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J Pediatr Neurosci. 2017 Jul-Sep; 12(3): 276–279.
doi: 10.4103/jpn.JPN_101_17: 10.4103/jpn.JPN_101_17
PMCID: PMC5696670
PMID: 29204208

Pallister–Hall Syndrome

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Abstract

Polydactyly is a relatively common abnormality in infants. However, it can be a marker of a wide variety of neurological and systemic abnormality. Hence, it is important for pediatrician and physician to have insight into the various association of this apparently innocuous anomaly. In this write-up, we report an extremely rare syndrome associated with polydactyly that is Pallister–Hall syndrome. A 10-month-old male child born by lower segment cesarean section presented with global delay associated with microcephaly, frontal bossing, hypertelorism, flat nose, short philtrum, incomplete cleft in the upper lip and hard palate, polydactyly, and syndactyly. The child presented with repeated vomiting and crying episodes. The patient was investigated which revealed a hypothalamic hamartomas. Pallister–Hall syndrome is a very rare autosomal dominant genetic disorder due to mutation in GLI3 gene in the short arm of chromosome 7 with variable penetrance and expressivity.

Keywords: *Hypothalamic hamartomas*, *Laurence–Moon–Biedl syndrome*, *Pallister–Hall syndrome*, *polydactyly*

Introduction

Polydactyly is not an uncommon phenomena in the new born. Awareness in to the various syndromes associated with it will be of use in planning investigation of a child with such an anomaly.

Polydactyly is categorized as preaxial triphalangeal when the 1st digit thumb has three phalanges: Preaxial duplication if the 1st digit is duplicated, postaxial Type A if well-defined extra finger which is wholly or partially articulated, and Type B if pedunculated postminimus or small finger. Postaxial Type B is relatively common with an incidence of about of about 1/531 infants.[1] A study among American blacks and whites showed postaxial duplication of the 1st digit is of polygenic inheritance and postaxial Type B is most common. American blacks with polydactyly had more neurological complications than whites.[2] It is categorized as postaxial hexadactyly when the 5th digit is duplicated and preaxial hexadactyly Type 1 when there is duplicated biphalangeal 1st digit and rare polydactyly for extra fingers in other sites.[3] This is also categorized as polydactyly isolated and polydactyly with other birth defects. The third type of approach is as combined if other limb defects including hypoplasia and dislocations are seen and multiple congenital abnormality type if other defects with other known cause for that are seen. Commonly associated defects are anencephaly, hydrocephalus, cyclopia, anophthalmia, microcephaly, spina bifida,

cleft lip and palate, optic atrophy, retinitis pigmentosa, esophageal atresia, anal and other gut abnormalities, gut malrotation, intersex, hypospadias, polycystic kidney, hydronephrosis, prune belly, etc., In this paper, we describe a very rare case of polydactyly associated syndrome.

Case Report

A 10-month-old male baby was the 2nd born to 3rd degree consanguineous parents. The child was delivered by cesarean section as the previous delivery too was lower segment cesarean section. The child cried immediately after birth and was noticed to have multiple abnormalities which they were advised to correct when the child is little older. However, the child did not attain head holding by 10 months, did not turn over, but just started babbling. Since 1-month relatives noticed that the child was holding on to head and crying on and off. The child was also coughing and vomiting. Hence, he was brought to our institution. Examination revealed head circumference of 47 cm[4] with frontal bossing. The child was obese and cheerful. There was ocular hypertelorism as evidenced by interpupillary distance approximately 44 mm.[5] The child had an incomplete ridge in the upper lip which was skin deep, and lips were still united. The incomplete ridge was extending throughout hard palate. Patietnt had flat bridge of nose, very short philtrum and lower jaw showed retrognathia, had a small chin with severe degree of tongue tie, bilateral equinovarus in the feet, both hands showed polydactyly post axial Type A with six fingers and an additional very small rudimnetary finger attached to both little finger and toe. Syndactyly was seen in the first toe and fingers [Figures 1a-d, 2 and 3]. With these features, a diagnosis of Laurence–Moon–Biedl syndrome or Pallister–Hall syndrome was made; as the child had probably headache, the child was investigated. The child was not cooperative for fundus examination. There were no other obvious oral, genital, or other system changes.

Patient and methods

Goggle visual evoked potential showed very poorly formed responses and with prolonged latency. Ultrasound abdomen was normal. Tandem mass spectroscopy and screening urine for abnormal metabolites, serum lactate, ammonia, cortisol, and thyroid function were normal. Magnetic resonance imaging T2-weighted images showed a slightly hyperintense mass lesion extending from hypothalamus to suprasellar region measuring 1.8 cm × 2 cm. It was isointense in T1 and slightly hyper in flair images [Figures 4 and 5]. Genetic assessment was not done due to lack of availability in Indian setup and financial constraint.

Pallister–Hall syndrome

This is an autosomal dominant disorder characterized by varying combinations of a spectrum of abnormalities which include bifid epiglottis, larynx, imperforate anus, polydactyly, dysmorphic face in the form of small ears pointing backwards, small retroverted nose, with flat nasal bridge, vertical groove in the middle of the upper lip philtrum, small tongue, and hypothalamic hamartomas causing hypopituitarism, micropenis, lethargy, hypoglycemia, electrolyte dysfunction, and metabolic acidosis. They also can have natal teeth, multiple frenula in the cheek, short limbs, dislocated hips, dysplastic lung, and kidney.[6] It was first described in 1980 by Judith Hall and Philip Pallister. And so far, only 100 cases reported in literature.

Genetics

Ninety-five percent of patients show mutation GLI3 gene in the short arm of chromosome 7. This has variable penetrance and expressivity, but within a family, the phenotype remains constant. Different allelic mutations in the same gene can present with different syndromes such as acrocallosal syndrome, preaxial polydactyly Type IV, Greig cephalopolysyndactyly syndrome, and oral-facial-digital syndrome.

Treatment

When infants manifest features of hypopituitarism, management with thyroxin and steroids is indicated. Hypoglycemia and electrolyte imbalance needs to be corrected. Surgery is mostly deferred as it is a malformation and not a tumor. Raised intracranial pressure, seizure also needs to be monitored. Genetic counseling is essential.

Acrocallosal syndrome

Characterized by macrocephaly, hypertelorism, seizures, and mental retardation.

Greig cephalopolysyndactyly syndrome

Polydactyly of fingers and toes, syndactyly, abnormal shape of skull; a high-arched palate, frontal bossing; broad nasal bridge; ocular hypertelorism are features of this syndrome.

Oral-facial-digital syndrome

Epicanthic folds, poly- and syn-dactyly, multiple frenula under the tongue, cleft in the tongue, palate and lip, broad nose, mental retardation, and abnormal dentition are seen.

Other differential diagnosis of different genotype

Holt-Oram syndrome, McKusick-Kaufman syndrome, hydrolethalus syndrome, Laurence–Moon–Biedl syndrome share some features clinically.

McKusick-Kaufman syndrome

These patients present with polydactyly, cardiac abnormalities, cysts in abdomen, abnormal secretions accumulation in vagina, mutation in 20 *p* 12 is seen.[7]

Holt–Oram syndrome

Show abnormalities of the heart with deformity of bones of the forearm and thumb which may be rudimentary, absent or show extra bone called triphalangy, extra scaphoid bones, hypoplastic limbs, humerus clavicles etc. are other features seen.[8]

Hydrolethalus syndrome

Severe neurodevelopmental problems, macrocephaly, small jaw, small nose and small eyes, cardiac and pulmonary dysplasias are the features of this syndrome.[9]

Laurence–Moon–Biedl syndrome

It presents usually with mental retardation, retinitis pigmentosa, polydactyly, obesity, and hypogenitalism. They can have microcephaly, optic atrophy, spina bifida, renal abnormalities, and very rarely hypothalamic hamartomas. Bardet-Biedl syndrome (BBS) is a close differential diagnosis and is characterized by cognitive impairment, genitourinary malformations, rod-cone dystrophy, truncal obesity, male hypogonadotropic hypogonadism, postaxial polydactyly, complex female genitourinary malformations and renal abnormalities.[10]

Discussion

There are several neurodevelopmental disorders associated with polydactyl. They are differentiated both by phenotypic and genotypic characters. It is importance to understand at least some of them as it will help us in guiding parents regarding the risks in subsequent pregnancies as well as prognostication in a given case. Our child has unique features in the form of macrocephaly, cleft in lip and palate, and tongue tie which are distinguishing features clinically from Laurence–Moon–Biedl syndrome [Table 1].

Conclusion

Polydactyly is a marker associated with several neurological disorders. Correct diagnosis is made by the associated abnormalities looked for with high degree of suspicion clubbed with genetic testing whenever possible. This will help in planning treatment, prognostication, and also properly guiding parents for subsequent pregnancy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

We would like to thank the Department of Neurology, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India.

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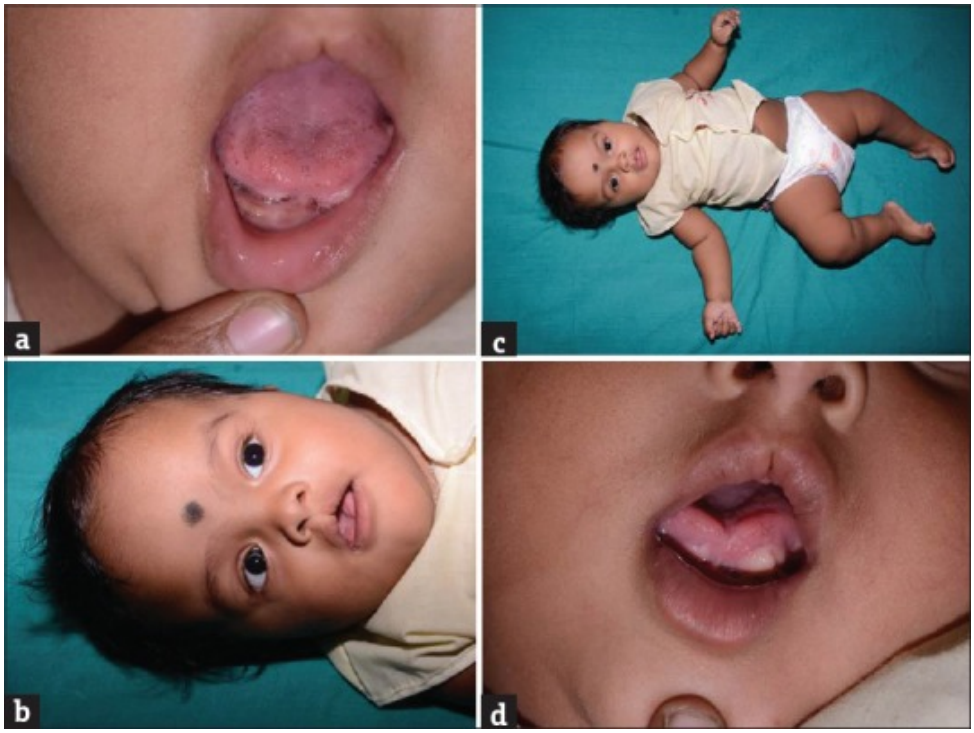
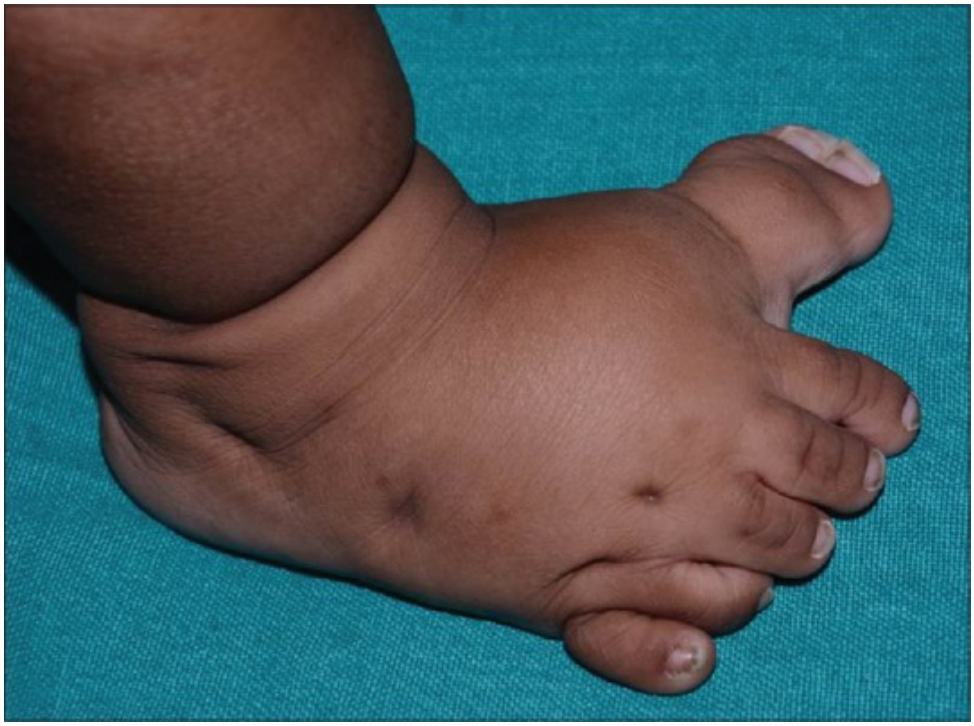
Figures and Tables

Figure 1



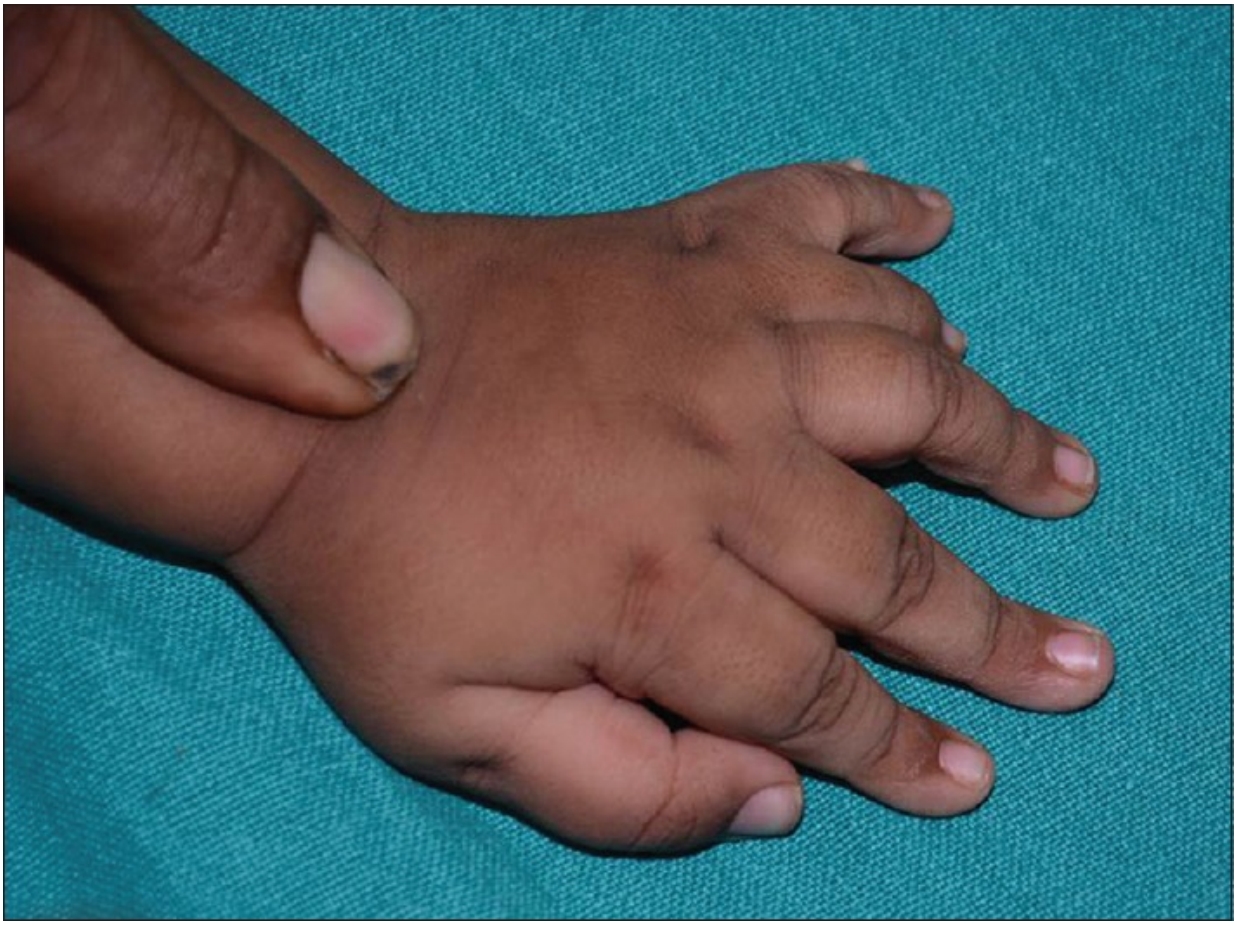
(a) Tongue tie. (b) Frontal bossing macrocephaly with small upper lip and philtrum. (c) Cleft in the upper lip and hard palate. (d) The picture of whole baby

Figure 2



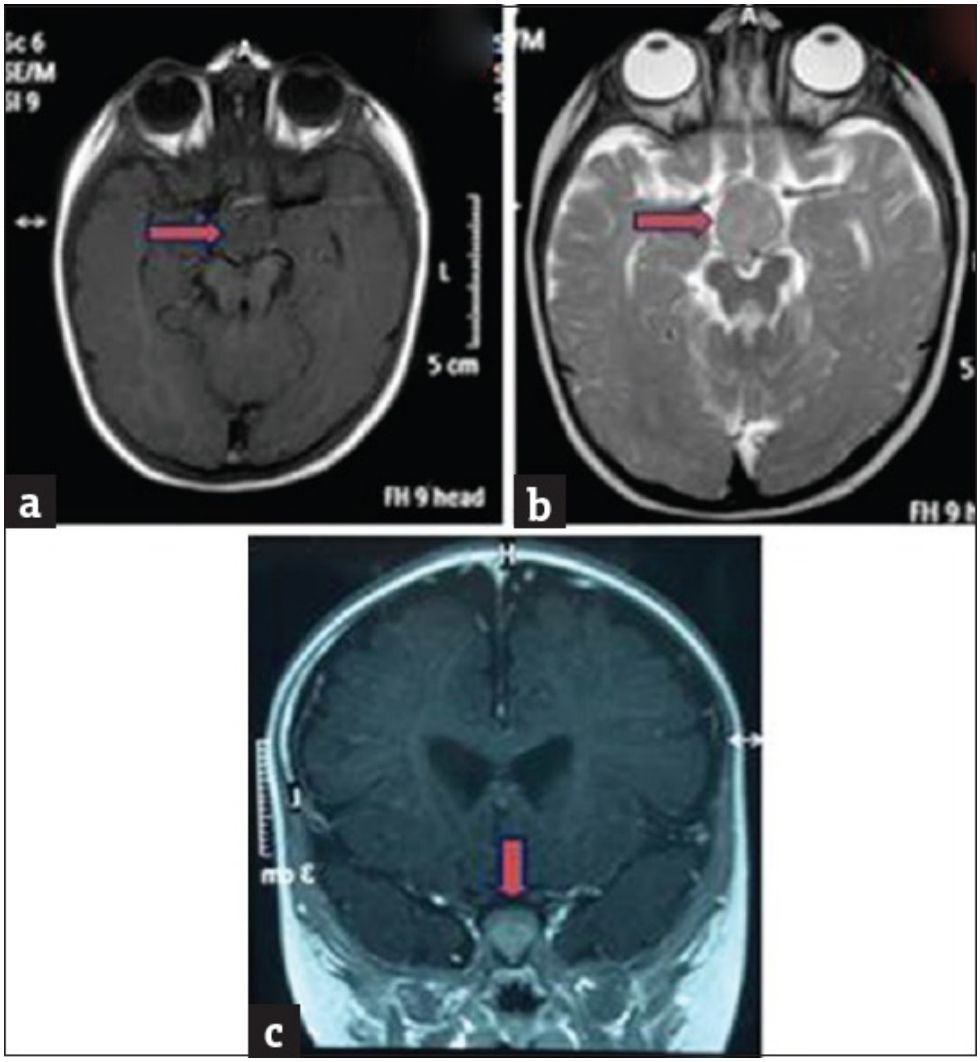
Syndactyly of big toe and postaxial Type A polydactyly

Figure 3



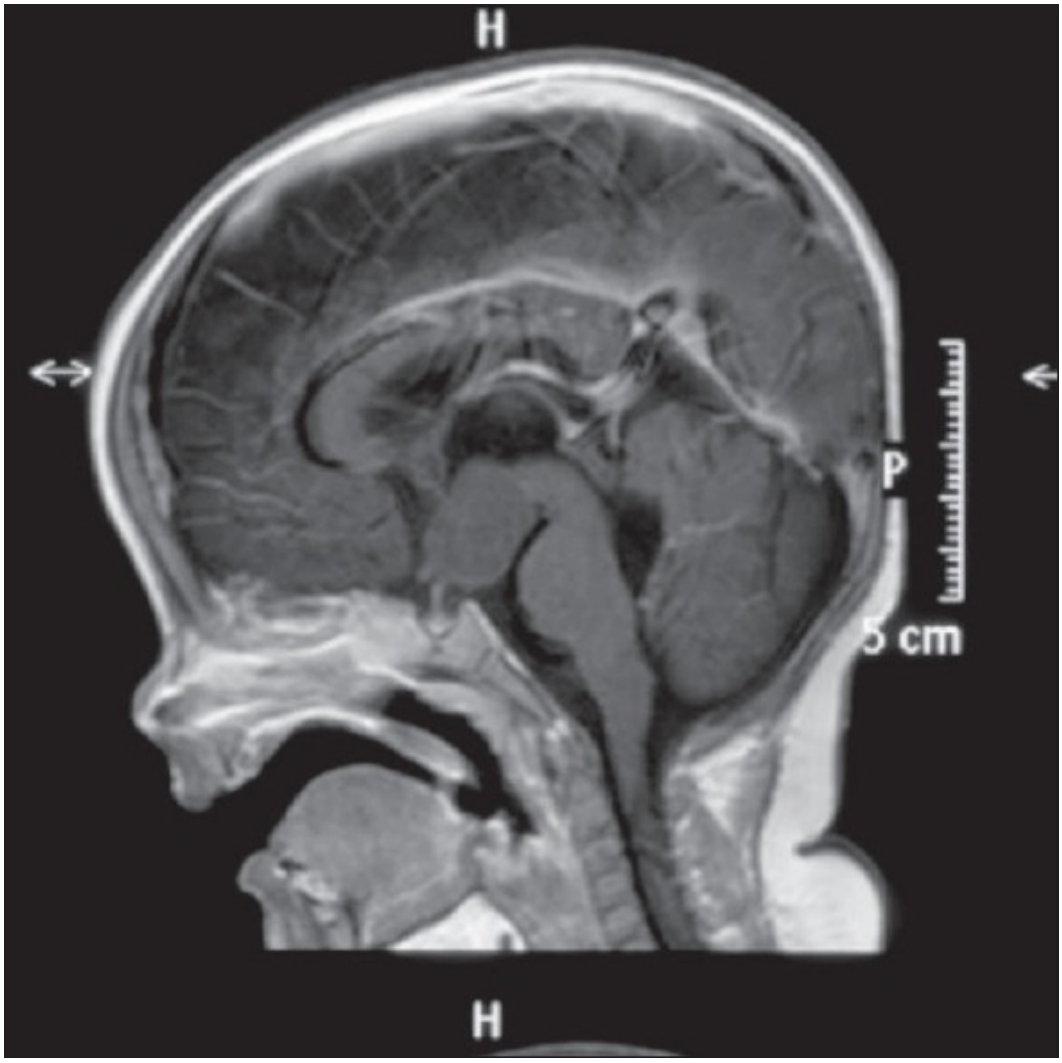
Postaxial Type A polydactyly with an additional small rudimentary finger attached to little finger

Figure 4



(a) shows T1 axial isointense mass in suprasellar region 4 (b) T2 axial hyperintense mass and 4 (c) coronal section fluid-attenuated inversion recovery hyperintense mass in the suprasellar region

Figure 5



T1 sagittal section shows isointense mass extending from hypothalamus to sellar region

Table 1

The differences between LMB syndrome and PH syndrome

Laurence–Moon–Biedl Syndrome	Pallister–Hall syndrome
Microcephaly	Macrocephaly
Retinitis pigmentosa	Optic atrophy
No cleft lip and palate	Cleft in lip and palate
Other system generally normal renal reported +/-	GIT and renal changes
AR BBS gene mutation	AD.GL13 gene chromosome 7

GIT: Gastrointestinal tract, AD: Autosomal dominant