Rare case report: A Chinese boy with MDPL cause by *POLD1* gene mutation

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INTRODUCTION

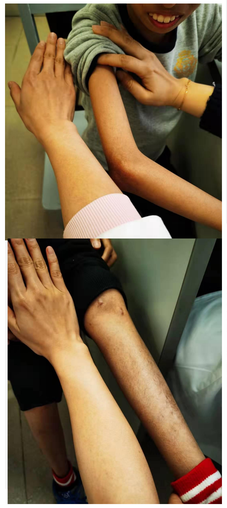
Mandibular hypoplasia, deafness, progeroid features, and lipodystrophy (MDPL) syndrome is a genetic disorder which was first recognized in 2010. MDPL syndrome is comprised of mandibular hypoplasia, deafness, progeroid features, lipodystrophy, hypogonadism and metabolic disorders. It is caused by an autosomal dominant mutation in the polymerase delta 1 (*POLD1*) gene, with <30 genetically confirmed cases to date.

AIM

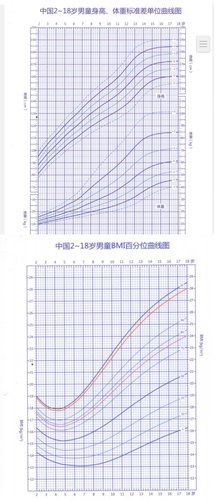
To learn more about this rare disease, and identify it as soon as possible.

CASE

A 13.42-year-old boy came to our clinic for his short stature. He was born at full term to non-consanguineous parents with a normal birth appearance (birth weight 3.2kg and birth height 50cm). He had a poor appetite and grew very slowly (no actual data was recorded). His intelligence and motor development were normal. He was nearsighted, while no hearing lost or hyposmia were noticeable. His height was 132.6cm (-3.9SD) and his weight was 20kg (-2.2SD for Ht). His BMI was 11.37kg/m2. He couldn't close his mouth probably due to mandibular hypoplasia. Subcutaneous fat loss was noted predominantly on his extremities. His testes were 1ml and soft in texture. The stretched penile length was 2.5cm. Laboratory investigations revealed results within the reference ranges for the electrolyte, renal, liver, glucose, insulin, adrenal and thyroid function, without dyslipidemia. GH provocative tests revealed that his maximum serum GH was 3.36 ug/L (L-Dopa and Pyridostigmine bromide). IGF-1 was 126.45ng/mL. The baseline follicle-stimulating hormone (FSH) was 16.56 IU/L and luteinizing hormone (LH) was 4.31 IU/L. The luteinizing hormone-releasing hormone (LHRH) test showed 24.73 IU/L in FSH and 18.55 IU/L in LH in 60mins. The testosterone was 0.17ng/ml. His bone age was 9 yrs.



Patiient's upper and lower limbs



Patient's heigh, weight and BMI in Chinese growth chart

	Recorded value	Normal range
IGF-1, ng/mL	126.45	<–2 SD
FSH, IU/L	16.56	1.00-8.00
LH, IU/L	4.31	2.00-12.00
Stimulated FSH, IU/L	24.73	
Stimulated LH, IU/L	18.55	>5
Testosterone, ng/ml	0.17	1.58-8.77
GH provocative tests (L-dopa and pyridostigmine bromide)	maximum GH 3.36 ug/L	<10
Bone age, year	9	13.5±1

METHOD

Whole exome sequencing (WES) was performed for his severe short stature, lipodystrophy and hypogonadism. WES revealed a de novo three-base deletion (c. 1812-1814delCTC, p.Ser605del) in the *POLD1* gene, which is located in Exon15, 19q13.33. Moreover, it's the most common kind of *POLD1* gene mutation, which is 75% (18/24) up to date.

CONCLUSIONS

We report a rare case of MDPL syndrome cause by *POLD1* gene mutation, whose chief complain was short stature. It strongly supports that severe short stature (< -3 SDS for the population or > 3 SD lower than mid-parental target height) should require genetic testing, especially along with other abnormalities.

REFERENCES

MDPL, mandibular hypoplasia, deafness, progeroid features, and lipodystrophy; POLD1, polymerase delta 1.
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MDPL, mandibular hypoplasia, deafness, progeroid features, and lipodystrophy; MMR, mismatch repair; POLD1, polymerase delta 1; POLE, Polymerase Epsilon.
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