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EDITORIAL OPEN ACCESS

Acute diabetic wound treatment with adipose derived stem cells

Yusuf Kenan Coban, Orhan Gazi Dinc, Serap Topaloglu

THE ACUTE INFECTED DIABETIC WOUND PROBLEM

Type 2 diabetes mellitus is a multi-systemic disease accompanied by microvascular and macrovascular complications. Diabetic patients often exhibit impairment in the healing of acute wounds. Multifactorial mechanisms play role in the impaired healing of diabetic wounds. Microvascular disease, biochemical abnormalities, limited joint mobility, increased susceptibility to infection, diabetic skeletal disease and microangiopathy are the main factors. Infected ulcerative wounds show purulence and two or more signs of inflammation such as warmth, edema, pain, lymphangitis, erythema and lymphadenopathy. Wagner classification describes these ulcers with associated involvement of tissue destruction in foot. If ulcer is deep to tendon it is stage 2. If stage 2 is with abscess it is stage 3. Stage 4 and 5 are localized or total foot gangrene. Figure 1 shows possible scenario that happens within acute infected foot gangrene.

Control of infection, improve microangiopathic/ macroangiopathic complications and the management of neuropathic ulcer are main targets in the struggle with diabetic foot ulcer. The removal of callus, reduction of weight bearing forces, and management of ischemic foot are done with medical or surgical therapies. Figure 2 shows the main factors which plays role in diabetic

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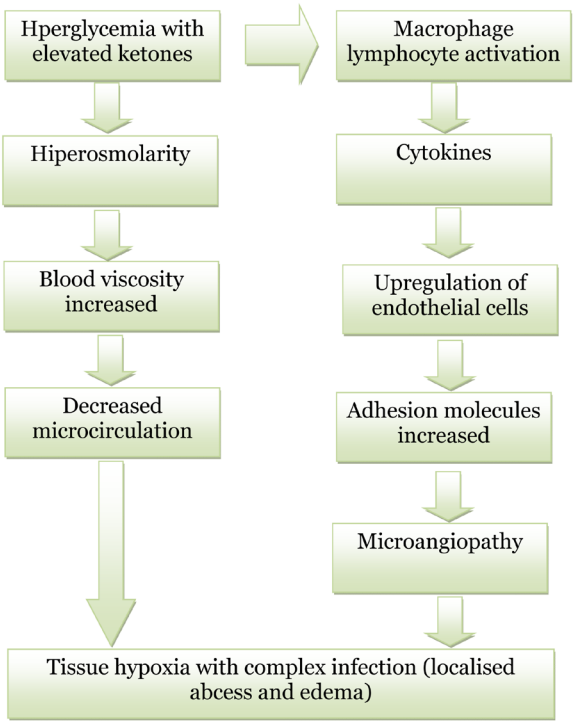

Figure 1: Possible scenario occurs within acute infected foot gangrene.

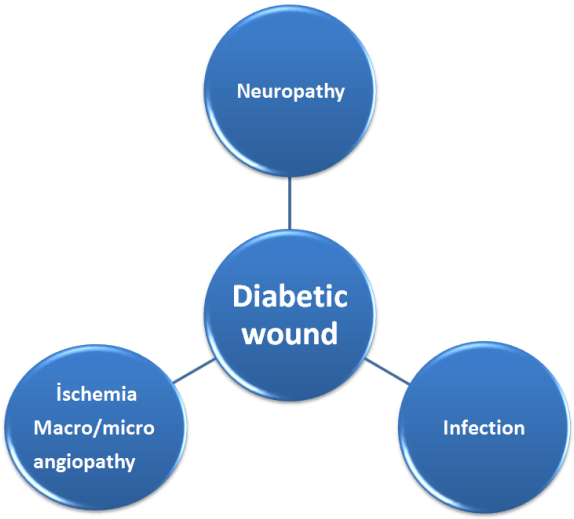

Figure 2: Main factors playing role in diabetic foot ulcer.

wound. Medical treatment consists of aspirin (100 mg/day), analytic antibiotherapy against infection, control of hyperglycemia with insulin treatment and decreasing local edema with negative pressure wound therapy. After control of local negative factors within 10 days' management of acute infected gangrene, early surgical debridement and application adipose derived stem cell to the soft tissue defects is the therapy modality which we use in our clinic recently. An active energetic management of wound care with an early application of adipose derived stem cells (ADCs) therapy may save the patient from major amputation.

ACUTE MEDICAL MANAGEMENT ALONG WITH AGGRESSIVE WOUND CARE OF THE DIABETIC WOUND

Diabetic ketoacidosis induced inflammation has been a recent focus of investigation. It has been suggested that ketones are directly involved in promoting proinflammatory factors and eliciting systemic inflammation [1]. Hyperosmolar hyperglycemic syndrome (HHS) and diabetic ketoacidosis are diabetic medical emergencies that require immediate attention. Although they have certain common features they differ in hyperglycemic status and presence of ketoacidosis. The underlying difference is that in HHS, there is still some residual insulin secretion that prevents ketosis [2]. Diabetic ketoacidosis occurs from a relative or absolute insulin deficiency and characterized by accumulation of acidic ketones and glucose in the bloodstream. Urgently, rehydration fluids and insulin must be given. The role of elevated ketones in macrophage and lymphocyte activation cytokine release and perturbation of endothelial cells in the capillaries has been reported in type 1 diabetic patients [3]. In turn, vascular endothelium plays a key role in amplification of inflammation by increased cytokine/chemokine production and subsequent upregulation of proadhesive phenotype [6]. Increased serum adhesion molecules have been reported in diabetic patients [5]. So, strict control hyperglycemia is absolute indication to stop the progress of microangiopathy/macroangiopathy in these patients. Another keystone in medical management of acute edematous foot gangrene is anticoagulant treatment which must be started at time of admission of patient.

We routinely use negative pressure wound therapy for every case of acute purulent ulcerative diabetic foot (Figure 3). This therapy modality provides evacuation of stagnant purulent collection and furtherly brings positive factors from systemic circulation to the wound site. Both local infection control and edema resolution is obtained at the same time period. A period of 10–15 days following to admission is generally enough to have a prepared wound for ADCs application.

Figure 3: (A) An acute infected diabetic foot gangrene at time of admission, (B) Following to 10 days' medical and negative pressure wound therapy the wound is seen as resolute edema with necrotic great toe of the right foot of the 45-year-old diabetic patient, and (C) Left, 14 days after adipose derived stem cell therapy to wound sites a well granulation covering the defective are is seen right; (D) One month later, near complete healing secondary to skin grafting.

THE FUTURE OF ADIPOSE DERIVED STEM CELL THERAPY IN DIABETIC FOOT ULCER

The treatment of acute diabetic wounds remains unsatisfactory, although new therapy modalities are being developed. There is clinical need for developing more effective treatment strategies. In particular, adipose derived stem cells (ADCs) exhibit an excellent potential for wound healing. Several studies have shown their various advantageous properties of paracrine secretion activity, immunomodulatory effects and ability to differentiate into fibroblasts and endothelial cells [6–8]. Human bone marrow-derived stromal cells (hBMSCs) and human adipose derived stromal cells (hADSCs) are used in cell-based therapy. The ADCs represent an attractive alternative of pluripotent cells with characteristics similar to BMSCs. Adult stem cells have prolonged self renewal

capacity with the ability to proliferate and differentiate into various cell types [9]. Data relating to the stem cell therapy and processes associated with adipose derived stem cells (ADCs) and bone marrow stromal cells (BMSCs) has developed remarkably in the past 10 years. The paramount importance of blood supply in the healing of wounds has been long appreciated. Recent research has highlighted the unique role of stem cells in neovascularization following injury because of their characteristics. Increased capillary density after ADCs injection around the wound bed is obvious with naked eye. There are at least two mechanisms involved in contribution of ADCs to the reconstruction of local blood vessels including direct differentiation into vascular vessels and secretion of angiogenic growth factors [10]. The longevity of ADCs therapy in acute diabetic wound necessitates larger clinical series. For the future, there are questions to be answered; firstly it has been demonstrated that BMSCs, the numbers significantly decrease with age [11]. If this is true for ADCs, the use of ADCs in elderly population might be problematic. Secondly, stem cells are present in many if not all tissues of adult animals and contribute to the tissue renewal. In chronic disease state, the number of these cells is not clearly known. So the use of it and its restriction must be delineated with controlled studies. Now, BMSCs have an important but not yet fully understood role in wound healing. ADCs may play the same role for the acute diabetic wounds.

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Keywords: Adiposederived stem cell, Diabetic foot ulcer, Therapy

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Author Contributions

Yusuf Kenan Coban – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Orhan Gazi Dinc – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Serap Topaloglu – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

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