



*Mini review*

## Endocrine manifestations in Joubert syndrome—literature review

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**Abstract:** Joubert syndrome (JS) is a heterogeneously inherited, rare, autosomal recessive disorder characterised by neonatal breathing dysregulation, developmental delay, hypotonia, abnormal eye movements and a distinctive cerebellar and brainstem malformation called the molar tooth sign (MTS). Patients with JS may develop hypothalamic-pituitary dysfunction, leading to growth hormone deficiency, hypothyroidism, adrenal insufficiency and hypogonadism. This review summarizes the screening, diagnosis, and management of these conditions in JS.

**Keywords:** Joubert syndrome; hypothyroidism; adrenal insufficiency; panhypopituitarism; micropenis

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### 1. Introduction

Joubert syndrome (JS) is a rare, autosomal recessive disorder, caused by the affected structure or function of primary cilia, which are highly specialised sensory organelles essential for cellular signal transduction. They are critical for signal transduction processes essential in the development of the nervous system, kidney tissue, retina, and bile ducts [1–3].

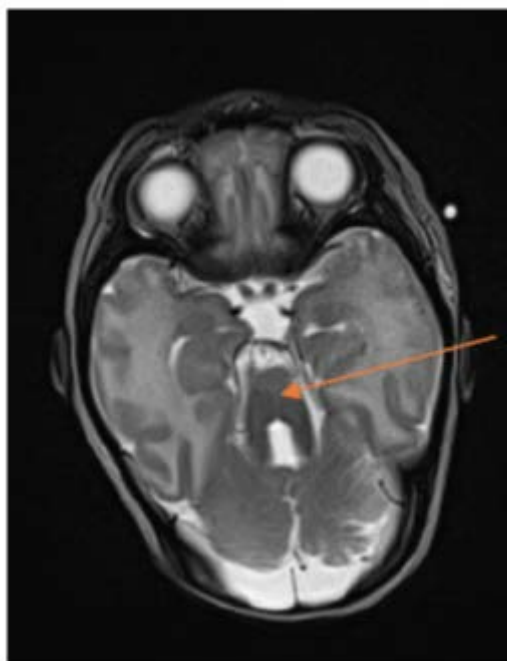
This subcellular sensory organelle is present in the structure of nearly all cell types; therefore, its defects lead to different pathologies. The patients' phenotype and course of the disease can greatly vary depending on the type of mutation and expression.

Clinical suspicion of JS may be set in an early stage of life, in which the circumstances of hypotonia is accompanied by episodic tachypnoea and/or apnea with abnormal eye movements [3,4].

Radiologically, molar tooth sign (MTS), which is a hallmark feature of JS, is revealed on axial views from cranial magnetic resonance imaging (MRI) alongside cerebellar vermis aplasia/hypoplasia,

thick and horizontally oriented superior cerebellar peduncles, and often deepened interpeduncular fossa, which taken together, confirm the diagnosis of JS [4] (Figure 1).

Anatomical malformations, including hypoplasia and midline cleft of the cerebellar vermis, lead to various abnormalities of the central nervous system (CNS) [5,6]. To date, both pituitary agenesis and pituitary aplasia have been reported in patients with JS [7–9].



**Figure 1.** Axial brain MRI presenting JS cardinal feature: molar tooth sign (MTS) characterized by elongated, thickened, superior cerebellar peduncles, vermian hypoplasia and abnormal deep interpeduncular fossa.

Pituitary aplasia and dysplasia may occur as a part of brain malformations leading to several endocrinopathies, including growth hormone deficiency (GHD), central adrenal insufficiency (CAI), central hypothyroidism (CH), hypogonadotropic hypogonadism (HH) and poor bone mineral density (BMD). To date, an imbalance of pituitary hormones was reported in various studies concerning JS [3,4,10–20]. This paper reviews the literature related to hypothalamic-pituitary dysfunction in JS, with an emphasis on diagnosis and treatment.

## 2. Methodology

We performed a literature review regarding the presence of endocrine manifestations in patients with JS. The diagnosis of the main disease was made based on clinical presentation, typical MRI features and, if possible, molecular identification. We searched for MEDLINE via the PubMed database between 1975 and October 2023. The search criteria used in the Medical Subject Headings (MeSH) were as follows: “Joubert syndrome” [All fields] AND “endocrine”, “pituitary”, “panhypopituitarism”, “adrenal”, “adrenal insufficiency”, “growth hormone”, “growth hormone deficiency”, “hypothyroidism”, “micropenis” or “microphallus”. The term “Joubert syndrome” was

present in 998 papers, and searched associations were found in 18 publications. We analysed the original papers, case reports and literature reviews in English. 19 papers included presentations of both JS and endocrine disorders.

### 3. Endocrine manifestations

The main endocrine abnormalities present in individuals with JS and detailed in the following paragraphs include the following: GHD, central hypothyroidism, CAI, micropenis, and HH [4,18,21,22]. The possibility of a diagnosis may vary depending on the age of the patient, starting with new-borns and going up to adulthood.

### 4. Neonatal period

Multiple pituitary insufficiency may be diagnosed as early as in the neonatal period, in the case of hypoglycemia, failure to thrive, or micropenis [23,24]. When it comes to hypoglycemia, its symptoms in neonates vary and may range from non-specific symptoms such as poor feeding, sleepiness, and jitteriness to lethargy, seizures, apnea and comas [25].

#### 4.1. Central adrenal insufficiency

The diagnostic pathways concerning dysfunction of the hypothalamic-pituitary-adrenal axis include the assessment of cortisol and adrenocorticotrophic hormone (ACTH), typically by the use of a low-dose (1 mcg) synthetic ACTH stimulation test. CAI was detected by decreased values 30 and 60 minutes after injection of the corticotropin analogue. In neonates, pituitary function and the response of adrenal glands may be evaluated during hypoglycemia (plasma glucose under 50 mg/dl); significantly lowered levels of ACTH and cortisol confirmed CAI [26,27]. Random levels of cortisol did not have a diagnostic value as the diurnal rhythm of cortisol starts in 6–12 months [27]. Disorders of mineralocorticoid, salt and aldosterone balance are absent as their synthesis is under the control of the renin-angiotensin system [26].

Replacement treatment involves a chronic intake of oral doses of 15 mg/m<sup>2</sup> hydrocortisone, adjusted with clinical follow-up, and monitoring growth rate, weight gain and blood pressure.

In the case of acute adrenal insufficiency, an immediate intravenous hydrocortisone (HC) administration is crucial. The standard dose for newborns starts at 50 mg/m<sup>2</sup> HC, and progressed to a maintenance dose of 50–100 mg/m<sup>2</sup> HC daily.

#### 4.2. Growth hormone deficiency

GHD is the most common endocrine disorder in JS and is found to be another cause of hypoglycemia in neonates. In normal subjects, low glucose leads to a rise in levels of GH and cortisol. Once a peak of GH is absent, GHD can be diagnosed, followed by the confirmation of low insulin-like growth factor type 1 (IGF-1) levels. The evaluation of blood samples during sleep is pointless, as the entrainment of GH secretion does not occur until after three months of age [28].

GHD does not affect birth weight and length [23]. Children with confirmed GHD require early recombinant human growth hormone (rhGH) treatment, which are administered by daily subcutaneous

injections. Doses are adjusted stepwise, and are controlled by IGF-1 and insulin-like growth factor binding protein-3 (IGFBP-3) concentration.

#### 4.3. Central hypothyroidism

All neonates with symptoms or signs of hypoglycaemia must also be checked for central hypothyroidism. In affected individuals, the TSH, fT4 and fT3 levels are all lowered due to insufficient stimulation by the pituitary of the thyroid gland. Apart from lowered glucose levels, patients are mostly asymptomatic. Early replacement treatment with levothyroxine helps maintain the best neurodevelopmental prognosis.

#### 4.4. Hypogonadotropic hypogonadism

Endocrine findings in male newborns with JS include micropenises and cryptorchidism [18]. Minipuberty, which is a postnatal transient activation of the hypothalamic-pituitary-gonadal (HPG)-axis, enables the evaluation of gonadal function in infants suspected of hypogonadism. A physiological peak of luteinizing hormone (LH) and follicle stimulating hormone (FSH) resulting in increased levels of sex hormones is present in healthy infants between 14 days of life and the end of the third month of life.

In the case of lowered LH, FSH and testosterone levels, special attention should be given to proper genital exams so as to determine appropriate therapeutics [4]. Then, in case of low testosterone and micropenises, low doses of testosterone (25 mg) administered intramuscularly may positively correlate with penile growth/elongation. Niceta et al. reported the benefits of topical administration of 2.5% dihydrotestosterone gel [11].

### 5. Childhood

#### 5.1. Growth hormone deficiency

When it comes to the diagnosis of GHD during childhood, systematic measurements and growth monitoring with standard charts are fundamental [4]. Laboratory testing should be considered in the case of clinical suspicion of growth disturbances. Endocrine evaluation is based on IGF-1 and IGFBP-3 serum level, stimulation tests for growth hormone and the assessment of bone age advancement [15]. Once a patient begins rhGH treatment, an emphasis should be placed on orthopaedic control for the presence of scoliosis.

Stephen et al. suggested an association between compound heterozygous mutations of *KIAA0753* in JS siblings and GHD [15]. Expression of this protein may be responsible for the formation and functioning of the pituitary gland, as Hammarsjo et al. reports the presence of two JS patients with small pituitary glands and the *KIAA0753* mutation [29].

#### 5.2. Puberty

A study conducted by Bachman et al. claims a possibility of either precocious or delayed puberty [4]. Nevertheless, Parisi et al. reported a typical onset of pubertal development in both

sexes [3]. In unclear cases of puberty, luteinizing hormone-releasing hormone (LHRH) stimulation with the use of tests may be crucial.

### 5.3. Obesity

A closer look has been taken on obesity due to gene linkage to syndromes known for excess weight. The presence of *CCDC28B*, which is a ciliopathy related gene, is a feature of another ciliary disorder, Bardet-Biedl syndrome (BBS), which has been also confirmed in JS [3]. Another gene, *INPP5E* may be a cause of both JS and a syndrome characterised by obesity, namely MORM (mental retardation, obesity, retinal dystrophy, and micropenis) [30–32].

GHD is an independent risk factor for additional weight as GH does regulate body composition. GHD results in an increased fat percentage and reduced fat-free mass, leading to abdominal obesity [33].

### 5.4. Other

In Healthcare recommendations for Joubert syndrome Bachman et al. does not clearly state about increased frequency of diabetes mellitus (DM), hypothyroidism, polycystic ovarian syndrome, ovarian failure in JS [4], though makes it vital to evaluate pubertal development and thyroid function.

## 6. Cases

A list of previous case reports that mention endocrine disorders in JS patients is provided in Table 1.

Akcan et al. reported an endocrine evaluation of a 13-day old JS newborn with hypoglycemia and a micropenis. CNS imaging revealed pituitary agenesis, and GHD was confirmed based on low levels of GH in stimulating tests and decreased levels of IGF-1 and IGFBP-3. Additionally, both basal and stimulated gonadotropins (short time human chorionic gonadotropin test) were dropped [16].

Lee et al. analysed JS affected families with the *CEP41* mutation: at least one endocrine disorder was present in four out of the eight presented cases, namely GHD, micropenises, hypoplastic scrotums and ambiguous genitalia [12].

Niceta et al. reported a patient born with a micropenis, cryptorchidism, and pituitary malformation (small anterior pituitary, ectopic posterior pituitary), thus presenting with transient hypoglycemia and GHD. Gonadotropin evaluation of an LHRH test at six months revealed a blunted gonadotropin response [11].

Sanders et al. examined three children from a Saudi Arabian family, all with mutation in *KIAA0556*, two of whom had endocrine comorbidities [9].

An endocrine assessment of two siblings with a mutation in *KIAA0753*, performed by Stephen et al. showed that both had GHD and responded well to rhGH therapy. Brain imaging proved an ectopic posterior pituitary gland in the first patient and a small pituitary gland and absent pituitary stalk at second [15].

As analysed by Van de Weghe et al., a single individual out of 11 patients with the *ARMC9* mutation showed GHD and a micropenis [13].

The presence of a micropenis in JS patient was also described in a case report by Asian et al.; however, the authors do not mention diagnostic pathways concerning pituitary function [34].

**Table 1.** The summary of endocrine manifestations in JS mentioned in literature.

Author	Sex	Gene	Hypoglycaemia	GHD	IGF-1	Micropenis	Additional information	MRI	Treatment
Akcan [16]	M	Not known	+	+	Low	+	-	-	rhGH
Lee [12]	M	<i>CEP 41</i>	-	+	NA	+	-	-	NA
Lee [12]	M	<i>CEP 41</i>	-	+	-	+	-	-	NA
Lee [12]	M	<i>CEP 41</i>	-	-	-	+	-	-	NA
Lee [12]	M	<i>CEP 41</i>	-	-	-	+	Ambiguous genitalia, hypoplastic scrotum	-	NA
Niceta [11]	M	<i>KIF7</i> <i>KIAA0556</i>	+	+	Low	+	-	-	rhGH 2.5% DHT
Sanders [9]	F	<i>KIAA0556</i>	-	+	-	-	Hypothyroidism	Hypoplastic pituitary	rhGH
Sanders [9]	M	<i>KIAA0556</i>	-	+	-	+	Panhypopituitarism	-	rhGH
Stephen [15]	M	<i>KIAA0753</i>	-	+	Low	-	-	Ectopic posterior pituitary gland	rhGH
Stephen [15]	F	<i>KIAA0753</i>	-	+	Low	-	-	Small pituitary gland, absent pituitary stalk	rhGH
Uzunhan [35]	M	<i>KATNIP</i>	-	+	NA	-	Hypothyroidism Undescended testicles	Ectopic neurohypophysis	NA
Van de Weghe [13]	M	<i>ARMC9</i>	-	+	-	+	-	-	-
Vilboux [17]	F	<i>CELSR2</i>	-	+	Low	-	-	-	-
Wolf [7]	M	<i>RPGRIPL</i>	-	+	-	-	Hypothyroidism Adrenal insufficiency	Pituitary agenesis	rhGH HC Thyroxine

Note: M: Male; F: Female; GHD: Growth hormone deficiency; IGF-1: Insulin-like growth factor 1; rhGH: Recombinant human growth hormone; DHT: Dihydrotestosterone; HC: Hydrocortisone; NA: Not admitted.

Vilboux et al. described a girl with JS and biallelic mutations in *CELSR2*, severe growth retardation, GHD and an IGF-1 deficiency (serum level lower than -2SD). Apart from that, she had normal thyroid function, no clinical signs of adrenal insufficiency and no structural anomaly of the pituitary gland on brain MRI [17].

In the publication of Wolf et al., a single male patient with the *RPGRIP1L* mutation presented pituitary insufficiency due to pituitary agenesis. He required hormonal replacement therapy consisting of rhGH, hydrocortisone and thyroxine [7].

The case of a mutation in the *KATNIP* gene diagnosed with GHD, CH and undescended testicles was described by Uzunhan et al. [35]. The patients' MRI revealed ectopic neurohypophysis.

Sumathipala et al. [36] also described ectopic neurohypophysis in a patient with biallelic variants in *KIAA0586*, though this patient had a normal endocrine profile.

There is an interesting report by Graber [37] describing a JS girl with congenital hypothyroidism due to thyroid dysplasia. It emphasizes the validity of the distinction between primary and secondary hypothyroidism in patients with developmental delay and hypotonia.

Among reports on large study groups, Bachman-Ganescu et al. reported the prevalence of endocrine manifestations based on 440 JS affected individuals: 5 cases (0.9%) of panhypopituitarism, 4 cases (0.8%) of hypothyroidism, 10 males (1.9%) with micropenises and 11 (2.1%) with other endocrine features (i.e., Hashimoto's disease, insulin dependent diabetes mellitus, unknown type diabetes, ovarian failure, polycystic ovarian syndrome, GHD, elevated parathyroid hormone and absence of pituitary spot, premature puberty and borderline diabetes) [22].

## 7. Conclusions

Joubert syndrome is a multisystem disorder with a variable presentation. Our goal was to emphasise the role of endocrine system disorders and to raise awareness. Considering cases that have already been reported, it is crucial to analyse the image of the pituitary gland on MRI. The onset of endocrine symptoms may range from infancy to adulthood; therefore, it is important and fundamental to survey for disturbances during this period for early recognition. Awareness of hypoglycaemia and its connection with pituitary dysfunction and the need to assess hormonal balance should be priority. Prompt recognition of GHD, hypothyroidism or adrenal insufficiency should lead to hormone replacement as required, though the treatment for JS is symptomatic and supportive.

## Use of AI tools declaration

The authors declare that they have not used Artificial Intelligence (AI) tools in the creation of this article.

## Conflict of interest

All authors declare no conflicts of interest in this paper.

## References

1. Brancati F, Dallapiccola B, Valente EM (2010) Joubert syndrome and related disorders. *Orphanet J Rare Dis* 5: 20. <https://doi.org/10.1186/1750-1172-5-20>

2. Guemez-Gamboa A, Coufal NG, Gleeson JG (2014) Primary cilia in the developing and mature brain. *Neuron* 82: 511–521. <https://doi.org/10.1016/j.neuron.2014.04.024>
3. Parisi MA (2009) Clinical and molecular features of Joubert syndrome and related disorders. *Am J Med Genet C Semin Med Genet* 151: 326–340. <https://doi.org/10.1002/ajmg.c.30229>
4. Bachmann-Gagescu R, Dempsey JC, Bulgheroni S, et al. (2020) Healthcare recommendations for Joubert syndrome. *Am J Med Genet A* 182: 229–249. <https://doi.org/10.1002/ajmg.a.61399>
5. Parisi M, Glass I (2003) Joubert syndrome, In: Adam MP, Feldman J, Mirzaa GM, et al., editors, *GeneReviews® [Internet]*, Seattle: University of Washington.
6. Poretti A, Boltshauser E, Loenneker T, et al. (2007) Diffusion tensor imaging in Joubert syndrome. *Am J Neuroradiol* 28: 1929–1933. <https://doi.org/10.3174/ajnr.A0703>
7. Wolf MTF, Saunier S, O'Toole JF, et al. (2007) Mutational analysis of the RPGRIP1L gene in patients with Joubert syndrome and nephronophthisis. *Kidney Int* 72: 1520–1526. <https://doi.org/10.1038/sj.ki.5002630>
8. Aljeaid D, Lombardo RC, Witte DP, et al. (2019) A novel pathogenic variant in OFD1 results in X-linked Joubert syndrome with orofacioidigital features and pituitary aplasia. *Am J Med Genet A* 179: 1010–1014. <https://doi.org/10.1002/ajmg.a.61018>
9. Sanders AAWM, de Vrieze E, Alazami AM, et al. (2015) KIAA0556 is a novel ciliary basal body component mutated in Joubert syndrome. *Genome Biol* 16: 293. <https://doi.org/10.1186/s13059-015-0858-z>
10. Gana S, Serpieri V, Valente EM (2022) Genotype–phenotype correlates in Joubert syndrome: A review. *Am J Med Genet C Semin Med Genet* 190: 72–88. <https://doi.org/10.1002/ajmg.c.31963>
11. Niceta M, Dentici ML, Ciolfi A, et al. (2020) Co-occurrence of mutations in KIF7 and KIAA0556 in Joubert syndrome with ocular coloboma, pituitary malformation and growth hormone deficiency: A case report and literature review. *BMC Pediatr* 20: 120. <https://doi.org/10.1186/s12887-020-2019-0>
12. Lee JE, Silhavy JL, Zaki MS, et al. (2012) CEP41 is mutated in Joubert syndrome and is required for tubulin glutamylation at the cilium. *Nat Genet* 44: 193–199. <https://doi.org/10.1038/ng.1078>
13. Van De Weghe JC, Rusterholz TDS, Latour B, et al. (2017) Mutations in ARMC9, which encodes a basal body protein, cause Joubert syndrome in humans and ciliopathy phenotypes in Zebrafish. *Am J Hum Genet* 101: 23–36. <https://doi.org/10.1016/j.ajhg.2017.05.010>
14. Delous M, Baala L, Salomon R, et al. (2007) The ciliary gene RPGRIP1L is mutated in cerebello-oculo-renal syndrome (Joubert syndrome type B) and Meckel syndrome. *Nat Genet* 39: 875–881. <https://doi.org/10.1038/ng2039>
15. Stephen J, Vilboux T, Mian L, et al. (2017) Mutations in KIAA0753 cause Joubert syndrome associated with growth hormone deficiency. *Hum Genet* 136: 399–408. <https://doi.org/10.1007/s00439-017-1765-z>
16. Akcan N, Bas F, Poyrazoglu S, et al. (2019) Joubert syndrome with multiple pituitary hormone deficiency. *BMJ Case Rep* 12: e229016. <https://doi.org/10.1136/bcr-2018-229016>
17. Vilboux T, Malicdan MCV, Roney JC, et al. (2017) CELSR2, encoding a planar cell polarity protein, is a putative gene in Joubert syndrome with cortical heterotopia, microphthalmia, and growth hormone deficiency. *Am J Med Genet A* 173: 661–666. <https://doi.org/10.1002/ajmg.a.38005>
18. Parisi MA, Doherty D, Chance PF, et al. (2007) Joubert syndrome (and related disorders) (OMIM 213300). *Eur J Hum Genet* 15: 511–521. <https://doi.org/10.1038/sj.ejhg.5201648>



19. Lucas-Herald AK, Kinning E, Iida A, et al. (2015) A case of functional growth hormone deficiency and early growth retardation in a child with IFT172 mutations. *J Clin Endocrinol Metab* 100: 1221–1224. <https://doi.org/10.1210/jc.2014-3852>
20. Hardee I, Soldatos A, Davids M, et al. (2017) Defective ciliogenesis in INPP5E-related Joubert syndrome. *Am J Med Genet A* 173: 3231–3237. <https://doi.org/10.1002/ajmg.a.38376>
21. Parisi MA, Pinter JD, Glass IA, et al. (2004) Cerebral and cerebellar motor activation abnormalities in a subject with Joubert syndrome: functional magnetic resonance imaging (MRI) study. *J Child Neurol* 19: 214–218.
22. Bachmann-Gagescu R, Dempsey JC, Phelps IG, et al. (2015) Joubert syndrome: A model for untangling recessive disorders with extreme genetic heterogeneity. *J Med Genet* 52: 514–522. <https://doi.org/10.1136/jmedgenet-2015-103087>
23. Hawkes CP, Grimberg A (2013) Measuring growth hormone and insulin-like growth factor-I in infants: What is normal? *Pediatr Endocrinol Rev* 11: 126–146.
24. Gujral J, Yau M, Yang AC, et al. (2019) Primary cortisol deficiency and growth hormone deficiency in a neonate with hypoglycemia: coincidence or consequence? *J Endocr Soc* 3: 838–846. <https://doi.org/10.1210/js.2018-00386>
25. Rosenfeld E, Thornton PS (2023) Hypoglycemia in Neonates, Infants, and Children, In: Feingold KR, Anawalt B, Blackman MR, et al., editors, *Endotext [Internet]*, South Dartmouth: MDText.com, Inc.
26. Dempsher D (2008) Adrenal and pituitary insufficiency in the neonate. *NeoReviews* 9. <https://doi.org/10.1542/neo.9-2-e72>
27. Yiğit Ş, Türkmen M, Tuncer O, et al. (2018) Neonatal adrenal insufficiency: Turkish neonatal and pediatric endocrinology and diabetes societies consensus report. *Turk Pediatri Ars* 53: S239–S243. <https://doi.org/10.5152/TurkPediatriArs.2018.01822>
28. Vigneri R, D'Agata R (1971) Growth hormone release during the first year of life in relation to sleep-wake periods. *J Clin Endocrinol Metab* 33: 561–563. <https://doi.org/10.1210/jcem-33-3-561>
29. Hammarsjö A, Wang Z, Vaz R, et al. (2017) Novel KIAA0753 mutations extend the phenotype of skeletal ciliopathies. *Sci Rep* 7: 15585. <https://doi.org/10.1038/s41598-017-15442-1>
30. Jacoby M, Cox JJ, Gayral S, et al. (2009) INPP5E mutations cause primary cilium signaling defects, ciliary instability and ciliopathies in human and mouse. *Nat Genet* 41: 1027–1031. <https://doi.org/10.1038/ng.427>
31. Hampshire DJ, Ayub M, Springell K, et al. (2006) MORM syndrome (mental retardation, truncal obesity, retinal dystrophy and micropenis), a new autosomal recessive disorder, links to 9q34. *Eur J Hum Genet* 14: 543–548. <https://doi.org/10.1038/sj.ejhg.5201577>
32. Bielas SL, Silhavy JL, Brancati F, et al. (2009) Mutations in INPP5E, encoding inositol polyphosphate-5-phosphatase E, link phosphatidyl inositol signaling to the ciliopathies. *Nat Genet* 41: 1032–1036. <https://doi.org/10.1038/ng.423>
33. Roemmich JN, Huerta MG, Sundaresan SM, et al. (2001) Alterations in body composition and fat distribution in growth hormone-deficient prepubertal children during growth hormone therapy. *Metabolism* 50: 537–547. <https://doi.org/10.1053/meta.2001.22510>
34. Aslan H, Ulker V, Gulcan EM, et al. (2002) Prenatal diagnosis of Joubert syndrome: A case report. *Prenat Diagn* 22: 13–16. <https://doi.org/10.1002/pd.220>

35. Uzunhan TA, Ertürk B, Aydın K, et al. (2023) Clinical and genetic spectrum from a prototype of ciliopathy: Joubert syndrome. *Clin Neurol Neurosurg* 224: 107560. <https://doi.org/10.1016/j.clineuro.2022.107560>
36. Sumathipala D, Strømme P, Gilissen C, et al. (2020) Sudden death in epilepsy and ectopic neurohypophysis in Joubert syndrome 23 diagnosed using SNVs/indels and structural variants pipelines on WGS data: A case report. *BMC Med Genet* 21: 96. <https://doi.org/10.1186/s12881-020-01024-y>
37. Graber JJ, Lau H, Sathe S (2009) Teaching neuroimages: molar tooth sign with hypotonia, ataxia, and nystagmus (Joubert Syndrome) and hypothyroidism. *Neurology* 73: e106. <https://doi.org/10.1212/WNL.0b013e3181c679ba>



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