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Case Report

Rare Cause of Chyleus Ascitus: Noonan Syndrome: About A Case

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Abstract

Noonan syndrome is a genetic disorder characterized by facial dysmorphism and several birth defects including lymphatic abnormalities. There are familial cases and sporadic cases. In practice, it is sometimes very difficult to confirm the diagnosis, as the manifestations are variable and & quot; subtle & quot; for the non-specialist. We report the case of a patient in whom the diagnosis was made late at the age of 37 years and whose reason for consultation was an increase in abdominal volume related to chylous ascites. Chylous ascites in Noonan syndrome seems to be more frequent than expected hence the need to know how to evoke this syndrome in its presence especially since there is a typical dysmorphic picture.

Keywords: noonan syndrome, lymphatic abnormalities, chylous ascites..

INTRODUCTION

Noonan syndrome or male turner syndrome is very rare [1]. Prevalence at birth varies between 1 / 1,000 and 1 / 2,500 live births [2]. It is transmitted in an autosomal dominant fashion, with variable expression [3]. However, the proportion of sporadic cases (neomutations) exceeds 80% [3]. We report the case of a patient in whom the diagnosis was made late at the age of 37 years and whose reason for consultation was an increase in abdominal volume.

OBSERVATION

This is a 37-year-old female patient with a history of asthma since childhood on Salbutamol and inhaled corticosteroid therapy admitted for increased abdominal volume in which the cardiovascular examination as well as the examination of the liver were strictly normal.

In addition, the remainder of the clinical examination was noted:

- A small height of 151 cm with a weight of 50 kg,
- Edentulous patient with limited opening of the mouth,
- Hypertelorism, ptosis and low implanted ears,
- A micrognathia, a short neck,
- An elongated triangular face with accentuation of the nasolabial folds,
- Asymmetric deformed thorax with superior pectus carinatum, inferior pectus excavatum, and dorsal kyphoscoliosis,
- Edema-ascitic syndrome with puffiness of the face, discreet edema of the upper and lower limbs taking the cup and a sloping dullness of the flanks,
- Dry skin, with keratosis pilaris of the limbs and brittle hair,
- Lymphedema of the lower right limb reaching up to the thigh with sign of stemmer +, placard of the right leg surmounted by lymphatic vesicles with fistula and lymphorrhea, tense calf with reduced sloshing, threadlike and elongated appearance of the "marfanoid" fingers

For her ascites, the patient benefited from:

- Abdomino-pelvic ultrasound: normal size liver with regular contours, homogeneous density without suspicious focal lesion, absence of dilation of VBIH and VBP, porous trunk and VSH permeable and of normal caliber, vena cava of normal permeable caliber, homogeneous spleen of normal size, kidneys of homogeneous density with well differentiated regular contours and of normal size with absence of dilation of the excretory cavities, homogeneous pancreas with fine wirsung, homogeneous adrenals without detectable hypertrophy or nodule, anechoic peritoneal effusion of great abundance, empty bladder wall and contents not visible uterus of normal size

7x3x5 cm, homogeneous echostructure, regular outlines, without visible focal lesion unseen ovaries

- Study of ascites fluid:

Milky chylous appearance
Transudate liquid with prot at 10g / L
PNN-predominant 60 cells / mm3 white blood cells (100%)
Red blood cells <3 elements / mm3
Triglycerides = 5.44g / L
Absence of yeasts, gram coloration: -
Expert gene -
Culture: no germs

- Pelvic MRI: normal size uterus with normal emptiness line, normal looking ovaries, absence of suspicious pelvic mass, presence of large ascites, absence of lymphadenopathy
- TTE: undilated cardiac chambers, LV of good systolic function without disturbances in kinetics with 70% LVEF, normal filling pressures, RV of good overall systolic function, no PAH, dry pericardium.
- 24h proteinuria = normal
- Alpha 1 antitrypsin clearance measurement: normal
- Exploratory laparotomy: under GA, dorsal decubitus, subumbilical incision, exploration: chylous ascites, presence of calcified mesenteric granulations, large omentum without anomalies, healthy peritoneum, absence of mass, unrolled small intestine: no abnormalities at the limit of exploration , biopsy of mesenteric granulations, omentum biopsy, sampling of ascitic fluid, careful hemostasis.

For his lymphedema of the lower right limb:

- X-ray of the right leg : normal
- Venous ultrasound of the lower limbs = superficial and deep venous axes permeable and of compressible appearance by compression maneuvers with a color Doppler signal present and respiratory modulation observed, permeable internal jugular vein, absence of parietal infiltration and endoluminal thrombus, presence of " significant infiltration of the soft parts of the limb concerned = absence of signs in favor of deep vein thrombosis => class II compression stockings, 10 vascular lymphatic drainage sessions

DISCUSSION

In about half of the patients, the disease is caused by missense mutations of the PTPN11 gene located on chromosome 12, resulting in a gain in function of phosphotyrosine phosphatase SHP-2 (protein tyrosine phosphatase, non-receptor type 11) [2]. Recently, mutations in other genes of the RAS MAPK pathway (KRAS, SOS1, RAF1 and RIT1 genes) and more rarely SHOC2, NRAS, RRAS, CBL, SOS2, RASA2 and LZTR1 have been identified in a small proportion of patients with Noonan syndrome [2,3]. The diagnosis of Noonan syndrome is clinical [4]. The sensitivity of the tests allowing to look for all the known genes makes it possible to confirm the diagnosis only in less than 75% of the patients [5].

It is characterized by facial dysmorphia, short stature, congenital heart disease, skeletal malformations and delayed acquisitions [6]. The clinical symptoms are very rich, sometimes with a discreet picture, which can be responsible for delayed diagnosis [6]. Especially since typical facial features tend to normalize with age and may be difficult to recognize in adulthood [7]. It is the best known and most frequent syndrome with lymphatic involvement [8]. The link between genetic mutation and lymphatic network abnormalities remains poorly understood to date [8]. Treatment requires multidisciplinary collaboration [9].

It includes symptomatic treatment, management of complications and growth hormone on specialist advice, but often no medical treatment is offered in adulthood [5]. The prognosis is conditioned by damage to vital organs, primarily the heart [9]. Lymphatic abnormalities, most commonly peripheral lymphedema, are present in less than 20% of individuals with Noonan Oinfants and disappear during the first years of life or develop in adolescence or adulthood [11] which was the case in our patient who reported the onset of lymphedema at the age of 31.

Lung, testicular or intestinal lymphangiectasia, lymphedema of the scrotum or vulva, and chylous effusions from the pleural space and peritoneum are less frequently reported [12, 13].

Prenatal, chylothorax is a classic call sign when it is bilateral, associated with a hygroma and the karyotype is normal [14, 15]. A prenatal molecular genetic diagnosis was reported in a study initiated by Schlüter and his colleagues in the presence of large cystic hygroma glues, massive pleural effusion and ascites at 23 weeks gestation in a fetus with a karyotype. Normal (46, XX) [16]. A study of 10 children (6 boys and 4 girls) with Noonan syndrome, all but one with a concomitant form of congenital heart disease, revealed pleural effusions confirmed to be chylothorax either by their general appearance or by criteria of laboratory (triglycerides> 110 mg / dL) in 9 children. One of these nine children also had chylous ascites and another presented with ananasarch state. The other remaining child had only ascites [17].

Chylous ascites in Noonan syndrome then seems to be more common than expected. It is necessary to know how to evoke this diagnosis in case of chylous ascites and typical dysmorphic picture. In our patient, dysmorphic and orthopedic features were guiding elements. The clinical signs of the disease, apart from heart disease, are discreet at birth and assert themselves with growth, so that the average age at

diagnosis is between five and ten years: failure to thrive, skin pigmentation abnormalities, delay in acquisitions [8].Sometimes the diagnosis can be even later in front of a discreet clinical symptomatology.

Marmouch *et al*., Reported the case of a man discovered to have Noonan syndrome at the age of 38 who consulted for infertility [1]. In our patient the diagnosis was also made late at the age of 37 years.

CONCLUSION

Our observation illustrates a Noonan syndrome discovered late at the age of 37 by chylous ascites. A search for associated abnormalities did not reveal any malformations, particularly of the heart and kidneys, or autoimmune dysthyroidism. Noonan syndrome is characterized by heterogeneous phenotypic manifestations. With a prevalence of one in 1000-2500, Noonan syndrome is a disorder that most physicians will encounter during their career.

The patient's presentation can range from mild to severe. The typical dysmorphic syndrome, the striking chest deformity allowed us in addition to the genetic study to confirm the diagnosis in our patient.

Chylous ascites occurring in a syndromic setting remains rare. The complexity of the lymphatic network and its close link with venous development mean that many avenues remain to be explored to improve the understanding of lymphatic function and to explain the occurrence of this ascites. Regular detailed follow-up with a multidisciplinary approach is often necessary to treat medical and developmental complications of Noonan syndrome.

The understanding of the molecular genetic causes of Noonan syndrome has advanced significantly over the past decade. We hope that with further research, targeted pharmacogenomic approaches will be developed based on a detailed understanding of the different disease-causing changes in RAS - MAPK.

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