Bardet Biedl Syndrome

Not only what but also how matters?

Narjess Boutalbi, Nihad Selim, Mohamed Said Nait Abdallah, Nadira Bouchair | Clinique pédiatrique sainte Thérèse , CHU Annaba
Narjess.boutalbi@gmail.com

Introduction

- Bardet-Biedl syndrome (BBS) is a multiorgan genetic disease which is a part of ciliopathies. The French National Authority of Health (HAS) published in March 2019 a new National Diagnostic and Care guideline for Bardet Biedl syndrome. However, in practice, we faced many difficulties in the screening and the multidisciplinary care of BBS complications.
- We report our experience with siblings composed of an eight-year-old boy and an 18-month-old girl suffering from BBS. Our objective is to manage obesity, hypogonadism, vision disorders, intellectual disability, and behavioral disorders.
- While the SBB clinical diagnosis seems well defined, the genetic determinism of BBS remains complex, especially that there is a need for an early diagnosis to guide the patient and overcome medical and social problems.

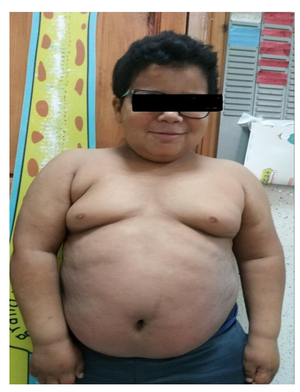
Observation

We report the case of a sibling resulting from a consanguineous marriage with an 8-year-old boy presenting:

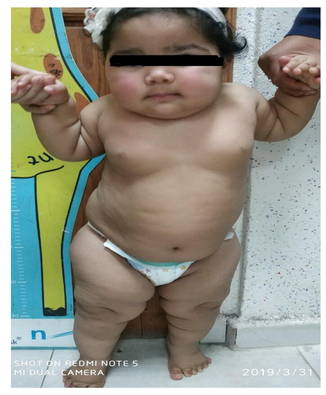
- Weight: 52 kg, height: 126 cm, BMI : 33 = obesity (Fig 1.A)
- Syndactyly at both feet (Fig 1.B)
- Hypogonadism, with a micropenis (Fig 1.C)
- Dvelopmental delay: acquisition of walking until the age of 3 years, very limited vocabulary, learning disabilities. The child is not in school.
- Convertible strabismus, cataract. The fundus objective is advanced retinopathy pigmented both tubal vision, visual acuity lowered.
- At this stage: No disorders of carbohydrate metabolism. Renal ultrasound was normal, as well as serum creatinine

The 18-month-old sister presents:

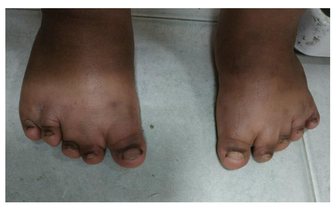
- Obesity BMI: 25.5 size: 80 cm Weight: 17kg (Fig 1.D)
- post-axial polydactyly at both feet (Fig 1.E)
- Small lip hypoplasia
- The lack of acquisition of standing and walking
- No carbohydrate metabolism disorders or renal impairment detected at this stage



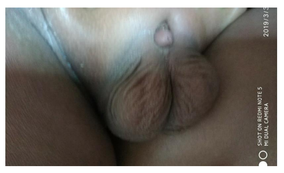
(A)



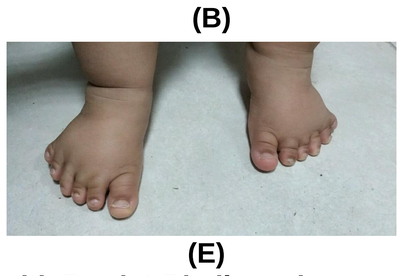
(B)



(C)



(D)



(E)

Fig 1 :Some images representing patients with Bardet-Biedl syndrome.

Diagnosing BBS

- The diagnosis is based on the combination of four primary criteria, including at least one of the first two [1] .
- Molecular confirmation of BBS has evolved over the last decade to next-generation sequencing gene panels containing all known BBS genes. The frequency at which molecular confirmation is achieved has increased accordingly from approximately 40–80% (Table 1). [2]

ii. Diagnostic features

Primary features	*Frequency*
Rod-cone dystrophy	93%
Polydactyly	63–81%
All four limbs:	21%
Upper limbs only:	9%
Lower limbs only:	21%
Obesity	72–92%
Genital anomalies	59–98%
Renal anomalies	53%
Learning difficulties	61%
Secondary features	
Speech delay	54–81%
Developmental delay	50–91%
Diabetes mellitus	6–48%
Dental anomalies	51%
Congenital heart disease	7%
Brachydactyly/ syndactyly	46–100%/8–95%
Ataxia/ poor coordination	40–86%
Anosmia/hyposmia	60%

Fig 2: Frequency of diagnostic features [3]

BBS type	Gene name	BBS type	Gene name
BBS1	*BBS1*	BBS11	*TRLM32*
BBS2	*BBS2*	BBS12	*BBS12*
BBS3	*ARL6*	BBS13	*MKS1*
BBS4	*BBS4*	BBS14	*CEP290*
BBS5	*BBS5*	BBS15	*WDPCP*
BBS6	*MMKS*	BBS16	*SDCCAS*
BBS7	*BBS7*	BBS17	*LZTFLI*
BBS8	*TTC8*	BBS18	*BBIPI*
BBS9	*BBS9*	BBS19	*IFT27*
BBS10	*BBS10*	BBS20	*IFT172*
		BBS21	*CSorf37*

Table1: Known genes causin BBs [3]

Management and difficulties

Fig 3: BBS requiring assessment [4]

Annual assessment	*At least once and more often if required*	*If required*
• Weight • Blood pressure. • Renal, thyroid, liver function tests, glucose and lipid profile. • Ophthalmology review. • Endocrinology review. • ERG of patient >5 years old	• Review by a clinical geneticist. • DNA for molecular diagnostics. • nephrology review . • Renal USS • Dietetics review • Developmental and educational assessment. • Hearing evaluation. • Clinical psychology review	• Oral glucose tolerance test • Referral to speech therapy • Echocardiography/ referral to cardiology • Referral to mental health services • Referral to orthodontist

- A multidisciplinary approach is required to manage BBS. Although research is in progress, there still no targeted treatment for BBS.
- Complications associated should be treated symptomatically.
- Difficulty performing ophthalmological examinations visual fields, optical coherence tomography requiring patient cooperation due to age and intellectual deficit. Weight management is also a big challenge in front of learning difficulties.

Future therapies for BBS

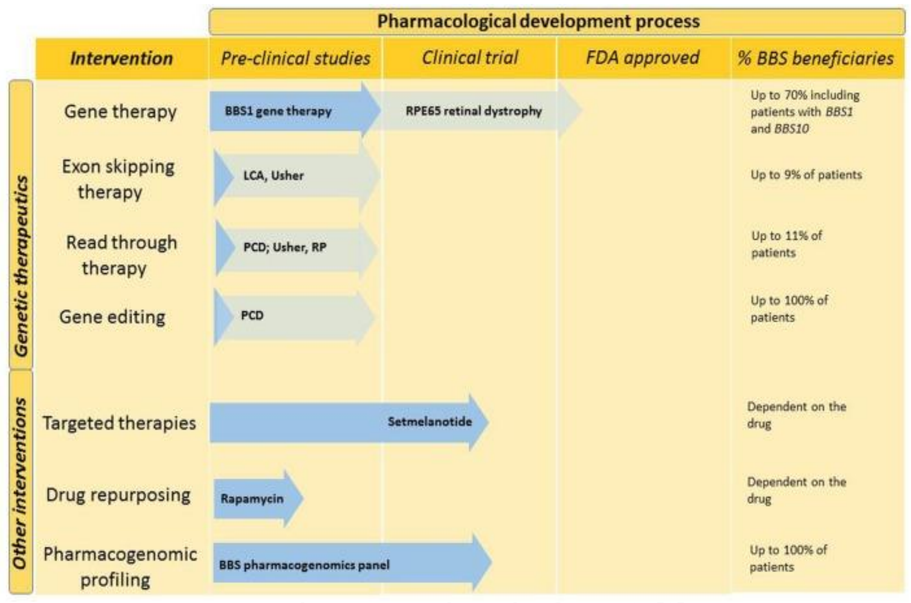


Fig 4: Future therapies for BBS [3]

References

[1] Protocole National de Diagnostic et de Soins concernant le syndrome de Bardet Biedl, Haute autorité de santé 2019

[2] Forsythe E, Beales PL. Bardet-Biedl syndrome. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Mefford HC, Stephens K, Amemiya A, Ledbetter N, editors. , editors. GeneReviews(R). Seattle, WA: (2003).

[3Forsythe E, Kenny J, Bacchelli C, Beales PL. Managing Bardet-Biedl Syndrome-now and in the future. Front Pediatr. 2018;6:23.

[4] Forsythe E, Beales PL. Bardet–Biedl syndrome. Eur J Hum Genet 2013;.

58ESPE P3-189
Multisystem endocrine disorders
Narjess Boutalbi
Poster presented at:
PosterSessionOnline.com