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Clinical Significance Of The C-786t Polymorphism Of The Nos3 Gene In Purulent-Necrotic Lesions Of The Lower Extremities Associated With Diabetes Mellitus

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Abstract: Purulent-necrotic lesions of the lower extremities developing against the background of diabetes mellitus are currently considered one of the most pressing problems of modern medicine. These complications are characterized by high rates of disability and limb amputation. In recent years, the role of genetic factors in the development of this pathology has gained particular importance.

In the present study, a comparative analysis of the genotype frequency distribution of the C-786T polymorphism of the NOS3 gene was conducted among patients with diabetes-associated purulent-necrotic foot lesions who underwent surgical or conservative treatment. The results demonstrated that the unfavorable C/C genotype of the NOS3 gene was more frequently observed in patients who required surgical treatment, whereas the wild-type T/T genotype may be associated with a milder course of the disease and better effectiveness of conservative therapy. The C-786T polymorphism of the NOS3 gene may serve as a significant genetic marker for predicting purulent-necrotic complications developing in patients with diabetes mellitus.

Keywords: Diabetes mellitus, diabetic foot syndrome, purulent-necrotic lesions, NOS3 gene, C-786T polymorphism, genetic markers, surgical treatment, conservative treatment.

1. Introduction: Diabetes mellitus is a nosological entity whose prevalence is increasing worldwide, and its late complications significantly reduce patients' quality of life. Diabetic foot syndrome is one of the most severe and socially significant complications of diabetes mellitus. In such cases, the development of purulent-necrotic processes often necessitates surgical intervention and is associated with a high risk of major amputations [3,4].

Recent studies indicate that microcirculatory disorders, endothelial dysfunction, and polymorphisms of genes related to nitric oxide synthesis play an important role in the pathogenesis of this condition [2,5]. The endothelial nitric oxide synthase enzyme encoded by the NOS3 gene is crucial for regulating vascular tone and tissue perfusion. Therefore, studying the C-786T polymorphism of the NOS3 gene is highly relevant for assessing disease severity and developing individualized treatment strategies [1,6].

2. Methods

A total of 201 individuals were included in the study. Among them, 103 patients constituted the main group, which was further divided into two subgroups based on clinical classification criteria:

- **Group 1:** 58 patients with type 2 diabetes mellitus (T2DM) and purulent-necrotic lesions of the lower extremities;
- **Group 2:** 45 patients with T2DM without purulent-necrotic lesions of the feet.

The comparison group consisted of 98 conditionally healthy individuals.

Aim of the Study. To conduct a comparative analysis of the genotype frequency distribution of the C-786T polymorphism of the NOS3 gene among patients with purulent-necrotic lesions of the lower extremities associated with diabetes mellitus who underwent surgical or conservative treatment, and to assess the clinical significance of this genetic marker.

3. Results And Discussion

During the study, localization of purulent-necrotic processes was analyzed in 58 diabetic patients with purulent-necrotic foot lesions. Deep phlegmon of the forefoot was identified in 19.0% of patients (11/58), distal gangrene of the great toe and forefoot in 12.1% (7/58), combined gangrene of the great toe with deep

forefoot phlegmon in 31.0% (18/58), and gangrene of the toes in 8.6% of cases. These pathological processes were noted to occur more frequently compared to other localizations. Additionally, phlegmon of the lower leg was observed in 5 patients (8.6%), gangrene of the heel and lower leg in 2 cases, isolated heel gangrene in 3 patients, and localized dry necrosis of the toes and heel in 12.1% of cases.

A comparative analysis of the frequency distribution of the studied genetic markers was conducted between diabetic patients with purulent-necrotic foot lesions who underwent surgical treatment and patients without such lesions who received conservative therapy. As shown in Figure 4.6, the unfavorable C/C genotype of the C-786T polymorphism of the NOS3 gene was detected in 17.6% of surgically treated patients, while it was absent in 82.4% of patients in this group.

In contrast, the unfavorable C/C genotype was not detected in patients who received conservative treatment.

Analysis of genotype frequency distribution demonstrated that the heterozygous C/T genotype was present in both groups, accounting for 41.2% in the surgical treatment group and 14.3% in the conservative treatment group. Although the differences did not reach statistical significance, a trend toward a 4.2-fold higher frequency of the C/T genotype was observed in surgically treated patients compared to those treated conservatively ($\chi^2 = 1.9$; $p = 0.2$; OR = 4.2; 95% CI: 0.47–37.5).

Conversely, the wild-type T/T genotype was significantly less frequent among surgically treated patients compared to those receiving conservative therapy (41.2% vs. 85.7%, respectively) ($\chi^2 = 4.9$; $p = 0.03$; OR = 0.1; 95% CI: 0.013–1.04).

4. Conclusion

The unfavorable C/C genotype of the C-786T polymorphism of the NOS3 gene may be associated with a more severe course of purulent-necrotic foot lesions in patients with diabetes mellitus and an increased need for surgical treatment. In contrast, the wild-type T/T genotype may exert a protective effect and be associated with a relatively milder disease course. These findings highlight the importance of genetic studies in developing individualized prognostic assessments and treatment strategies for patients with diabetic foot syndrome.

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