Case Study: Novel Approach to HIV-Associated Neuropathy Platelet Rich Plasma Successful in Treating HIV-Associated Peripheral Neuropathy

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Abstract: Distal symmetrical peripheral neuropathy (DSPN) is the most common neurologic complication of Human Immunodeficiency Virus (HIV) infection. DSPN is a distressing pain syndrome and infected patients have limited treatment options for alleviating symptoms. Platelet Rich Plasma has been found to be effective in relieving pain associated with chronic and acute musculoskeletal conditions as well as arthritic conditions. We tested the hypothesis that platelet rich plasma alleviates symptoms of HIV-associated DSPN. A 50year-old African American patient was referred for long-standing bilateral leg neuropathy. The patient was treated with an injection of platelet rich plasma therapy ever two weeks for 12 weeks. The treatment outcomes were pain intensity, pain relief, sensory perception, quality of life, mood, and function. After the first therapeutic injection of platelet rich plasma, the patient reported significant improvement in pain relief, sensory perception, and range of motion. The therapy was effective in relieving pain so the patient discontinued use all other pain medications including Vicodin and Neurontin.

This case report provides evidence that platelet rich plasma is effective in relieving painful numbness, tingling and burning related to HIV-associated DSPN. Platelet rich plasma may be a valuable option for treatment of symptoms associated with DSPN among HIV patients.

Keywords: Distal symmetrical peripheral neuropathy, H.I.V. neuropathy, neurogenic growth factors, platelet-rich-plasma, nerve pain.

INTRODUCTION

Distal Symmetrical Peripheral Neuropathy (DSPN) is the most common neurologic complication of HIV infection. DSPN can be categorized as Primary HIV-associated DSPN or Antiretroviral Therapy Toxic Neuropathy (ATN) [1,2] which has increased in frequency with the advent of this class of medications. DSPN affects approximately 57% of HIV patients [1] and is characterized by painful numbness, muscle weakness, depressed reflexes and impaired temperature homeostasis. Treatments options for temporary symptomatic relief include Memantine [3], Peptide-T, Amitriptyline, Gabapentin, topical Capsaicin 8%, recombinant human growth factor, and smoked cannabis [4]. However, the results of clinical trials indicate few are efficacious and most are financially burdensome to patients [5-7]. Therefore, there is an urgent need for adequate and affordable therapeutic options for DSPN.

Increasing evidence supports the hypothesis that platelet rich plasma may reduce neuropathic pain by triggering the cascade of events that occur in wound repair [8-10]. Platelet enriched plasma contains a high concentration of platelets, clotting factors and growth factors [11,12]. These growth factors, released by platelets, help to facilitate wound repair. In this research, we propose to test the hypothesis that platelet rich plasma alleviates symptoms of HIV-associated DSPN in a case report.

CASE PRESENTATION

A 50-year-old African American female presented to a PlasmaGenix affiliated clinic after being referred by her HIV specialist, for evaluation and possible treatment of her neuropathy. She presented with a chief complaint of bilateral foot and leg pain, numbness, tingling, and burning sensation which persisted for 15 years. She also reports that her symptoms are more pronounced on the left lower extremity. The patient also stated that she has difficulty walking for extended periods of time and has been in a state of constant and severe pain since her symptoms began. She rated the pain as an 8 out of 10 on the pain scale. The medications the patient was taking for pain include Vicodin, Neurontin, Lyrica, Capsaicin and Fentanyl patch but has not experienced symptomatic relief.

The symptoms have significantly decreased her quality of life. The patient is distressed and depressed by her situation since she used to be physically active

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prior to the DSPN. DSPN was diagnosed in the patient based on the Semmes Weinstein monofilament examination. A 5.07mm S-W monofilament was placed perpendicular to the following areas with enough pressure to cause the nylon filament to bend in the shape of the letter "C": The plantar metatarsal 1,3 and 5 areas as well as the plantar skin of the great toe. The monofilament was held in place for approximately 1 second. The patient was unable to sense the monofilament on the plantar great toe area as well as the plantar 5th metatarsal area bilaterally. Additionally, further neurologic testing was performed using a 128-Hz tuning fork. After causing the tuning fork to vibrate, the base of the tuning fork was placed at the medial and lateral malleolus as well as the first metatarsal phalangeal joint areas bilaterally. The patient showed diminished vibration sensitivity particularly at the medial malleoli bilaterally.

She was diagnosed with HIV in 1985 and her HIV has been well managed. Her CD4 count at the time of her visit was over 500 cells/mm3 and she was not on anti-retroviral therapy. The patient's past medical history included type 2 diabetes mellitus and left leg liposarcoma for which she underwent partial quadriceps resection and radiation. Because of the liposarcoma, she has developed a left-sided limp and has become sedentary. The patient's hemoglobin A1c was 7.5% at the time of treatment and her diabetes was managed with Humalog 100 units and Lantus 100 units. The patient was on no other medications at the time of treatment.

During the physical exam, she appeared her stated age and her vitals were within normal limits. During the neurological exam, she was alert and oriented and her speech was clear and fluent. Her cranial nerves were grossly intact. No pronator drift was noted, motor strength was 5/5 for upper extremities and 4/5 for lower extremities with greater strength in the right lower extremity than the left. Posture was normal but her ability to stand was limited. Gait was limited to small to medium steps and the patient had a left-sided limp. Light touch, pinprick, position sense, monofilament testing, and vibration sense were diminished in the lower extremities.

Patellar and Achilles reflexes were hypoactive and elicited with reinforcement. The following pulses were present: Dorsalis Pedis: 1+ Bilaterally, Posterior Tibial: 1+ Bilaterally. Skin was cool to the touch in the lower extremities and no digital or leg hair was present. Additionally, the skin was mildly atrophic and non-elastic. There were no evidence of ulcerations or fissures.

PROTOCOL AND MANAGEMENT

The patient was provided with detailed information about the procedure including potential risks and complications such as swelling and pain at the injection sites. After written informed consent was obtained, the injection sites were prepped using 65% alcohol. Using a butterfly blood collection set with a 21gauge needle, approximately 20MLs of whole blood were collected in 2-10 ML test tubes. Utilizing an adaptation from a published platelet processing protocol [13], each tube was then deposited into the centrifuge (Figure **1**). The centrifuge was then set for 10 minutes at 3600 RPM. After the centrifuge process was complete, both platelet rich and platelet poor plasma were extracted from each test tube and combined with .5MLs of a proprietary mixture of a platelet aggregator and platelet activator yielding approximately 10 ML's of the combined mixture. This mixture was then placed into a 10 ML syringe with a 27gauge needle. The injection sites were identified below the knee along the L4 and L5 skin dermatomes bilaterally. Approximately three 2 ML injections were administered along the L4 dermatomes and two 2 ML injections along the L5 skin dermatomes bilaterally. Each injection site was massaged thoroughly in effort to disperse the neurogenic growth factors evenly. The injection site were covered with bandages and the patient was monitored for approximately 10 minutes before being discharged and given post therapeutic materials and follow-up appointment for two weeks.

TREATMENT OUTCOMES

Treatment outcomes were measured using the *PlasmaGenix Treatment Efficacy Treatment Scale* (Table **1**) for 12 weeks and the following variables were followed and recorded throughout treatment:

1. Pain intensity: 1-10 (10 being the worst pain)

2. Pain relief: None, Moderate, Significant.

3. Sensory Perception: Vibratory, Proprioception, Simmes-Weinstein monofilament being within normal limits or diminished.

4. Quality of life: According to the Karnofsky performance status scale [14].

5. Mood: 1-10 (10 being the worst mood)

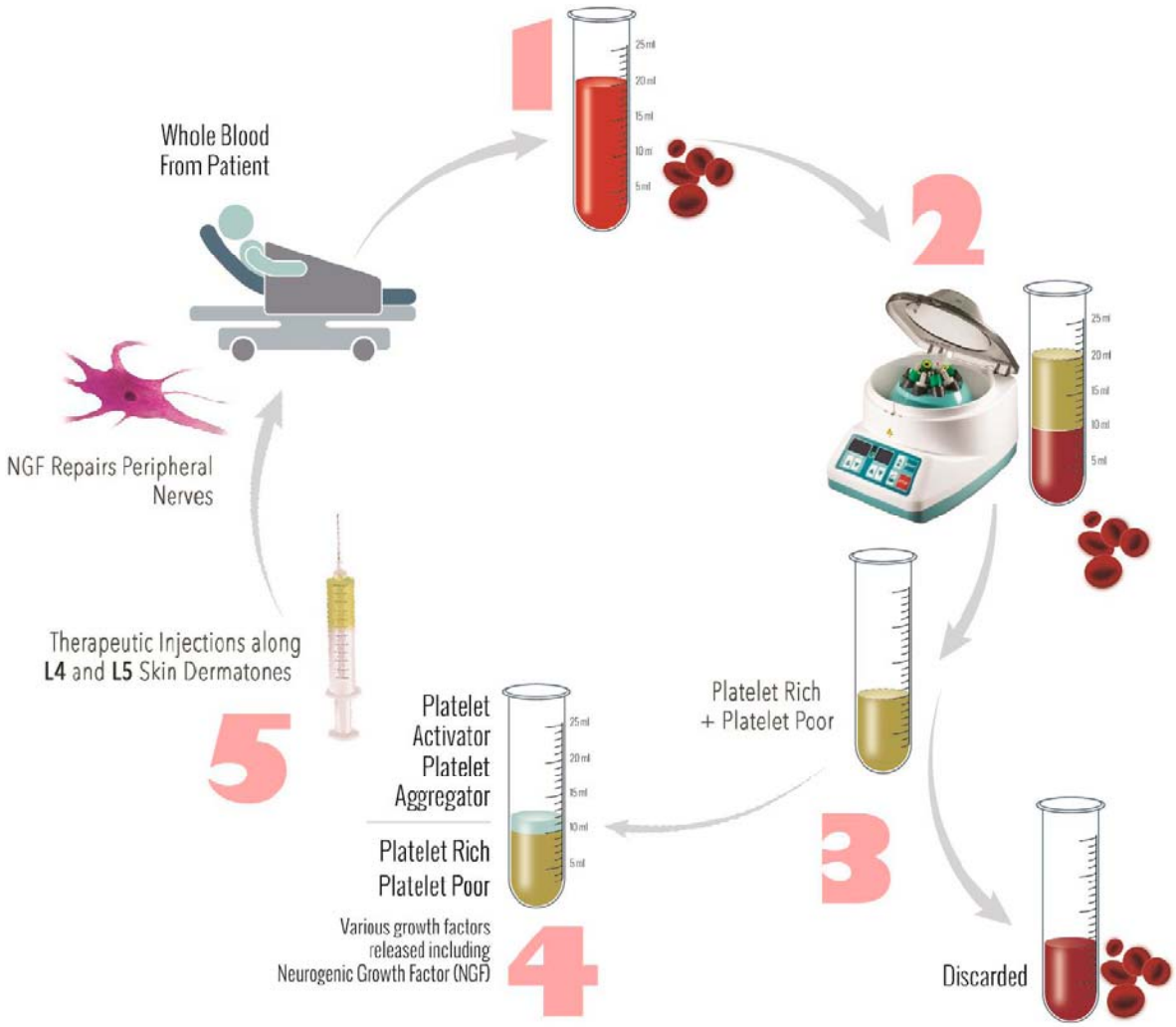

Figure 1:

6. Function: flexibility, standing longevity, walking distance being characterized as diminished, improved or same.

Within the first 2 weeks of treatment, the patient reported moderate relief of her pain and an improvement in flexibility and ability to walk. Within 4 weeks, the patient reported significant relief of her pain and improved function. Within 6 weeks, the patient reported significant relief of her pain and improved function, quality of life and mood.

Within 6 weeks, the patient reported significant relief of her pain and improved function, quality of life and mood. Additionally sensory perception was found to be improved on medical exam and minimal hair growth was appreciated. These observations are documented.

Three months (12 weeks) after the first injection, the patient reported to not be limping anymore, being able to bend her left leg (which she had not been able to do for over 10 years), and able to sit cross-legged. She is now able to walk up a flight of stairs with more ease due to increased mobility and hopes to be able to go hiking again in the near future.

DISCUSSION

In this investigation, we report the case study of a patient whose symptoms were completely relieved following a proprietary new protocol and treatment plan based on the regenerative properties of Activated Autologous Platelet Rich Platelet Poor Plasma (AAPRPP).

Several studies have demonstrated the positive effect of platelet rich plasma when administered in humans. Evidence which supports efficacy of platelet rich plasma includes case studies [15,16], cohort studies [17,18,19], and a randomized controlled trial [20].

Table 1: Efficacy Measurement Scale

	Treatment #1 1st Week	Treatment #2 3rd Week	Treatment #3 5th Week	Treatment #4 7th Week	Treatment #5 9th Week	Treatment #6 11th Week
Pain Intensity	5-10	4-5	0-4	No Pain	No Pain	No Pain
Pain Releif	Moderate	Significant	Significant	Significant	Significant	Significant
Sensory Perception	VIB Prob Mono-Fil Diminished	VIB Prob Mono-Fil Diminished	VIB Prob Mono-Fil Diminished	VIB (WNL) Prob (WNL) MonoFil (WNL)	VIB (WNL) Prob (WNL) MonoFil (WNL)	VIB (WNL) Prob (WNL) MonoFil (WNL)
Quality of Life	70	80	85	90	90	95
Mood	3	5	8	9	9	9
Function	Flex: Limited Standing: Walking: Limited	Flex: Improved Standing: Improved Walking: Improved	Flex: Improved Standing: Improved Walking: Improved	Flex: Improved Standing: Improved Walking: Improved	Flex: Improved Standing: Improved Walking: Improved	Flex: Improved Standing: Improved Walking: Improved

1. Pain Intensity: 1-10 with 10 worst.
2. Pain Releif: Significant, moderate, some, no improvement.
3. Sensory Perception: vibratory, proprioception, simmes-weinstein monofilament.
4. Quality of Life: See karnofsky performance status scale [14].
5. Mood: 1-10 (1 worse with 10 feeling the best).
6. Function: Flexibilty, standing longevity, walking distance.

The randomized controlled trial conducted in the United States evaluated the role of platelet rich plasma as a treatment for diabetic foot ulcers [21]. Study participants included diabetes patients between the ages of 18 and 95 years suffering from an ulcer. 72 patients were randomized to receive standard of care with platelet rich plasma gel or saline gel. During a 12 week period, wounds healed in 68.4% of the platelet rich plasma group compared to 42.9% of the saline gel group. Furthermore, patients healed wounds in the platelet rich plasma group by a mean of 4.5 days less than the saline gel group.

The benefits of recombinant nerve growth factor in neuropathy have been shown previously. This study shows the benefits of autologous growth factors derived from activated platelets [22, 23]. A clinical trial would be beneficial to measure the possible mechanism of action of platelet rich plasma on peripheral nerves. Neurogenic growth factors may be released during the activation phase of the platelet rich plasma preparation. Additionally, quantitative studies such as nerve conduction studies and skin biopsies to measure peripheral nerve density may be helpful in identifying ways to provide interventions to prevent peripheral neuropathy development in HIV patients. This method would offer a valuable alternative to current and ineffective treatment options. Important advantages are that this method of treatment is easy to use, has point of care administration, and relatively quick and painless application which facilitates compliance. Another inherent advantage is that AAPRPP is derived from the patient's own blood, reducing the risk of allergic or adverse reactions other than minimal injection site tenderness.

In summary, platelet rich plasma may act directly on neurons to promote axon regeneration thereby alleviating neuropathic pain. The present research provides evidence that platelet rich plasma may be used to treat HIV-associated neuropathy which adds new data to the extant literature on this topic.

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