

## Noonan Syndrome with Hepatitis B Virus Association—A Rare Case Report

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### Abstract

Noonan syndrome affects many area of the body characterized by the unusual facial characteristics, short stature, skeletal malformations, or defects, bleeding disorder and many other signs. This syndrome occurs 1 in 2000 populations. We present a case of 29years old male patient suffering from Noonan syndrome (a genetic disorder) associated with Hepatitis B with hepatosplenomegaly with jaundice.

**Keywords:** Noonan syndrome, Hepatitis B virus, genetic disorder, hepatosplenomegaly.

### Introduction

Noonan's syndrome is a congenital disorder affecting multi system of the body. It is characterized by the unusual facial features, short stature, skeletal disorder, heart defects, bleeding disorder and many other signs and symptomatology.

The individual who is with NOONAN's syndrome present with features of deep groove between the nose and mouth, widely spaced eyes and appear like mongoloid and low set ears and rotated backward. These individual may also have high arched palate, poor alignment of the teeth and small jaw. Most of the children of NOONAN's syndrome also exhibit short and webbed neck with low hair lines at the back of the neck. [1], [2].

50 to 70% NOONAN children may have short stature due to growth hormone irregularity even though these abnormality is not evident when they born later on their growth is retarded. On examination of the chest of the NOONAN's reveal pectus carinatum or pectus excavatum and also they have scoliosis occasionally. Congenital pulmonary valve stenosis is more common with NOONAN's syndrome occasionally they have Hypertrophic Cardiomyopathy. Bleeding disorder are often associated with NOONAN's syndrome early bruising, gum bleeding, epistaxis or prolonged bleeding followed by injury or surgical intervention. Women with NOONAN's syndrome may develop excessive bleeding during menstrual cycle or during childbirth. [3], [4].

Adolescent male with NOONAN's syndrome may attain delayed puberty and decreased pubertal growth with undescended testis with the absence of secondary sexual characteristics. Children with NOONAN's syndrome

have normal intelligence but a few children may need special educational need due to intellectual disability. They also born with visual and hearing difficulty. Infants with NOONAN's syndrome may be born with puffy hands and feet caused by lymphedema, which may dissolve itself as the infant with NOONAN's grow up. They may also develop feeding problem which may go off as the children grow up. [5]

### Case Report

A 29year old male presented to our OPD with chief complaints of abdominal distension, abdominal pain and breathlessness for 20days.

The abdominal distension was gradual in onset and progressive in nature limited more to the upper abdomen associated with a vague abdominal discomfort limited to right and left hypochondriac region which was non radiating mild to moderate in intensity.

Breathlessness was intermittent present even at rest not associated with chest pain or palpitations.

On examination patient was conscious, oriented, Hypertelorism, webbing of neck, low hair line, high arched palate, low set ears, depressed nasal bridge were present. His vitals were stable. No pallor. Icterus was present. No cyanosis, clubbing lymphadenopathy. Pitting pedal edema is present. His height was 164cm, weighed 53kgs and his arm span was 154cm. Pectus carinatum was present with mild thoracic scoliosis. Cardiovascular system examination revealed S1 and S2 with wide fixed 2<sup>nd</sup> heart sound, No murmur was noted. Respiratory system examination had a normal vesicular breath sounds with no adventitious sounds. The central nervous system was normal. On examination short stature, pot belly, wide set nipples, short neck, subnormal

intelligence, slanting eye was noticed. Abdominal examination on inspection had a upper abdominal fullness with umbilicus normal in position, no scars were present. Skin over the abdomen were normal.

On palpation patient has hepatomegaly 10cm below the right costal margin, left lobe predominantly enlarged compared to the right one, firm in consistency, non tender, surface was normal, edge was rounded, bruit present. Splenomegaly was also present 5cm below Left costal margin, splenic notch was palpable, firm in consistency. With this physical examination a provisional diagnosis of NOONAN's syndrome with hepatomegaly and jaundice was made.

### Investigation

Investigations were done. His complete blood count revealed. Total count- 7,700, Neutrophils 70%, Lymphocytes 26%, Eosinophils 2%, Monocytes 2% and peripheral smear study showed mild to moderate hypochromia with microcytosis, few normocytes and anisocytosis. Ultrasound abdomen was done which showed a massive enlargement of Liver with Left lobe being predominantly involved measuring 14cm. The portal vein was 1.8cm in diameter. The main portal vein was thrombosed including the Left branch and part of right branch. Echo pattern was coarse and nodular. Hepatic artery was 7mm in diameter. The Intra hepatic part of IVC was normal without thrombosis. The spleen was enlarged measuring 23cm and echo pattern was normal. The Gall bladder had a Phrygian cap like appearance with sludge present. The ultrasound abdomen revealed a massive hepatomegaly, portal vein thrombosis, splenomegaly. His renal and Liver function tests were normal. With this our diagnosis was revised and working diagnosis was made as NOONAN's syndrome with hepatosplenomegaly with jaundice and portal vein thrombosis.

### Discussion

This condition is inherited in an autosomal dominant pattern, which means one copy altered gene in each cell is sufficient to cause the disorder. In some cases, a affected person inherits the mutation from one affected parent. Other cases result from new mutation in the gene and occur in people with no history of disorder in the family. [6]

Mutation in the PTP N11, SAS1, RAF1, CRAS, NRAS and BRAF cause NOONAN's syndrome. Most cases results from mutation in PTP N11, SAS1 or RAF1, PTP N11. [7]

PTP N11 accounts 50% of all cases of NOONAN's syndrome. SAS1 accounts 10-15% of all cases of NOONAN's syndrome. RAF1 accounts 5-10% of all cases of NOONAN's syndrome. CRAS accounts 2% of all cases of NOONAN's syndrome. ( more severe form or atypical form). [8]

### Differential Diagnosis

Familial Turner's syndrome  
Female Pseudo Turner's syndrome  
Male Turner's syndrome  
NOONAN-EHMKE-syndrome  
Pseudo-Ulrich Turner's syndrome  
Turner's syndrome in female with X syndrome  
ULRICH-NOONAN's syndrome  
Watson's syndrome  
William syndrome  
Leopard syndrome

Congenital disorder in human being discovered and always go with the name of the discoverer where as, what is the use of the suffering individual. Are we competent enough to treat them or prevent them right from the budding stage that is intrauterine life of the fetus by advanced technology either apply and correct them to overcome the life long sufferer of the genetically inherited disorder or destroy them in the intrauterine level. [9]

MONOGENIC DISEASE- an inherited disease controlled by a single pair of genes

### Conclusion

The cause of NOONAN's syndrome remaining 20% unknown. The PTP N11, SAS1, RAF1, CRAS, NRAS and BRAF genes all provide instructions for making protein that are important in signaling pathways needed for proper formation of several types of tissue during development. These proteins also play a roles in cell divisions, cell movement and cell differentiation( the process by which cells mature to carry out specific functions). [10] Mutation in any of the genes listed above cause the resulting protein to be continuously active, rather than switching on/off in respond to cell signals. This constant activation disrupts the regulation of system that controls cell growth and division, leading to the characteristic feature of NOONAN's syndrome.

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