

## **DOWN SYNDROME AND DI GEORGE SYNDROME: A CASE REPORT**

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**Abstract:** *We present a case report of a newborn girl that was admitted at the University Childrens Hospital Braşov Romania, for dehydration and cyanosis. She also presented with the characteristic features of Down syndrome associated to symptomes of Di George syndrome. She presented with persistent hypocalcemia, IgA hypogamaglobulinemia and tymus agenesis that was seen on the radiographic image. Down syndrome is associated with multiple malformations but was rarely associated with Di George syndrome in the literature. We also review the main issues related with these diagnoses.*

**Key words:** *Down syndrome, Di George syndrome, diagnoses.*

### **1. Introduction**

Down syndrome is the most common genetic disease having a very distinct pattern of phenotypic presentation, making the diagnosis evident during the newborn period [2]. It is also a common cause of intellectual disability at children. There are several case reports regarding the occurrence of Down syndrome together with other genetic malformations but few with Di George syndrome.

### **2. Patient and method**

We present a newborn girl admitted at the age of 23 days at the Newborn Department of the University Children's

Hospital Braşov, for failure to thrive, marked cyanosis, difficult breathing.

She was born after a normal gestation of 39 weeks, birth weight of 2850 grammes, APGAR 9, breastfed for 2 weeks after that she received milk formula. She received the BCG and hepatitis B vaccine at the Maternity being discharged from there with the diagnosis of Down syndrome and cardiac malformation.

The patient was admitted for the above mentioned symptomes and presented at the clinical exam mediocre state, fever 38.5 degrees Celsius, diffuse cyanosis, signs of dehydration, a systolic murmur that was audible on the whole cardiac area, oxygen saturation of 75-80% without oxygen that under oxygen raise to 85-90%, persistent crepitan rates, a normal abdomen, normal

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stools, marked hypotonia, dysmorphic characteristic features corresponding to Down syndrome. The main dysmorphic features were brachycephaly with flat occiput, epicanthal folds and upslanting palpebral fissures, low nasal bridge, downturned mouth with protruding tongue, low-set ears, broad neck, and small hands with transverse crease.

The lab exams at admittance showed the following: leucocytes  $16600/\text{mm}^3$  with a predominance of neutrophils 85%, hemoglobin level 16.2g/dl, hematocrit level 46.9%, trombocytes  $279000/\text{mm}^3$ , CRP=2.04 mg/dl, Na/K=132/5.8 mmol/l, Ca=8.50mg/dl, ferrum level of 226 $\mu\text{g}$ , urea level of 57.8mg/dl, creatinine level of 1.34 mg/dl, LDH 1157 U/l, GOT/GPT=52/69U/l.

Immunoglobulin A (IgA) remained persistently low at a level of 0.39g/l while immunoglobulin G (IgG) raised from 6.30 g/l to normal level during the hospitalization period.

Cultures were taken and revealed nasal and pharyngeal swab *Staphylococcus aureus* MRSA, conjunctival swab *Haemophilus influenzae*, urine culture positive for *Klebsiella* ESBL. Blood culture was negative. The radiography showed alveolar pneumonia.

Echocardiography showed a complete atrio-ventricular channel at admittance but was repeated during hospitalization period.

The diagnosis at that moment was:

1. Alveolar pneumonia
2. Atrioventricular channel
3. Down syndrome
4. Prerenal insufficiency due to dehydration
5. Urinary tract infection with *Klebsiella* ESBL.

Treatment was started with feeding tube with high calory formula (Infasource courtesy of Nestle), perfusion, albumin, ceftriaxon, aerosols and oxygen, vitamins, calcium supplementation.

Table 1

	5.05		6.05	7.05	9.05			10.1		11.1	12.1
pH	7,20	7,27	7,34	7,35	7,16	7,11	7,25	7,14	7,26	7,20	7,35
PCO <sub>2</sub> mmHg	54,3	52,5	40,3	43,1	53,1	49,9	56,6	66,5	51,7	56,0	53
PO <sub>2</sub> mmHg	50	33	54	32	34	28	37	38	37	52	53
HCO <sub>3</sub> mmHg	21,4	24,8	22,1	23,8	19	15,9	21,6	22,8	23,4	21,9	28,4
BE	-7,3 / -6,6	-3,2 / -2,2	-3,4 / -3,7	-2,1 / -2,0	-10,2 / -9,2	-13,8 / -13,8	-6,3 / -6,0	-7,5 / -6,4	-4,3 / -3,9	-6,3 / -6,3	-0,4 / -0,3
SaO <sub>2</sub> %	76	54,5	86	78,6	49,4	42,4	60,7	54,6	61,5	77,6	83,2

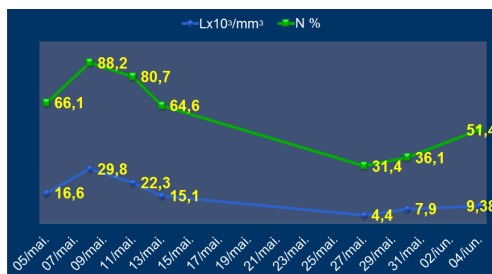


Fig. 1.

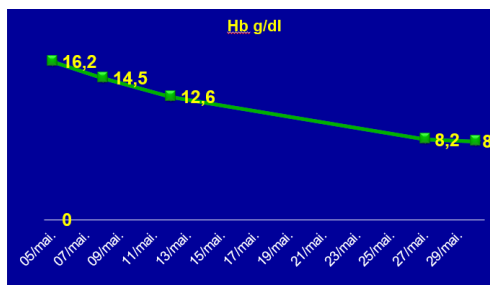
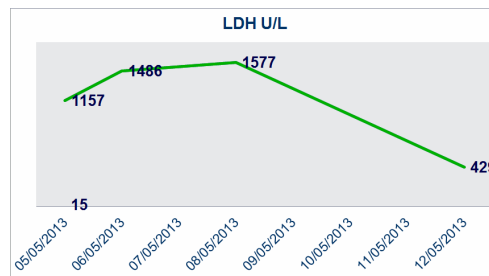
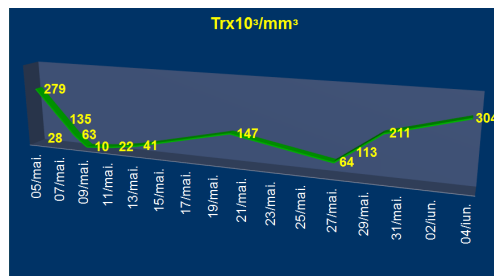


Fig. 2.



Under treatment the evolution was difficult with persistence of low degree fever so second radiography was performed and revealed the complete resorption of one of the opacities but one still persisted with a mild cardiomegaly. At this radiography it was clearly seen the absence of the thymus. This correlated very well with the hypocalcemia and hypogammaglobulinemia (IgA) all three main features for Di George syndrome.

Second echocardiography established the diagnosis of large atrial septal defect, ventricular septal defect, mild pulmonary hypertension.

The transfontanelar and abdominal ultrasound were normal.

The final diagnosis was:

1. Alveolar pneumonia
2. Complex cardiac disease (atrial and septal defect, mild pulmonary hypertension)
3. Di George syndrome (thymic agenesis, hypocalcemia and hypogammaglobulinemia)
4. Down syndrome
5. First degree malnutrition.

Treatment continued with partial tube feeding, ceftriaxon and vancomycin for a period of 14 days, vitamin A and D, Furosemid 5mg/kg/day, ACE inhibitors 1mg/kg/day, intermittent oxigen supplementation. She received complex feeding with special milk formula

(Infasource courtesy of Nestle) adapted for toddlers suffering of failure to thrive.

Under this treatment the evolution was favorable and she was discharged at parents request continuing to come at regular check-ups.

### 3. Discussion

Di George syndrome occurs in a number of 1:4000 births and we assist at an increasing number of this syndrome due to the fact that parents affected by the disease bear their own children [12]. Down syndrome on the other hand remains the most common genetic disorder despite the prenatal diagnosing or the termination of pregnancy. The incidence of Down syndrome remains at 1:1000 births in the whole world [4], [17].

Most of the Di George syndrome cases are sporadic but around 10% of the deletions are inherited ones [20]. Usually Di George syndrome is considered to be the result of an abnormal embryologic development of the third and fourth pharyngeal arch resulting in congenital defects which mainly affect the thymus, parathyroid and to varying degrees the heart [1], [15].

At half of the patients we may found a hemizygous deletion of 22q11.2 while in other cases the diagnoses is made on clinical and lab examination [11]. Aproximately 90% of the patients

suffering of Di George have a common deletion region of 3 Mb which contains approximately 40 genes and around 10% of the patients present with a smaller one of around 30 genes that is 1.5 Mb. [3].

Di George syndrome is mainly associated with T-lymphocyte immunodeficiency. However a study of Patel et al. found that 6% of the children having Di George syndrome suffered from hypogammaglobulinemia [18]. The prevalence of Down syndrome increased during 1979-2003 in ten american regions by 31.1% [18].

The higher prevalence of Down syndrome with increasing mother's age is not really fully understood. There are several hypotheses trying all to explain the occurrence of the syndrome. The most used hypothesis for explaining this is that the ovum of the mother is also ageing [5]. Another hypothesis is the one that states that hormonal imbalance causes a less development of microvasculature which are needed around thematuring follicles. This will decrease the oxygen and also the intracellular pH of the oocyte. There are two important consequences of this fact, one is a smaller spindle and the other one is the displacement and disjunction of the chromosome [7]. The last but not least one is more extended and states that hormonal imbalance may suppress the maturation of the oocyte during the follicular phase having as a result the disjunction of the chromosome. Seasonal reproduction pattern may be seen in humans and this may also explain the seasonal reproduction errors [10]. There are several studies describing seasonal variation in sperm and ovulation production, in early pregnancy termination or spontaneous abortion [8], [24]. Other studies have shown the high incidence of endocrinologic mainly thyroid dysfunction for children with Down syndrome [13]. Children with Down have an increased risk for endocrinologic,

cardiac, hematologic, psychiatric, neurologic and audiologic problems compared with the normal population [6], [19].

Studies report a higher number of heart malformations associated to Down syndrome alone rather than associated to other genetic syndrome [16]. Also it was shown that children with Down syndrome are at higher risk for hospitalization since early age due to respiratory diseases and also failure to thrive with a longer hospital stay [9]. This was the case for our girl, she was admitted at an early age, 23 days and her hospitalization period exceeded 40 days.

Survival for the first year at children suffering of Down syndrome has improved dramatically in last years from under 50% in the 1942-1952 to over 90% in the nineties [14]. The mean age for death due to different complications in Down patients increased in the later years to 50 years of age [22].

However, there are very few reports regarding the occurrence of Down syndrome together with Di George syndrome mainly the ones that are published point out the incidence of cardiovascular disorders and their surgical outcome. The spectrum of cardiac malformation is also very vast for Di George as well as for Down syndrome [21].

Most of the studies have been interested mainly in the survival pattern of the chromosomal malformations of children. However, while Down syndrome by itself was not a risk factor for children having conotruncal heart problems, the 22q11.2 syndrome appeared to influence the results of surgical cure at children this particular ones having a higher mortality rate [23].

At our patient we present the association of the two syndromes complicated the evolution of the newborn due to alveolar pneumonia having a prolonged

hospitalization period with a poor response at antibiotic treatment due to thymic agenesis.

#### 4. Conclusion

We present a case report of a Down syndrome case associated to Di George syndrome whose evolution was good after treatment with calcium and supportive cardiac treatment along with antibiotics but needed a prolonged hospitalization period.

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