A Rare Combination of Bardet-Biedl And Meckel Syndrome: A Case Report

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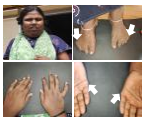
INTRODUCTION

- Bardet–Biedl syndrome(BBS) and Meckel Syndrome (MKS) are rare ciliopathies genetic disorder
- In BBS, 90% of renal abnormalities can be the cause of morbidity and mortality[1]; renal cystic dysplasia is a salient feature in MKS[2]
- Approx.18 genes (*BBS1-BBS18*) linked to BBS; *BBS1 & 10* are commonly mutated and *BBS2, 3 & 12* genes reported unusually[3]
- Approx. 14 genes are linked to MKS, most reported genes are *CEP290, MKS1, CC2D2A, TXNDC15, B9D2*[4]
- X-linked retinitis pigmentosa GTPase regulator-interacting protein 1 (*RPGRIP1)*[5] and Exocyst Complex Component 3-Like Protein 2 (*EXOC3L2)*[6] are ciliogenesis genes, mutation were not reported in BBS and MKS

SUBJECTS AND METHODS



III:6

IV:1

IV:2

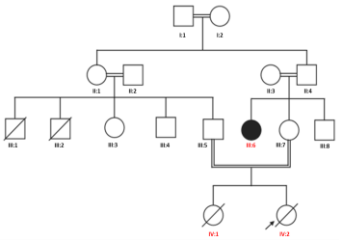


Fig. 1

- An 18-month-old female baby (Proband - IV:2) presented with lower respiratory infection to the hospital. 2nd girl baby born to 2nd degree consanguineous marriage
- Proband had dysmorphic features like joint contractures, low set ears, high arched palate, widespread nipples, hyperkalemia, left Congenital talipes equinovarus (CTEV), polydactyly, hypertelorism, situs solitus, microphthalmia, and retrognathia. Antenatal scans showed bilateral ventricular, also had dextrocardia, Atrial septal defect and ventricular septal defect, bilateral ventricular dilatation, mild hydrocephalus, renal pelvicalyceal dilation, renal parenchymal, and mild hydronephrosis. she died at 20 months of age
- Girl baby(IV:1) also had congenital defects like fetal ascites, bilateral hydroureteronephrosis, bilateral hydronephrosis, polydactyly, dilated large bowel, fetal placentomegaly, and polyhydramnios. She died at 3 months of age due to non-immune hydrops dysplastic kidney
- Affected individual(III:6) – she had global development delays/intellectual disability and other complications like hypertelorism, retrognathia, obesity, polydactyly, joint constructures. Currently, she is 23 years old without any medical illness or treatment

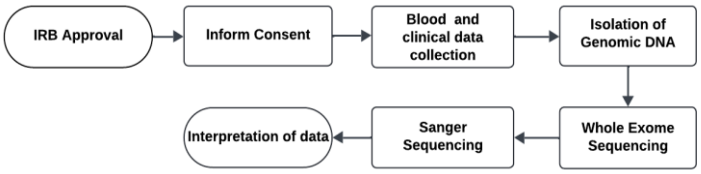


Fig. 2

- SNHAR ethical clearance IRB No: 42/06/05/23
- We collected the 2ml of blood samples from the family members
- WES was done for proband and affected individual
- For further confirmation, we sent samples for sanger sequencing of candidate genes such as *RPGRIP1* and *EXOC3L2*

RESULTS

Whole Exome Sequencing

Syndromic Disorder	Proband/ Affected individual	Mutation (AA changes)						
BBS	Gene	***BBS2***	***BBS4***	***BBS9***	***BBS10***	***BBS12***	***MKKS***	
	Proband	R413X; I289V; S70N	I182T	A333T; A455T; A364T	P539L	R386Q; D467N	G532V; R517C	
	Affected individual	R413X; I289V; S70N	I182T	A333T; A455T; A364T		R386Q; D467N		
MKS	Gene	***RPGRIP1L***	***B9D1***	***B9D2***	***CEP290***	***TMEM67***	***TMEM216***	***TMEM231***
	Proband	R744Q	H187Y; P167L	I11M	R1746Q	I604V; I523V	R147T; R86T	S26R, L6V
	Affected individual	R744Q		I11M		I604V; I523V		

Table:1- The list of Mutated genes in BBS and MKS identified in proband and affected individual.

Mutation Analysis for proband

1. *RPGRIP1*(exon 5: c.A574G:p.K192E)
2. *EXOC3L2* (exon12:c.G2372A:p.R791Q)

Sanger Sequencing

EXOC3L2

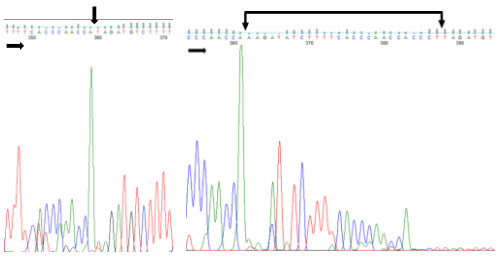


Fig. 3- Affected individual

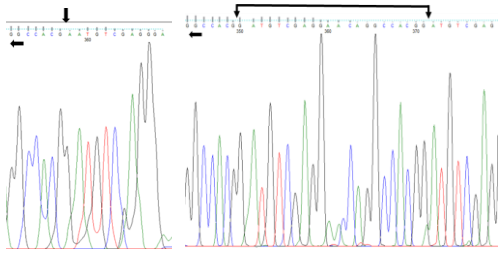
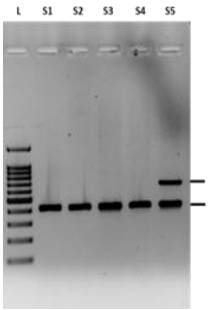


Fig.4- Proband

Fig.5- Control

Fig.6- Proband

RPGRIP1



L-Ladder S1- Positive control
S2- Proband S3- Father
S4- Mother S5- Affected individual

Fig: 7

FUTURE PROSPECTS

- We have given Sanger sequencing of *the RPGRIP1 and BBS2* gene
- We plan to identify the *RPGRIP1* and *EXOC3L2* genes and its role/effects in ciliopathy

CONCLUSION

- Proband carries six genes associated with BBS and seven genes associated with MKS, it lead to the combination of both ciliopathies
- We observed the uniqueness of the mutations in ciliary genes *RPGRIP1* and *EXOC3L2* in proband

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