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Role of Coxsackie virus B in Type 1 Diabetes- Brief Review

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Abstract

Diabetes is the chronic disease, which is known to develop due to the genetic autoimmune disorder leading to the destruction of the insulin producing β-cells or low production of insulin. Beside the role of the genetic factors in the genesis of the diabetes, other external environmental factors also known to be the cause. Studies revealed the association of the viral infection with the diabetes. Literature revealed the enterovirus mainly the Coxsackie virus has been found to be associated with the development of the diabetes. Studies showed the higher cellular immune response to the antigens of the Coxsackie virus B (CVB), at the onset of the diabetes. Experimental evidence of animal studies also favored the role of CVB. In the current scenario, we like to review the role and the presence of CVB in diabetic patients.

Introduction

Diabetes mellitus is considered as an autoimmune disorder, in which the immune cells recognize the insulin producing pancreatic beta cells and destroy them. Along with the genetic factors, non-genetic environmental factors also play its role in genesis of the diabetes. Studies revealed that the viral infections are considered as the major candidates for the development of the diabetes disorder. From past several decades the association of viral etiology with the diabetes has been studied. The association of the viruses with diabetes was studied including cytomegalovirus (CMV), Parvovirus, encephalomyocarditis virus and retroviruses [1-4]. Studies of association have been put forward between the Rota virus and diabetes and pointed out that the concurrence of the Rota virus infection and development of the autoantibody in children was reported [5] but was challenged by studies conducted by the Blomqvist et al. [6], leading to lack of evidence of association of the Rota virus in the etiopathogenesis of the diabetes.

Role of Enterovirus in Diabetes

Literature revealed that the diabetes has been found to be associated with the enterovirus. Studies including the meta-analysis found the significant association between diabetes and enteroviruses and confirmed using the application of molecular techniques [7]. The presence of Coxsackie virus higher titers of the neutralizing antibodies in serum found in the recent onset diabetic patients [8]. The increase in the rate of the autoimmunity has been found to be high in diabetic cases and has been associated with the enteroviruses [9]. Studies revealed that the enterovirus is involved in the initiation of the islet autoimmunity as well as progression to the glycemic stage [10].

Further CVB RNA has been detected during the onset or course of the diabetes [11]. The higher cellular immune response to the CVB has been demonstrated in the patients [12]. Not only was the immune response, the CVB isolated from the deceased child with diabetic ketoacidosis. Inoculation with the homogenates from the patient's pancreas into mouse, monkey and human cell cultures lead to the isolation of the virus and was related to a diabetogenic variant derived from Coxsackievirus B4 [13]. The presence of the CVB has been demonstrated in the pancreatic tissues of the diabetic patients [14]. Persistent enteroviral infection in the intestine might contribute to the pathogenesis and destruction of the beta cells of the pancreas. A study conducted by the Oikarinen isolated enterovirus from the intestinal biopsy from the 75% of the diabetic patients compared to the 10% in controls [15].

The beta cells of the pancreas express the enterovirus receptors including poliovirus receptor and integrin alpha 2 and beta3. Infections by viruses that target the beta cells bind to the promoters leading to the strong inflammation within the islets may thus

represent the initial step in the induction of autoimmunity [16]. Enteroviral infections are capable of unmasking the beta cells for the recognition of the $CD8^+$ T cells leading the production of the interferon production promoting the beta cell destruction [17].

A study conducted by Badia-Boungou et al. has demonstrated the presence anti-CV-B4 activity in saliva of patients with type 1 diabetes and concluded that it might acts as a useful marker to study the role of CV-Bs in the pathogenesis of the disease [18]. Further confirming, Engelmann et al. demonstrated the changes in the microRNA profile in the pancreatic cell due to persistent infection with CVB [19]. The direct demonstration of CVB in pancreatic tissue has been demonstrated using the application of the short fluorescent labeled oligonucleotide probes proving the direct role of CVB in genesis of the diabetes [20].

To conclude the CVB has been evolved as one of the important factor in the Type 1 diabetes and further studies are needed to establish its role and has to evaluated with the application of enteroviral vaccines which may acts as a potential therapy for preventing the Type 1 diabetes.

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