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Case Report

Success of topiramate to slow progression of Blount disease in a toddler: A case study ☆,☆☆

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ABSTRACT

Rates of Blount disease and childhood obesity have increased in parallel, although the co-management of this acquired comorbidity and obesity is not well described. This report shares the course of a toddler with severe obesity who experienced rapid and persistent weight gain without success from nutrition and behavior changes. After repeat subspecialty evaluation, the patient was ultimately diagnosed with signs of early-onset Blount disease, urging the need for adjunct medical therapy. Initiation of topiramate was shown to achieve weight neutrality and improve the patient's body mass index (BMI), appearing to halt the progression of Blount disease and avoiding escalation to surgical treatment. This report suggests topiramate can be an effective and well-tolerated medication in young patients with a pressing need for weight intervention.

Introduction

Blount disease is a progressive growth disorder that results in proximal tibial asymmetry and genu varum malalignment [1,2]. Early-onset Blount disease is positively associated with higher body mass index (BMI) and is becoming more common as the rate of childhood obesity increases [3–7]. First-line treatment with lifestyle modifications can fall short of achieving weight neutrality or weight loss, thereby prompting the need for adjunct medical therapies. We report the case of a toddler with early-onset Blount disease in the setting of severe obe-

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sity refractory to behavioral interventions. Ultimately, weight neutrality was achieved with the initiation of topiramate, and may have halted further progression and avoided the need for surgical correction.

Case report

A 21-month-old female with no significant medical history was referred to the pediatric metabolic syndrome and prevention clinic by her primary care physician for severe obesity and abnormal weight gain of approximately 1 year. At the initial consult age 21 months, her height was 84 cm (60th percentile for age and sex), body weight 22 kg (>99th percentile), and body mass index (BMI) 30.32 kg/m^2 (>99th percentile) (Fig. 1). BMI is expressed as >99th percentile since the percent of the 95th percentile is not available under the age of 2 years.

Birth and family history were unremarkable. Borderline gross motor delay (walked at 16 months) was noted, but otherwise the patient had normal development. The patient lived at home with her mother and 4 older siblings (ages 4, 5, 11, 16). Per her mother, the patient expressed continued hunger (e.g., crying, visible anger) following meals and often requested snacks upon seeing others eat during the day. Her diet consisted of processed grains (e.g., cereal, rice), beans, soup, fruit, and chips; frequent sugar-sweetened beverages (SSB) and reduced-fat milk supplemented her meals. On physical exam, slight bowing of bilateral legs was noted. Initial lab work, including thyroid-stimulating hormone (TSH) and cortisol, was within normal limits. Behavioral approaches focused on scheduled meals and snacks were discussed along with recommendations for outpatient dietician and physical therapy.

At 3-month follow-up, there was continued concern for the appearance of her legs and feet in addition to low muscle tone at physical therapy. Subsequent evaluation by pediatric orthopedics was consistent with physiologic genu varum and reassurance was provided. Over the next year, the patient's BMI steadily increased to 33.7 kg/m^2 (184% of 95th percentile, or %BMI$_{p95}$), and efforts to enroll the patient in the hospital's family-based intensive health behavior and lifestyle treatment program (IHBLT) were unsuccessful. Medical genetic testing was negative for genes associated with early-onset obesity, and history and physical features were deemed inconsistent with syndromic conditions such as Prader-Willi, Bardet-Beidl, or Alström.

At age 3, the patient returned for follow-up at pediatric orthopedics, where hip-knee-ankle radiographs (Fig. 2A) demonstrated continued left-sided genu varum with early signs of Blount disease; plans were made for close monitoring of signs that would warrant surgical intervention with hemiepiphysiodesis. Specialty evaluation at an outside hospital supported the diagnosis of left genu varum; documentation indicated a concern for a limb length difference of 7 cm and metaphyseal diaphyseal angle of 12 degrees. Radiographs from this visit were unavailable for review. A recommendation for a left knee-ankle-foot orthosis (KAFO) was made. Imaging at our institution showed a 1 cm leg length discrepancy. At the family-based clinic, an in-depth discussion with the mother concerning the urgency of addressing weight gain resulted in shared decision-making to trial low-dose topiramate (15 mg sprinkle capsule, twice daily) to lessen her appetite. The goal was to observe for weight status improvement while simultaneously addressing family habits and feeding practices.

Over the next year, the patient and her family participated in monthly multidisciplinary visits through the IHBLT program. Per mother, medication use was not consistent, and she questioned if the medication was helping. Reassurance of weight stabilization on growth charts during clinic visits increased medication frequency over time, as evidenced by regular medication refills. There were no adverse side effects attributed to medication use. Year-over-year improvements were noted in BMI (33.7 vs. 28.6, 184% vs. 158%%BMI$_{p95}$) and Z-scores (8.19 vs. 5.01), while weight was nearly unchanged (34.0 vs. 34.7 kg) compared with before starting topiramate. Height growth velocity continued along the 94-98th percentile. Continued improvement in BMI and weight stabilization was seen at follow-up (BMI 27.4, Z-score 4.41, %BMI$_{p95}$ 152%, 34.9 kg). At age 4, repeat radiographs showed overall improvement in mechanical access and the slope of the medial metaphyseal region (Fig. 2B).

Discussion

Blount disease is an acquired condition characterized by the slow development of epiphysiodesis, leading to hallmark findings of asymmetry and permanent bowing of the lower extremities [2]. Early-onset or infantile Blount disease is often bilateral and occurs between ages 2 to 4; associated risk factors include early ambulation before 10 months, male sex, and black race [2,7,8,11]. Overweight and obesity are chief risk factors for disease progression, largely attributed to excessive load and increased compressive forces on the joints and bones, which are typically amplified on the medial tibial physis [2,9]. Moreover, decreases in ossification and mechanical strength are associated in children with obesity, which may contribute to disease development alongside underlying genetic predisposition [2,10]. Measurements including metaphyseal angle >10° and BMI >22 kg/m^2 have been shown to have strong predictive value of early-onset Blount disease, rendering sensitivity and specificity as high as 95% and 100%, respectively [11]. Our patient met both these criteria to support her eventual diagnosis of Blount disease and the crucial need for thoughtful and expedient intervention.

Güven et al. described 7 cases of otherwise healthy children (age range from 17 to 30 months) who experienced excessive weight gain and outward bowing of legs, ultimately diagnosed with early-onset Blount disease [7]. Patients were noted to have rapid weight gain starting after the transition to supplementary nutrition and early toddling before age 1; all patients were referred for dietary counseling and orthopedic evaluation [7]. Interestingly, while our patient appeared to be conditioned to eat around household members (asking for food from her siblings), likely starting with solid food introduction, she had delayed walking that began at 16 months, which may have delayed diagnosis or an obvious presentation.

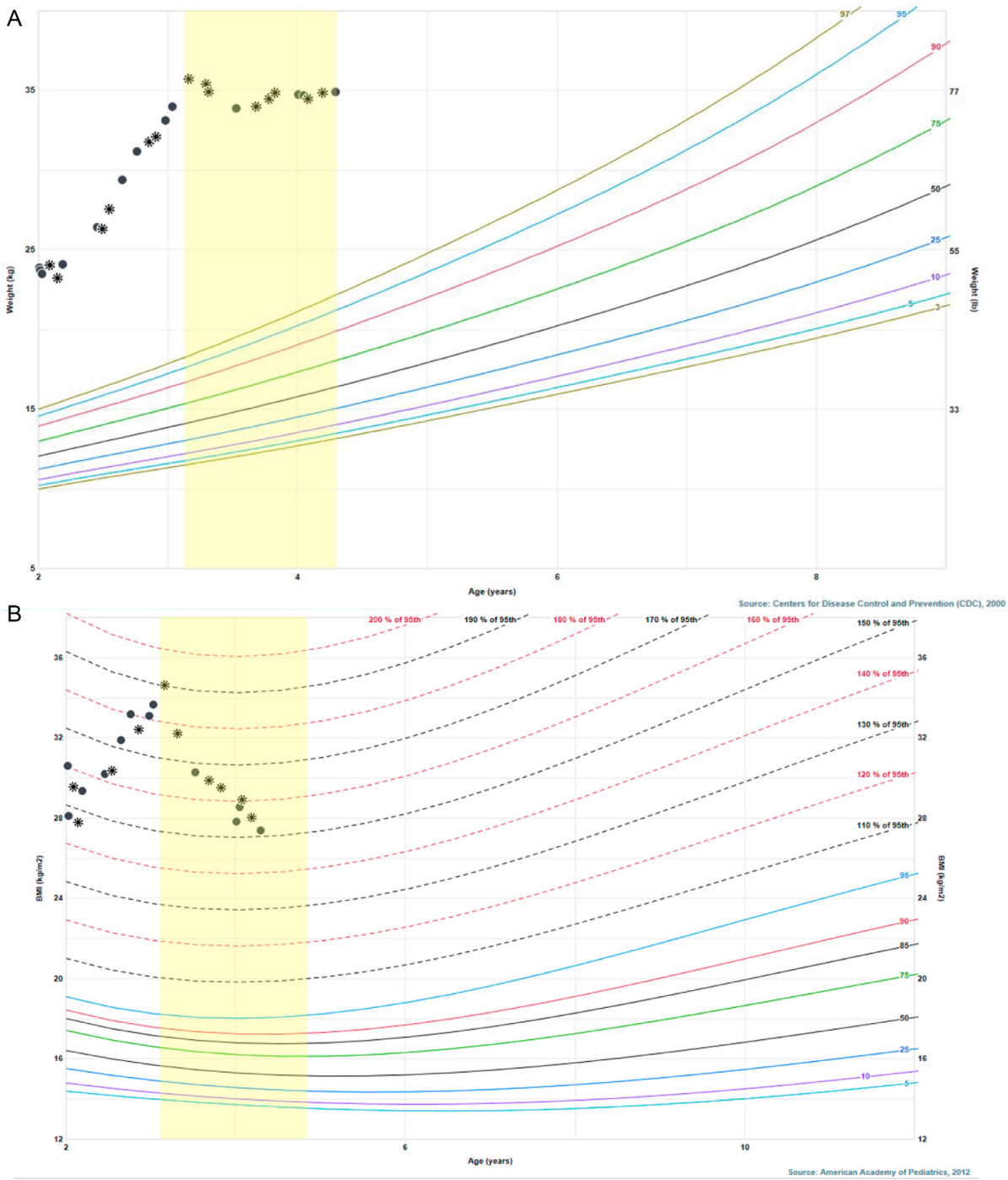

Fig. 1 – The growth charts (CDC Girls 2-20) of extended body mass index (BMI)-for-age percentiles demonstrate down-trending BMI and weight-for-age percentiles reveal stabilization of weight, both as a function of age. The administration period of topiramate is shown with the yellow band. Asterisks (*) indicate outside values while circles (•) indicate in-house values.

There is minimal research on targeting BMI to improve the prognosis of irreversible deformity of Blount disease [7]. Pace and Hennrikus found that weight loss was unsuccessful in a sample of postsurgical pediatric patients, including 22 with slipped capital femoral epiphysis (SCFE) and 11 with Blount disease, mainly due to difficulty implementing behavior changes recommended by the weight management program [12]. To our knowledge, this case report is the first description in the literature of successfully using anti-obesity pharmacotherapy to curb the advancement of Blount disease in a toddler.

Topiramate is a common antiepileptic medication used in children with a proven safety and efficacy profile for the treatment of neurologic disorders [13,14]. Currently, there is

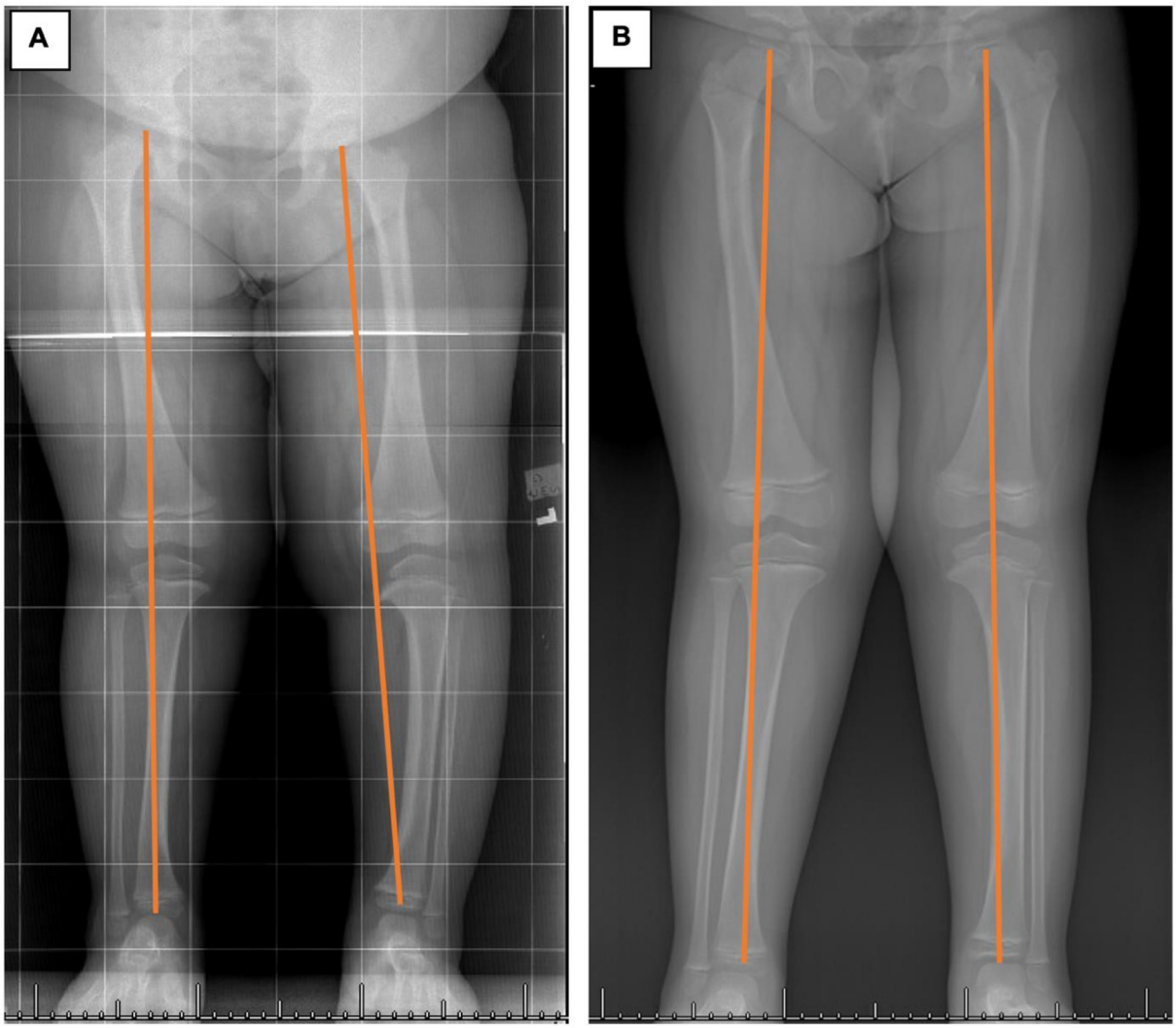

Fig. 2 – Hip-knee-ankle radiographs. (A) At age 3, anterior-posterior lower extremity films showed normal mechanical axis for age on the right with slight valgus positioning of the knee, abnormal bowing on the left with mild proximal medial tibial metaphyseal slope. (B) At age 4, repeat imaging showed overall improvement in mechanical access, left knee in mild valgus, though not symmetric with the right, with improvement in the overall slope of the medial metaphyseal region. Lower limb mechanical axis lines (in orange) are shown for comparison.

no consensus for the off-label use of topiramate as a single-agent anti-obesity medication in pediatric populations [15]. Topiramate's mechanism of action on gamma-aminobutyric acid (GABA) and glutamate, and possibly neuropeptide Y, results in the observed effect of appetite suppression [16,17]. Berman et al. described a case series of 5 children (mean 10.25 years ± 1.5 years) who all demonstrated a decreased $\%BMI_{p95}$ (mean −12% [−5% to −18%]) and improvements in overeating while on topiramate for 16 weeks; medication side-effects were limited to drowsiness in only 1 patient with no evidence of nephrolithiasis, metabolic acidosis, or paresthesia across all cases [15]. Our patient tolerated low-dose topiramate without complaint and achieved a decreased $\%BMI_{p95}$ with weight neutrality. Counseling on topiramate consistency and objective markers of progress on growth charts were discussed during visits to support medication adherence.

Regarding nonoperative management, while prolonged orthotic treatment is an option for children with Blount disease who are younger than 3 years, its usefulness and success is debatable, especially given the type of brace, length of time needed to treat (i.e., greater than 1 year), and patient discomfort while sleeping [2]. Our patient was able to eventually tolerate a KAFO used in Blount disease at night with her mother's encouragement as part of her conservative treatment plan. Continued behavioral changes along with close follow-up likely contributed to her successful outcome.

Pediatric obesity is well-recognized as a growing public health concern that warrants a holistic approach. Lifestyle counseling and support for behavior change as a primary intervention for pediatric obesity is outlined by the United States Preventative Strategic Task Force (USPSTF) and recommended by the American Academy of Pediatrics (AAP) Clinical Practice Guidelines (CPG) [18]. There is limited evidence

for anti-obesity medication use in very young children; at the time of this report, there are few options approved by the US Food and Drug Administration (FDA) for patients under age 18 and none under age 12 [19]. In times when anti-obesity medication is considered as an adjunct therapy to behavioral interventions, weight stigma may contribute to misunderstandings about the biopsychosocial nature of obesity and medications as unmerited substitutes for diet and exercise [19]. Our case report supports the role that judicial medication use can have in supporting nutrition and behavior changes for successful weight management, especially when complicated by rapidly developing comorbidities such as Blount disease.

Patient consent

Written, informed consent for publication of this case was obtained from the patient's parent.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2024.07.183.

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