Local administration of adipose derived stem cells for facet joint syndrome: 
Case report and discussion of the possible pathophysiological mechanisms

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Abstract

Facet joint syndrome is a common disabling condition. Degeneration of the motion segment leads to a loss of height of the segment resulting in an athrosis of the facet joint. The degenerative changes in the joint result finally in a chronic inflammatory process. Injection of corticosteroids and oral pain medication are of little value in the long-term treatment. Advances in regenerative medicine revealed immune-modulatory properties of stem cells.

In a 58 year-old male, suffering from facet joint syndrome and spinal canal stenosis, adipose derived stem cells were injected into the facet joint under fluoroscopic guidance. The patient remained pain free over a period of at least 6 months. Injection of adipose derived stem cells might be a promising novel therapy for facet joint syndrome.
**Introduction**

Lumbar spinal facet joints were first suggested in the medical literature as a source of low back and lower extremity pain in 1911. Since then, the so-called “facetogenic back pain” has become a widely accepted diagnosis, though still a controversial entity in the literature. The strongest support comes from investigations reporting successful relief of back pain following intra-articular or peri-articular joint injections. Estimates of the prevalence of lumbar facet joint pain based on single diagnostic blocks have been reported to range from 7.7% to 75% among patients reporting back pain. The facet joint syndrome is a degenerative process of the joints cartilage, involving the immune system, and producing local inflammatory reactions with synthesis of pro-inflammatory cytokines and metalloproteinases. Due to the inflammatory nature of the disease, injection of glucocorticoids into the affected joint has become a common treatment option. However the results of various studies suggest that these injections are of little value in the long-term treatment of patients with chronic low back pain.

Recently it could be shown that interactions of human bone marrow derived stem cells (MSCs) can inhibit or limit inflammatory responses and promote the mitigating and anti-inflammatory pathways. It was shown that when MSCs are present in an inflammatory environment they may alter the outcome of the on-going immune response by altering the cytokine secretion profile of dendritic cell subsets and T-cell subsets, thereby resulting in a shift from a pro-inflammatory environment toward an anti-inflammatory or tolerant cell environment. However bone marrow derived stem cells are not easy to access and puncture of the iliac crest is painful and accompanied with a substantial morbidity.

Several studies have found no significant qualitative differences such as growth kinetics and multi-lineage differentiation potential between adipose derived stem cells and bone marrow-derived stem cells. Therefore ADSCs seem to be ideal for treating degenerative inflammatory processes in the musculoskeletal system. Various injections of stem cells in bigger joints like the knee or hip are reported in human and veterinary medicine. To the best of our knowledge we report the first adipose derived mesenchymal stem cell (ADSC) injection for facet joint arthritis in the human.
Case report

A 58-year-old male presented with a history of nearly 10 years of facet joint syndrome. Several diagnostic and therapeutic injections of the facet joints L4/5 were performed. The pain resolved after nearly all injections however the pain free interval after each injection became shorter over time. At the time of presentation in our outpatient clinic he reported lower back pain with a severity of 8 on the visual analogue scale and mild radicular pain (L5) VAS of 2. The lumbar MRI revealed spinal canal stenosis at L4/L5 and severe facet joint arthrosis. Showing an enlargement of the joint and fluid collections within the joint in the T2 weighted image. (see figure 1 and 2)

Lipoaspiration was performed under sedation. Making a small incisions (3 mm in size) Then 200ml of modified Klein’s solution were injected into the abdominal fat tissue. (1 ml epinephrine 1: 1000, 20 ml Ultracain 2% , 12ml 8.4% sodium hydrogen carbonate to 1000 ml saline). Allowing the fluid to percolate uniformly through all layers for 10 minutes. Then 60 ml of fat were aspirated via micro-cannular liposuction. Leaving the incision wounds open to drain out fluid. A small amount of fluid was left back in the tissue and was allowed to drain slowly over two days. This residual fluid provided analgesia in the immediate postoperative period.

Stem cells were processed using the InGeneronARC™ Tissue Processing Unit. After preparation of the ADSCs they were injected under fluoroscopic guidance into the facet joints at L4/L5 on both sides.

The patient showed an immediate response in the pain level after 24 hours. The pain level decreased to VAS in the back of 0 at rest and a VAS at 2 during exercise. There was a minor improvement of the leg pain from 2 to 1 on the VAS. The pain levels did not change over a 6 months postoperative period. The patient remains pain free concerning the backache and suffers from minimal leg pain (VAS1 during exercise)
Discussion

In degenerative lumbar spinal disorders, pain is often caused by inflammatory reactions to degenerative changes. Inflammatory cytokines were detected in the facet joint, which generated arthropathic changes in degenerative lumbar spinal disorders. Subsequently lumbar pain is caused by chemical factors associated with inflammation such as inflammatory cytokines. This theory is supported by the fact that non-steroidal anti-inflammatory drugs and corticosteroids show a better clinical effect than opioids or other analgetics.\(^\text{10}\)

The immunosuppressive effect of stem cells is of great interest for the prevention of inflammatory reactions in degenerative diseases of the musculoskeletal system. Successful treatment has also been reported in mice with experimental autoimmune diseases, such as collagen-induced arthritis, the animal models of human rheumatoid arthritis and multiple sclerosis. However, conflicting results on the mechanisms developed by stem cells to suppress inflammation are still under debate.\(^\text{2, 22}\)

We employed in our case adipose derived stem cells, because it could be shown in several studies that there is no substantial qualitative difference between bone marrow derived and adipose tissue derived stem cells. The main difference, however, is the significantly higher number of regenerative cells in adipose tissue and ease of access to adipose tissue compared to bone marrow. Harvesting of adipose tissue is less invasive and yields high counts of regenerative cells. Bone marrow shows relatively low cell counts of regenerative cells and typically requires the expansion of MSCs in culture prior to use in clinical applications, resulting in alterations of gene expression.\(^\text{19}\) Adipose-derived stem and regenerative cells can be isolated in large numbers and administered back to the patient without cell expansion.\(^\text{18}\) Furthermore, minimally manipulated cells result in higher clinical safety and efficacy. Systematic studies confirm that, adipose-derived and bone marrow-derived stem cells meet the following criteria.\(^\text{21}\)

This case report indicates that ADSCs might be used for regulating inflammatory responses and could offer therapeutic benefit in degenerative diseases of the musculoskeletal system. Like Treg cells, ADSCs possibly migrate to the joints where they can act locally inside the inflamed synovium to decrease the proliferation and function of immune cells via the secretion of inhibitory soluble factors. They might also act systemically to suppress the host immune response through a shift in the Th1/Th2 cell balance, indicating that ADSC-induced immune suppression is not mediated by a single or unique mechanism.\(^\text{1}\) This may have important therapeutic applications far beyond the field of inflammatory degenerative diseases. However this is only a single case reported. Further studies are needed to examine the underlying biochemical reactions within the joint and the long term results of such injections.
Literature

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Figure 1. T2 weighted sagittal MRI of the 58-year old patient showing the underlying pathology with a spondylolisthesis grade I, facet joint degeneration and spinal canal stenosis.
Figure 2. T2 weighted axial MRI of the 58-year old patient showing severe facet joint degeneration and spinal canal stenosis