

**Case Study**

*IJCA*, Vol. 3, No. 3, Aug. 2017.13-15.

## Digeorge syndrome presenting with uncommon cardiac anomaly and hepatomegaly

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Received: 12 Jan 2017

Accepted: 25 June 2017

### Abstract

Digeorge syndrome is caused by microdeletion of a large region of chromosome 22q11.2 lead to the abnormal development of the third and fourth pharyngeal pouches. This syndrome is characterized by hypoparathyroidism, cellular immune deficiency secondary to thymic hypoplasia, congenital heart disease and dysmorphic facial features. In this case report, we describe a 4month old boy who presented with respiratory distress due to cardiac anomaly (Large PDA) that was hypocalcemic, thrombocytopenic, lymphopenic and had hepatomegaly and history of seizure in neonatal period.

Because of recurrent opportunistic infection, this infant was suspected of immune deficiency. He died after about 4 month hospitalization due to severe sepsis and multi organ failure feature. Genetic study confirmed chromosomal 22q11.2 deletion and Digeorge syndrome after his death.

**Keywords:** Digeorge syndrome, Cardiac anomaly, hepatomegaly

### Background

Digeorge syndrome is characterized by neonatal seizure, tetany and increased susceptibility to infection, because of underlying hypocalcemia and abnormal T-cell function.

This patient has hypocalcemia due to hypoparathyroidism and T-cell deficiency because of thymus hypoplasia.

Other clinical presentation is cardiac malformation particularly those involve outflow tracts.

Deletion of chromosome 22q11.2 is the most common genetic abnormality in this syndrome and has an incidence of 1 in 4000 newborns (1, 3).

Only 7% of all cases with 22q11.2 deletion are inherited from a parent in an Autosomal dominant manner thus the majority of cases developed by de novo mutation.

Common abnormalities included multiple transcription factor that regulate the thymus and parathyroid development.

The facial appearance of patient with Digeorge syndrome is characterized by hypertelorism, micrognathia, short philtrum with fish mouth appearance, antimongoloid slant and short palpebral fissures.

We reported an unusual case of Digeorge syndrome that presenting recurrent infection and liver dysfunction.

### Case report

A 4-month-old boy was referred from cardiac surgery center to our pediatric intensive care unit.

He was born term (39 week gestational age) with cesarean delivery and discharged early from

Table 1. CD Marker results

Flow cytometry	Result %	Reference value %	Absolute count(cell/mcl)	Reference Absolute count(cell/mcl)
Total CD4	9	39-57	143	720-1348
Total CD8	7	17-46	111	220-960

hospital after 24 hours.

In second day of life, admitted in neonatal intensive care unit with respiratory distress.

Echocardiographic evaluation showed large patent ductus arteriosus (PDA) with septal deviation to the left and moderate to severe TR and PH.

Hepatomegaly and cardiomegaly was present in second day. There was a history of seizure in neonatal period due to hypocalcemia.

PDA closure was done at the age of 2 month. After cardiac surgery, surgeons could not to extubate the patient because of recurrent infection, prolonged hospitalization and malnutrition.

The patient referred to the pediatric children hospital with probability of immune deficiency. He had positive blood cultures for fungal and bacterial microorganisms.

Patient had dysmorphic feature consist of coarse face, hypertelorism and saddle nose.

In physical examination there was abdominal distention, hepatomegaly, spider angioma, and hypospadias. Frequent fever were detected.

In the laboratory study results; serum calcium level was under the normal range.

Due to frequent fever, hepatomegaly and high serum ferritin level hemophagocytosis and HLH were considered. But bone marrow and further study showed no evidence of HLH.

The primary evaluation of immune system and CD marker study were performed. Lymphopenia and CD4 and CD8 deficiency with low serum IgG level were detected and the combined immunodeficiency was diagnosed. Laboratory result are listed below and in Table 1.

*WBC : 4200 (cell/micro liter)*

*Diff:*

Lymphocyte:930(cell/micro liter)

Neutrophyle:2300(cell/micro liter)

Monocyte:740(cell/micro liter)

Eosinophil: 200(cell/micro liter)

*Hemoglobin:10.2 g/dl*

*MCV:30%*

*MCH:88 FL*

*MCHC:30.9 Pg*

*Platelet Count: 30000 (cell/micro liter)*

*Calcium level: 5 mg/dl*

*IgA level: 0.3 g/l (0.7-3.5)*

*IgG level:9 g/l (6.5-13)*

*IgM level: <0.4 g/l (0.4-2.63)*

*Ferritin level: 1200 ng/ml*

*NBT test: 100% (90-100)*

*Urine and serum amino acid chromatography:*  
Normal pattern.

### Discussion

Digeorge syndrome was originally described in 1967 by Di George et al (1), Digeorge is a developmental defect caused by a micro deletion of chromosome 22q11.2 has an incidence of 1 in 4000 newborns (2-3).

It is also known as velocardiofacial syndrome or CATCH 22 syndrome to describe the classical features of this syndrome (C-Congenital heart disease, A-Abnormal facies, T-Thymus hypoplasia, C-Cleft Palate and H- Hypocalcaemia due to Hypoparathyroidism. Autoimmune disorders, skeletal defects, renal abnormalities (2).

Chromosome 22q11.2 deletion syndrome is associated with immunodeficiency involving mild to moderate deficiency in peripheral blood T-cells. Thymic hypoplasia (partial Digeorge syndrome) or aplasia (complete Digeorge syndrome) leading to defective T-cell function is one of the main features of Digeorge syndrome (4-6).

The hepatomegaly was not reported in clinical presentation of this syndrome. But the rare condition is described as atypical complete Digeorge syndrome that presented by liver dysfunction, lymphadenopathy, rash and T-cell deficiency, resembles Omenn syndrome. This condition has not been fully characterized (7,8).

Perhaps hepatomegaly in our case to be justified with such conditions or hepatomegaly in the future to be reported in other cases with Digeorge syndrome.

Hypocalcaemia most frequently manifests during the neonatal period and is considered one of the phenotypic characteristics of the Digeorge syndrome.

Congenital heart defects are the major cause of mortality in this syndrome and have been reported in 75% of patients. The primary cardiovascular anomaly always involved the aortic arch system or the arterial pole of the heart. Findings include

tetralogy of Fallot, aortic arch anomalies and ventricular and atrial septal defects (9-11). However, our case presented with another form of cardiac anomaly (Large PDA) which has been reported less before.

Because of unusual presentation and little suspicion for diagnosis of this syndrome; unfortunately the genetic study with delay was proposed.

With earlier diagnosis, this infant might have survived with bone marrow transplantation. Nevertheless genetic study for her parents will be done until the next child born healthy.

### Acknowledgement

The authors would like to thank Ali-Asghar Clinical Research Development Center, for editorial assistance.

*Conflicts of interest:* None declared.

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