A Multicenter, Retrospective, Case Series of Patients with Charcot Neuroarthropathy Deformities Undergoing Arthrodesis Utilizing Recombinant Human Platelet-Derived Growth Factor with Beta-Tricalcium Phosphate

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Statement of Purpose

Hypothesis: The hypothesis for this study was that the utilization of recombinant human platelet-derived growth factor bone grafting would lead to union in the majority of Charcot reconstruction cases.

Literature Review

The increased utility of operative intervention for complex limb salvage in entities such as Charcot neuroarthropathy has resulted in an awareness of the intricacies of bone consolidation, despite the availability and use of improved fixation constructs. Nonunion rates have been reported as high as 41% with high risk populations of patients including those with Charcot neuroarthropathy (1,2). In Charcot reconstruction, fusion is critically important in achieving the end goal of successful limb salvage.

Autograft, most commonly harvested from the iliac crest, has the advantages of good osteoinductive and osteoconductive properties, however, it brings with it potential complications such as donor site morbidity, bleeding, infection and persistent pain (3). Allografts provide a solution to the issues of harvesting autograft, but their drawbacks include the risk of disease transmission, nonuniform preservation practices, potential structural weaknesses, cost, variable availability, and possible increased risk of nonunion or failure (4,5).

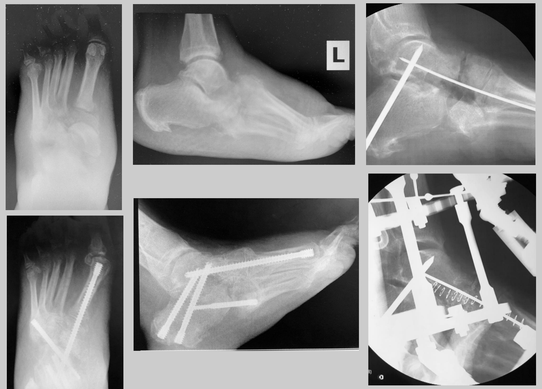
An ideal grafting material would be one that eliminates complications from harvesting and has osteoinductive and osteoconductive properties to facilitate faster healing of high risk joint fusions (6).

Platelet-derived growth factor (PDGF) is a graft material that has many of these desirable qualities in that it stimulates fibroblastic activity and the healing cascade (7). Recombinant PDGF-BB, is even more promising in its ability to stimulate bone growth. In combination with the osteoconductive properties of a beta-tricalcium phosphate scaffold (rhPDGF-BB/B-TCP), a powerful bone graft substitute is created which has shown comparable efficacy and non-inferiority to autograft in foot and ankle fusion rates (8).

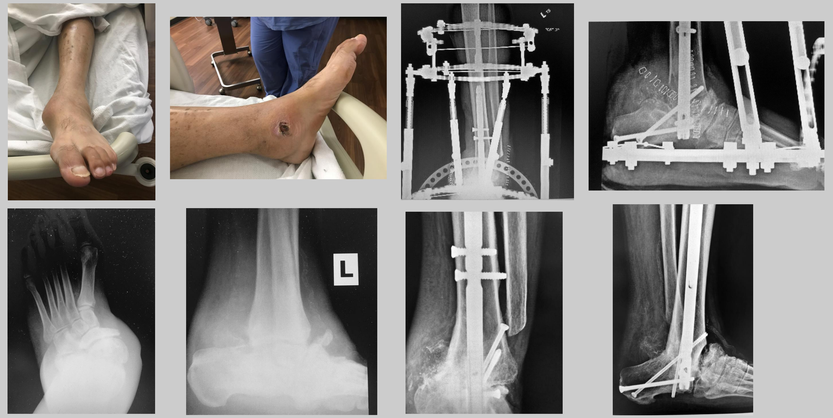
Methodology

Study Design: Level IV Retrospective Multi-Center Case Series
Conflict of Interest: Wright Medical (JL,RM,MC)
Population: N = 98 patients, Mean 14 month follow up.
Inclusion Criteria: All patients who underwent reconstruction of Charcot arthropathy utilizing rhPDGF-BB/B-TCP bone grafting for joint fusions from September 2015-2019.
Exclusion Criteria: Patients with less than 12 months of follow up at time.
Procedures: Reconstruction of Charcot Arthropathy utilizing rhPDGF-BB/B-TCP for augmentation of fusion sites.
Primary outcome: Primary outcomes for the study were: (1) fusion rates; (2) average time to fusion; (3) complications: wound healing, infection, amputation
Methods: Retrospective chart and radiographic review of all patients meeting the aforementioned inclusion criteria.

Procedures: Complex Charcot Arthropathy Reconstructions



Case 1: 50 y/o diabetic WF has unstable Charcot deformity on the right foot . She underwent a midfoot osteotomy with external fixation and beaming of the foot for a panpedal fusion with rhPDGF-BB/B-TCP. There was successful fusion achieved at 16 weeks



Case 2: 47 y/o diabetic HM developed a Charcot deformity in his left ankle and a wound on the medial side of his ankle. Patient underwent a talectomy with tibiocalcaneal fusion via IM Nail and external fixator with rhPDGF-BB/B-TCP. He achieved a successful fusion at 20 weeks.

Results: Primary and Secondary Outcomes

Table 1: Demographics

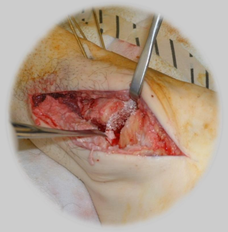
Variable	N
Patients	98 Patients (223 joints)
Sex	61 Males 37 Females
Average Age	63 years
Diabetic	76 Patients
Neuropathic (Non diabetic)	22 Patients
Smokers	25 Patients
Ulceration (preoperatively)	19 Patients

Table 2: Primary Outcomes

Primary Outcomes	N
Fusion Rate (Joints)	217/223 (97.3%)
Average Time to Fusion	13 weeks
Average Time to WB status	13 weeks
Average Follow up time	14 months
Death Following the Procedure	2 Patients
Nonunions (All ankle joints)	6 Patients
Complications: (Infection, Broken Hardware, Chronic Pain & Wound Healing)	24 Patients
Below the Knee Amputations	3 Patients
Adverse Reactions Pertaining to Grafting Material	None

Table 3: Case Results

Joints Fused	Procedures	Percentage
Ankle	46	20.62
Subtalar	54	24.22
Talo-Navicular	54	24.22
Calcaneal-Cuboid	32	14.35
Medial Column (Navicular-Cuneiform and Tarsometatarsal)	34	15.25
TibioTaloCalcaneal	2	0.89
Fibula	1	0.44



Intraoperative Application of rhPDGF-BB/B-TCP

Analysis & Discussion

A total of 98 patients underwent Charcot reconstruction with attempted arthrodesis of 223 joints using rhPDGF-BB/B-TCP. There was an 97.3% joint fusion rate (217/223) in the series with an average time to fusion of 13 weeks, with fusion being defined by radiographic consolidation and clinical findings. The average return time to weightbearing status was 13 weeks with follow up time ranging form 12-36 months. There were 6 nonunions in the series that all developed at the ankle joint with three patients requiring below the knee amputations. The overall complication rate in the study was 26.5% (26/98) for this high risk patient population. CT scans were obtained in 37/98 patients to assess for fusion versus nonunion. There were no adverse reactions or complications specifically related to the grafting material.

In 2013, DiGiovanni et al. published a prospective randomized control trial on the use of recombinant platelet derived growth factor in hindfoot and ankle fusions. In that study, 434 patients requiring hindfoot or ankle arthrodesis were randomized 2:1 into autograft or rhPDGF-BB/B-TCP groups. They reported fusion rates of 61.2% and 62% for the groups with fusion defined as > 50 % osseous bridging confirmed using CT scans. Glazebrook et al reported that only 25-30% osseous bridging was required for successful clinical outcomes as determined by SF-12, FFI and AOFAS clinical outcomes questionnaires (9). Clinical healing of 87.6% and 86.2% at fifty-two weeks. Fewer side effects were also reported in the PDGF group (8).

Fusion rates using recombinant human platelet-derived growth factor compared very favorably to historical autograft controls, especially in this high risk Charcot patient population (2). This series is, to our knowledge, one of the largest samples described in the literature, and that we had patients with follow up as long as three years, in spite of the comorbidities associated with these patients.

In conclusion, this case series review of using rhPDGF-BB/β-TCP for arthrodesis in patients with Charcot deformities demonstrated a high rate of fusion, reasonably short time to fusion, complication rates comparable to other interventions, and no adverse events related to the graft material, rhPDGF-BB/β-TCP, even in this high-risk patient population.

References

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