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Pediatric

Nijmegen Syndrome: About A Sighting

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Abstract **Case Report**

Nijmegen syndrome (NS) is characterized by progressive microcephaly, early growth deficiency that improves with age, recurrent respiratory infections, an increased risk for malignancy. Developmental milestones are attained at the usual time during the first year; however, borderline delays in development and hyperactivity may be observed in early childhood. Intellectual abilities tend to decline over time. Recurrent pneumonia and bronchitis may result in respiratory failure and early death. The diagnosis of NS is established in a proband with characteristic clinical features and biallelic pathogenic variants on molecular genetic testing and/or absent nibrin protein on immunoblotting assay. Early diagnosis is essential to prevent serious infections and unnecessary radiation exposure. There is no specific treatment.

Keywords: Nijmegen syndrome, chromosomal instability, early diagnosis.

BACKGROUND

Nijmegen syndrome is a rare autosomal recessive disease present at birth with microcephaly, facial dysmorphism increasing with age, growth retardation and risk of later complications such as blood diseases and infections.

The aim of this work is to highlight the clinical and biological characteristics of this rare entity.

OBSERVATION

We report the case of a 5 years old female infant from a followed pregnancy. The delivery was done vaginally. At birth she was hypotrophic, with a birth weight of 1800g. Her medical history is remarketed by a notion of repeated infections: recurrent low respiratory tract since the age of 2.5 years at a rate of 6 to 10 episodes/one treated with antibiotic therapy; recurrent gastroenteritis 4-6 episodes/year since the age of 3 years and dermatological lesions of the face since the age of 4 years.

The history of the disease dates back to the age of 2.5 years with the occurrence of recurrent febrile broncho- pneumonia which gave rise to several consultations (more than 20 consultations) treated with antibiotic therapy but without clinical improvement.

The last episode dates back to 7 days before without admission by the occurrence of a productive cough + greenish sputum in a context of fever. On physical examination she was febrile with a failure to thrive with a Weight= 15 kg (-2DS) - Height= 102 cm (-2DS) - PC= 42 cm (-3DS) and facial dysmorphism; superinfected left suborbital erythematomacular lesions and rales on pulmonary auscultation.

Faced with this picture of microcephaly, growth retardation, facial dysmorphism, repeated respiratory infections, combined immune deficiency, the diagnosis of Nijmegen syndrome is suspected.

Gamma globulines was administered in combination with antibacillairy treatment 2RHW/4RH and a therapeutic treatment of cotrimoxazole, relayed by preventive treatment with a good tolerance.

The evolution was favorable, the infant stabilized clinically.

Biological Examination

- **NFS:** HG: 10;1 g/dl MCV: 72.3 L MCH 22;9 L GB: 4900 E/ mm" PNN: 3200/ mm3 Lynphocytes: 1100/mm3 plaquettes: 380000/mm3.
- **EPP:** Significant decrease in gamma globulins: 2.3 g/l.

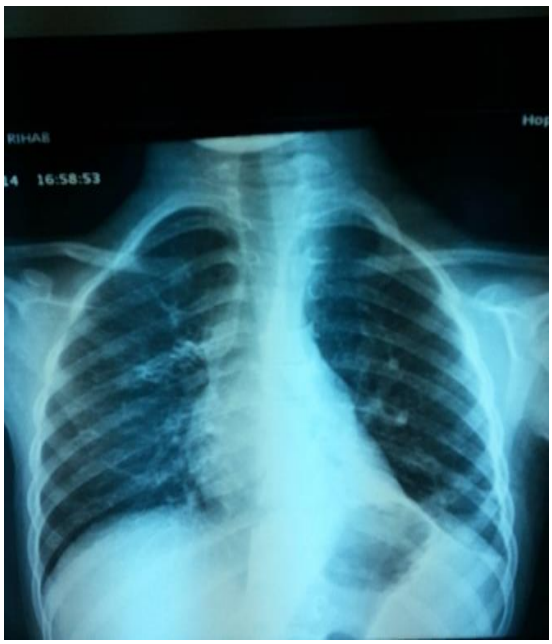
- **HIV:** Serology negative and Search of pneumocyctis jiroveci: negative**.**
- **ECBC:** Heamophilus influenza.
- **BK and IDR:** Negatives.

Ig weight assay

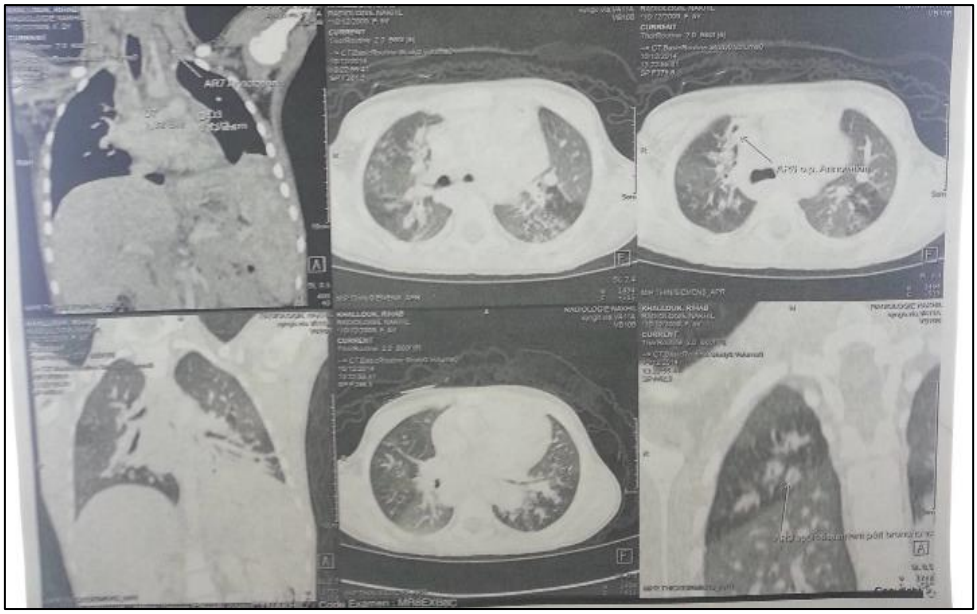
Type d'immunoglobuline	Résultat	Valeur normale
IgG	1.1 g/l	7 – 16 g/l
IgA	0.371 g/l	0.7 – 4 g/l
IgM	1.9 g/l	0.4 - 2.3 g/l
Kappa	0.457 g/l	1.7 – 3.7 g/l
Lambda	0.31 g/l	0.9 – 2.1 g/l

Typing of sub-populations Lymphocytic

Sous-populations lymphocytaires	Marqueurs	Taux lymphocytes En % des	Valeur absolue en 103/ µL †	Valeurs de référence*
Lymphocytes		100	1.1†	2,3 - 5,4
CD3	CD3+	57.0	0.6	1,4 - 3,7
T4	CD3+ et CD4+	34.3	0.38	0,7 - 2,2
T8	CD3+ et CD8+	16.2	0.18	0,49 - 1,3
B	CD3- et CD19+	25.2	0.28	0,39 - 1,4
NK	NK CD3- et (CD16+CD56+)	8.88	0.10	0,13 - 0,72



Chest X-Ray: Chest distension; domed apex; Lowering of domes; Ventilation disorders Left inferior atelectasis Image of bronchus dilation



CHEST CT: bilateral SD associated with multiple mediastinu, hilair and supraclavuculair ADPS

DISCUSSION

Nijmegen syndrome is a rare autosomal recessive disease; present at birth with microcephaly, facial dysmorphism increasing with age, growth retardation and risk of later complications such as blood diseases and infections.

It is due to mutations in the NBN gene (8q21-q24) responsible for the production of partially functional truncated fragments of nibrin, involved in the repair of double-stranded DNA damage [1].

The main signs are: microcephaly present at birth and progressing with age; facial dysmorphism (protruding face underlined by a tilted forehead and receding chin; upward oblique palpebral clefts, long and hooked or small nose with anteverted nostrils); Mild growth retardation; early ovarian failure in girls. Minor skeletal anomalies (clinodactyly of the 5th fingers, etc) A delay in language acquisition is common. The hair is fine and sparse improves with age. Congenital malformations of the kidney.

The other characteristic manifestations of the syndrome are an immune deficiency with repeated severe respiratory tract infections, a strong predisposition to malignant tumors (especially lymphoid) and radio sensitivity [1].

The diagnosis is based on the clinical picture and on the demonstration of chromosomal instability (spontaneous and induced), cellular hypersensitivity to ionizing radiation in vitro, combined immunodeficiency and bi-allelic mutations of NBN and total absence of whole nibrin. Molecular analysis confirms the diagnosis.

Early diagnosis is essential to prevent severe infections and unnecessary radiation exposure (diagnostic and therapeutic) [2].

There is no specific treatment. Multidisciplinary management is necessary because of the specific immune deficiency and radio sensitivity with long-term monitoring.

The prognosis is guarded, tumors being the major cause of death [3].

CONCLUSION

This observation underlines the value of early diagnosis, a key element in preventing the occurrence of severe infections and respiratory squeals.

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