Case Report

**Type 1 Diabetes Mellitus (T1DM) and Congenital CMV Infection**

Elizabeth K E* and Dhanya Unnikrishnan

*Department of Pediatrics, SAT Hospital, Govt. Medical College, Thiruvananthapuram, Kerala, South India

**Abstract**

T1DM due to molecular mimicry can occur following intrauterine infection. One-year-old girl, diagnosed case of congenital CMV infection, who discontinued valganciclovir, presented with brittle T1DM. As CMV PCR was positive, valganciclovir along with insulin was restarted and showed clinical improvement and glycemic control.

**Keywords:** Congenital CMV Infection; T1DM, Molecular Mimicry; Valganciclovir

**Introduction**

Congenital CMV infection is not uncommon. Association of CMV infection and T1DM is known [1]. An infant with congenital CMV infection, who discontinued antiviral therapy and later developed T1DM, is reported.

**Case Report**

One-year-old girl was referred with brittle T1DM. She was the 2nd child of third degree consanguineous marriage, with a birth weight of 2 Kg, born at 32 weeks of gestation. At 4 months of age, she was evaluated in the same hospital for growth retardation, severe pallor, hepatosplenomegaly, microcephaly, developmental delay and sensori-neural deafness, but had no chorrioretinitis. Her weight, height & head circumference were < -3 Z score: 3.5 Kg, 55 cm and 33 cm respectively. Her CMV IgM was positive and IgG was twice than mother's titre and urine showed CMV inclusion bodies. Her hemoglobin was 7 g/dl, WBC Count 3500/ cu mm, Platelets 90,000/cu mm, Bilirubin 2.2 mg/dl and AST/ ALT 420/280 U/L. She was started on valganciclovir and hearing aid was given, but discontinued medication and was lost to follow up. After 8 months, she presented with brittle T1DM. Her HbA1C was 12%. She had growth retardation, pallor, hepatosplenomegaly, sensorineural deafness, developmental delay and microcephaly. Her weight, length and head circumference were < -3 Z score: 6 Kg, 64 cm & 40.5 cm respectively. Hemoglobin was 6.8 g/dl, Platelets 100000/cu mm, Bilirubin 2 mg/dl, and AST/ALT 620/470 U/L.

CMV viral load test was estimated using laboratory-developed tests (LDTs) in the virology lab and the quantitative PCR DNA measured viremia in a range of 150-10,000,000 copies/mL. CMV PCR was positive in blood, saliva and urine. Urine viral load was maximum 69, 17416 copies/mL. In blood and saliva, it was 54, 00678 and 5196785 copies/ml, respectively.

She was already on dietary therapy and regular insulin, but hyperglycemia was uncontrolled. After starting valganciclovir, in 10 days, glycemic control was achieved on 0.7 units/Kg/day of regular insulin. While on treatment, her serial blood counts and liver function improved and on completion of antiviral therapy for 6 weeks, repeats CMV PCR was negative. At 4 months follow up, her Hb A1C dropped to 8%.

**Discussion**

T1DM results from a variety of causes; monogenic disorder to autoimmunity to environmental causes. Various viruses have been implicated in inducing autoimmunity and T1DM due to molecular mimicry and viral persistence [1, 2, 3, 4]. Association of congenital rubella syndrome and T1DM to increased islet cell surface antibodies has been reported [5]. Both congenital and post-natal CMV infection had been linked to T1DM [6,7,8]. CMV infection was shown to induce islet-cell antibodies that react with a 38 kD auto antigen present in human pancreas [9]. A CD4+ T-cell clone reactive to β-cell auto antigen glutamic acid decarboxylase - GAD65 isolated from a prediabetic patient with stiff man syndrome was found to cross-react with CMV DNA binding protein, revealing autoimmunity induced by molecular mimicry [10]. Strong correlation between CMV genome and islet cell auto antibodies detected in diabetic patients had suggested that persistent CMV infection may be a risk factor for T1DM [8]. This observation had been further evaluated on Swedish infant cohort with congenital CMV and T1DM [6].

CMV DNA estimation methods vary from lab to lab. As quantitative PCR DNA for CMV viral load assessment and reporting units vary according to the laboratory developed tests, comparisons can be done only using repeat tests in the same lab... It is understood that CMV DNA value of 100 000 copies/mL in a laboratory may be reported as 100 copies/mL (3 log10 difference) with a different LDT in another laboratory.

This case is reported for sensitization of paediatricians on this
association of T1DM and congenital CMV infection. This is important as congenital CMV infection is not uncommon and also highlights the missed opportunity as the child could not complete antiviral therapy at first instance. The observation that glycemic control could be obtained in 10 days of restarting valganciclovir was remarkable, which may be a boon to similar patients.

References