integration or differentiation into neurons. This mechanism allows for neuroprotection and functional recovery without the need for structural integration, which is technically more complex and carries higher risks of complications. This likely explains why, despite the absence of dramatic changes in motor scores, the patient demonstrated gradual recovery in independence and daily activity performance. Preclinical studies also support this view. For example, Jang et al. (2020) emphasized that MSCs can induce neuroregeneration through paracrine activity without differentiating into functional neurons, highlighting a mechanism of action consistent with the outcomes observed in this case.

In addition to paracrine effects, emerging studies have suggested that mesenchymal stem cells (MSCs), under specific microenvironmental conditions, may undergo transdifferentiation into dopaminergic neuronal phenotypes. This mechanism, referred to as direct transdifferentiation, involves the conversion of MSCs into cells exhibiting characteristics of A9 neurons from the substantia nigra, which are responsible for producing endogenous dopamine in the brain. This potential expands the therapeutic horizon of regenerative medicine. Barbuti et al. (2021) emphasized that the ability to generate authentic dopaminergic neurons that integrate into the nigrostriatal circuitry is crucial for achieving clinically meaningful long-term outcomes. This view is supported by Cha et al. (2023), who highlighted the importance of phenotypic and functional compatibility of transplanted cells to ensure sustained motor improvement. Although this evidence is largely limited to experimental models and has yet to be fully verified in humans, it provides a plausible biological rationale for the observed clinical improvements—even when therapy is administered systemically and non-invasively. The ability of MSCs to activate local neurogenesis pathways through cell–cell interactions and directional signaling also offers the possibility of functional regeneration without the need for complex genetic engineering.

Nevertheless, this report carries several important methodological limitations. As a single case study without a control group, the findings cannot be generalized to a broader population and are subject to observation bias and potential placebo effects. The lack of objective comparison limits the ability to isolate the specific impact of TPS on symptom improvement. Placebo effects in Parkinson's interventions have been reported to be significant, potentially increasing striatal dopamine release detectable via PET imaging (Jang et al., 2020). Moreover, the monitoring period, which spanned only four weeks, is insufficient to evaluate the sustainability of the therapeutic effects or the possibility of delayed adverse events. A meta-analysis by Wang et al. (2023) noted that most clinical benefits from cell-based therapies tend to emerge between six- and twelve-months post-intervention, underscoring the importance of extended observation for clinical validation.

The absence of supporting data such as neuroimaging or biomarker measurements also limits deeper mechanistic interpretations regarding TPS's mode of action in neuroregeneration. Many clinical trials involving cell transplantation incorporate evaluations such as PET-FDOPA and diffusion MRI to detect structural and functional changes in dopaminergic pathways, which can substantiate claims of biological efficacy (Cha et al., 2023). These limitations are consistent with findings from other studies that report while early clinical improvements may occur, long-term stability often requires follow-up treatments or supportive interventions such as adjunct neuro-motor rehabilitation.

Therefore, to support the clinical and scientific validity of TPS, more systematic follow-up studies are essential. These should include randomized controlled trials (RCTs) ranging from small to large scale, with extended monitoring periods. The development of objective biomarkers, standardized TPS administration protocols, and integration of neuroimaging technologies will be critical steps in building a robust scientific foundation for the broader clinical application of TPS in the future.

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CONCLUSION

This case report demonstrates that a single session of Hematopoietic Stem Cell (HSC)-based cell rejuvenation therapy using the Therapeutic Plasma Secretome (TPS) approach can yield meaningful short-term clinical improvements in an elderly Parkinson's patient with vascular comorbidities. The reduction in UPDRS-8 score and enhancement of daily motor functions provide preliminary evidence suggesting that TPS may offer genuine therapeutic benefits. However, as a single uncontrolled case report lacking objective data such as biological biomarkers or neuroimaging, these findings should be interpreted with caution. The possibility of observation bias and placebo effects cannot be ruled out. Furthermore, the limited follow-up period restricts the ability to assess the long-term sustainability of the observed therapeutic effects. Despite these limitations, TPS presents promise as a non-invasive and relatively accessible alternative to conventional stem cell approaches, particularly in settings with limited access to advanced medical technologies. To comprehensively validate the efficacy, long-term safety, and mechanisms of action of TPS, larger-scale randomized controlled trials with extended follow-up, along with the integration of biomarker assessments and neuroimaging, are essential as part of a standardized evaluation framework.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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