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Case report

Orthopaedic manifestations of Beckwith-Wiedemann syndrome: a case report

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Abstract

Beckwith-Wiedemann syndrome (BWS) is a genetic/epigenetic disorder with overgrowth and cancer predisposition, presenting with symptoms like macroglossia, abdominal wall defects, and limb length discrepancy (LLD). This case report details a 4-year-old female with BWS and a 3 cm LLD, treated with epiphysiodesis using eight-plates in her left femur and tibia. After two years, the plates were removed, achieving equal limb length. The report highlights effective surgical intervention for moderate LLD in BWS, emphasizing the importance of early diagnosis and comprehensive orthopedic management, applying general LLD treatment principles to patients with Beckwith-Wiedemann syndrome.

Keywords

Beckwith-Wiedemann Syndrome; musculoskeletal disease; hemihyperplasia

Introduction

Beckwith-Wiedemann syndrome is a growth disorder that can affect several parts of the body. Children with BWSp presenting with macrosomia are taller and/or larger than average even though the growth rate slows down after the age of eight. Less often the overgrowth disorder affects half of the body (hemihyperplasia).[1-5]

Case Presentation

A 4-year-old female with a known BWS (abnormal methylation of maternal DMR2 at 11p15) was re-

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ferred by a paediatrician for lateralized overgrowth. Other symptoms included diastasis recti, macroglossia, facial naevus flammeus, exophthalmos and left hemihyperplasia extending to the upper and lower extremities. Full leg x-rays were obtained to assess radiographic evaluation of the leg length discrepancy or any deformity of the legs that could affect the surgical management of the patient. Clinical evaluation showed 0,9cm length difference of the upper extremities and 3cm leg length discrepancy (Figure 1). We performed epiphysiodesis of the knee using eight-plates medially and laterally of distal femur and proximal tibia (Figure 2). At three months post-op, the patient reported no problem continuing regular daily activities and a new radiographic evaluation was obtained. The difference between the legs decreased to 2,6cm. The patient was tactically followed up in outpatient clinic and the limb's length was monitored (Figure 3). After two years of treatment the same leg length was achieved (Figure 4) and eight-plates were removed. Because of the possibility of Rebound phenomenon (reoccurrence of LDD), patient will be monitored in outpatient clinic until complete skeletal maturity.

Discussion

Beckwith-Wiedemann syndrome is caused by genetic or epigenetic defects around the

11p15.5 region that contains growth regulator genes. It affects 1 per 10,340 live births, with increased incidence of 1 every 4000 children conceived with assisted reproductive technologies (ARTs). Diagnosis is usually made in the neonatal period or early childhood[1]. Cardinal and suggestive features are used to make a clinical diagnosis or to refer a patient for genetic testing (Table 1).[8] Macrosomia (defined as height and/or weight >2SDS) is present in half of the BWS patients, and even though overgrowth is noted to slow down in late childhood, the final adult height tends to be greater than the parental target height. Growth charts are strongly indicated.[1,4,5] Lateralized overgrowth occurs in only 13% of BWS patients and it might include the upper and/or lower extremity. Cases of lateralized overgrowth with painful scoliosis have been reported. Along with the growth charts, an annual clinical evaluation for leg length discrepancy is strongly indicated and when present, should be referred for Orthopaedic evaluation. LLD ≤2cm can be corrected with shoe lifts, internal (1cm) or external (2cm).[6,7] LLD 2-5cm is indicative for surgical correction, reversible epiphysiodesis of the longer limp is usually the way to go in BWSp, as they tend to reach tall statures.[9,10] With closed growth plates femoral or tibial shortenings with IM nailing are the other options. LLD 5-20cm requires limp lengthening techniques with osteotomies and gradual distraction with external fixation or magnetic IM nail, although these techniques should only be considered for specific cases. Surgical correction of asymmetric overgrowth of the upper limbs is generally not indicated. Joint laxity has been reported to be around 70% in BWS patients in a study, but advanced bone age is only present in 3%.[5-9] In case of the reported patient, epiphysiodesis was proved an effective management of LLD, as during the period of treatment she had no complications and could continue doing her regular daily activities.

Conclusion

The broader implications of this report lie in its contribution to the evolving field of orthopedics, providing valuable insights into effective surgical interventions for moderate LLD in the context of BWS. As the understanding of genetic and epigenetic factors in BWS grows, the importance of early diagnosis and comprehensive management strategies becomes increasingly evident. This article serves as a practical guide for clinicians, offering evidence of the efficacy and tolerability of epiphysiodesis in addressing LLD in BWS patients. Epiphysiodesis of the femur and/or tibia is usually indicated for predicted LLD >2cm, preferably reversible epiphysiodesis with eight-plates is preferable. Limp lengthening should only be considered in specific cases.

Clinical message

Correction of LLD in Beckwith-Wiedemann syndrome follows the general rules of treatment of any limb length discrepancy.

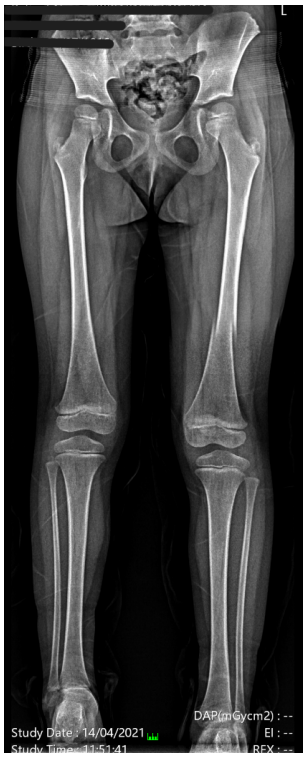

Figure 1. *Preoperative AP full-length leg radiograph*

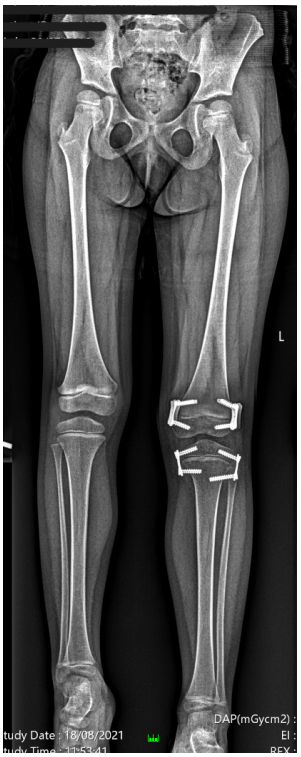

Figure 2. *Postoperative AP full-length leg radiograph*

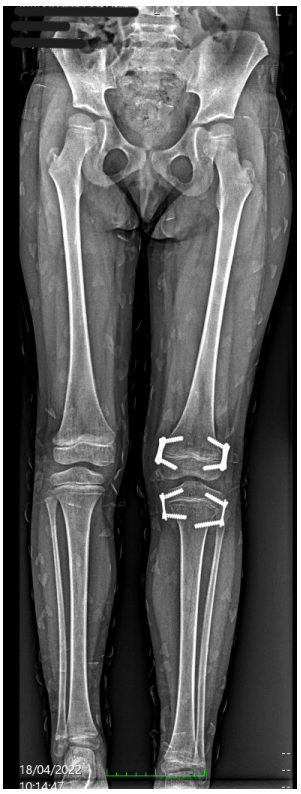

Figure 3. *1 year Postoperative AP full-length leg radiograph*

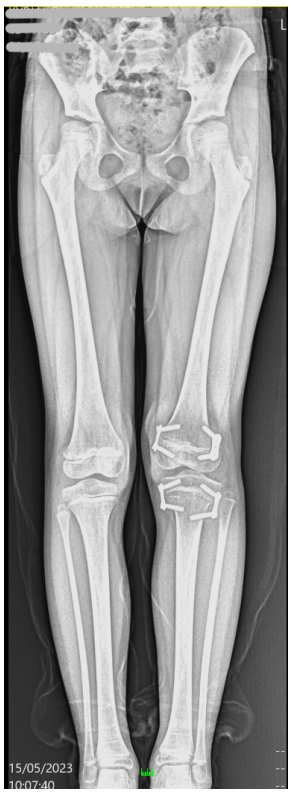

Figure 4. *2 years Postoperative AP full-length leg radiograph*

Table 1. Clinical features of Beckwith–Wiedemann Spectrum	
Cardinal features (2 points per feature)	**Suggestive features (1 point per feature)**
Macroglossia	Birth weight >2 SDS above the mean
Exomphalos	Facial naevus simplex
Lateralised overgrowth	Polyhydramnios and/or Placentomegal
Multifocal and/or bilateral Wilms tumour or nephroblastomatosis	Ear creases and/or pit
Hyperinsulinism (lasting beyond one week and requiring escalated treatment)	Transient hypoglycaemia (lasting less than a week
Pathology findings:adrenal cortex cytomegaly, placental mesenchymal dysplasia orpancreatic adenomatosis	Typical BWSp tumours (neuroblastoma, rhabdomyosarcoma, unilateral Wilms tumour, hepatoblastoma, adrenocortical carcinoma or phaeochromocytoma
-	Nephromegaly and/or Hepatomegal
-	Umbilical hernia and/or diastasis rect

Table 1 Clinical features of Beckwith–Wiedemann Spectrum[8]

An essential diagnostic tool for classical Beckwith-Wiedemann syndrome (BWS) is the standard deviation score, or SDS. For a clinical diagnosis, a score of ≥4 is required; however, molecular confirmation of an 11p15 anomaly is not required. For patients with a score of ≥2, including those with a traditional BWS score of ≥4, genetic testing is advised in order to further explore and validate the diagnosis of BWS. Individuals who have a score below two are not eligible for genetic testing. For patients with a score of ≥2, it is recommended to investigate alternate diagnosis options or refer them to a BWS expert for additional assessment if genetic testing produces negative results[8]

Competing interests

The author(s) declare that they have no competing interests.

Consent

We hereby confirm that written informed consent has been obtained from the patient's guardian for the publication of this case report. All identifying information has been omitted or altered to protect the patient's privacy.

Authors' Contributions

In the collaborative effort of this study, IO, DO, ET, EK all played integral roles encompassing the conceptualization and design of the research, the meticulous acquisition, comprehensive analysis, and insightful interpretation of the acquired data. IO assumed the responsibilities of drafting the manuscript, conducting the clinical examination of the patient and performing the surgery. IO also conducted the necessary diagnostic tests as part of this process. DO and EK, in addition to reviewing the manuscript critically for substantial intellectual input, actively participated in its drafting, further enhancing its intellectual content. ET's proficiency was evident in her assistance during surgery and in the patient's postoperative evaluation. The collaborative writing process involved all four authors, IO, DO, ET and EK who collectively lent their insights to the manuscript, ensuring its quality and significance. With unanimous approval, IO, DO, ET and EK all endorsed the final manuscript. They have embraced full accountability for the research, taking the responsibility to thoroughly investigate and resolve any queries regarding its accuracy or integrity.

References

1. Brioude F, Kalish JM, Mussa A, et al. Expert consensus document: Clinical and molecular diagnosis, screening and management of Beckwith-Wiedemann syndrome: an international consensus statement. Nat Rev Endocrinol. 2018;14(4):229-249. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6022848/
2. Gazzin A, Carli D, Sirchia F, et al. Phenotype evolution and health issues of adults with Beckwith-Wiedemann syndrome. Am J Med Genet A. 2019;179(9):1691-1702. https://onlinelibrary.wiley.com/doi/10.1002/ajmg.a.61301
3. Gerber LH, Chaudhry U, DeBaun M. Joint laxity, scoliosis, and thoracic cage abnormalities in children with Beckwith-Wiedemann syndrome. Eur J Pediatr. 2001;160(2):143-144. https://link.springer.com/article/10.1007/s004310000650
4. Stricker SJ, Hunt T. Evaluation of leg length discrepancy in children. International Pediatrics. 2004;19(3):134-146. http://www.int-pediatrics.org/PDF/Volume_19/19_3/134_146_ip1904.pdf
5. Wang KH, Kupa J, Duffy KA, Kalish JM. Diagnosis and Management of Beckwith-Wiedemann Syndrome. Front Pediatr. 2020;7:562. Published 2020 Jan 21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6990127/
6. Pappas JG. The clinical course of an overgrowth syndrome, from diagnosis in infancy through adulthood: the case of Beckwith-Wiedemann syndrome. Curr Probl Pediatr Adolesc Health Care. 2015;45(4):112-117. https://www.sciencedirect.com/science/article/pii/S1538544215000280?via%3Dihub
7. Mussa A, Di Candia S, Russo S, et al. Recommendations of the Scientific Committee of the Italian Beckwith-Wiedemann Syndrome Association on the diagnosis, management and follow-up of the syndrome. Eur J Med Genet. 2016;59(1):52-64. https://www.sciencedirect.com/science/article/pii/S176972121530046X?via%3Dihub
8. Brioude F, Kalish JM, Mussa A, et al. Expert consensus document: Clinical and molecular diagnosis, screening and management of Beckwith-Wiedemann syndrome: an international consensus statement. Nat Rev Endocrinol. 2018;14(4):229-249. https://www.sciencedirect.com/science/article/pii/S176972121530046X?via%3Dihub#bib23
9. Dimeglio A. Growth in pediatric orthopaedics. J Pediatr Orthop. 2001;21(4):549-555. https://journals.lww.com/pedorthopaedics/citation/2001/07000/growth_in_pediatric_orthopaedics.26.aspx
10. Stevens PM. Guided growth for angular correction: a preliminary series using a tension band plate. J Pediatr Orthop. 2007;27(3):253-259. https://journals.lww.com/pedorthopaedics/abstract/2007/04000/guided_growth_for_angular_correction__a.1.aspx

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