CANADIAN JOURNAL OF UROLOGY

Tech Science Press

Doi:10.32604/cju.2026.077945
CASE REPORT

Beckwith–Wiedemann syndrome and medullary sponge kidney: a case report of two rare but related entities

Alberto Zambudio-Munuera,[1] María del Carmen Cano-Garcia,[1,2] Africa Navarro-Garcia,[1] Jose Luis Martin-Rodriguez,[3,4] Miguel Angel Arrabal-Polo[1,2,4]*

[1]Urology Department, San Cecilio University Hospital, Granada, Spain
[2]Kidney Stones Unit, Urology Department, San Cecilio University Hospital, Granada, Spain
[3]Radiology Department, San Cecilio University Hospital, Granada, Spain
[4]Instituto Investigación Biosanitaria de Granada, Grupo UROMET, Granada, Spain

ZAMBUDIO-MUNUERA A, CARMEN CANO-GARCIA Md, NAVARRO-GARCIA A, MARTIN-RODRIGUEZ JL, ARRABAL-POLO MA. Beckwith–Wiedemann syndrome and medullary sponge kidney: a case report of two rare but related entities. *Can J Urol* 2026;33(4):999–1005.

Background: *Beckwith–Wiedemann syndrome (BWS) is a congenital overgrowth disorder that may be associated with renal abnormalities, although benign renal manifestations presenting in adulthood are less well characterized.*
Case description: *We report the case of a 20-year-old woman with genetically confirmed BWS who was diagnosed with medullary sponge kidney (MSK) during adulthood after imaging evaluation for suspected renal abnormalities. Contrast-enhanced computed tomography and intravenous urography demonstrated characteristic medullary collecting duct dilatation with nephrocalcinosis, consistent with MSK, associated with hypercalciuria and hypocitraturia. Medical management with thiazide diuretics and potassium citrate achieved metabolic control and stable imaging findings.*
Conclusion: *This case highlights the importance of considering MSK in patients with BWS and underscores the role of appropriate imaging and metabolic evaluation for accurate diagnosis and long-term management.*

Key Words: Cacchi-Ricci disease, Beckwith-Wiedemann syndrome, kidney anomalies, case report

Introduction

Beckwith–Wiedemann syndrome (BWS), first described in 1964, is a congenital multisystem disorder characterized by generalized or segmental somatic overgrowth, macroglossia, neonatal hypoglycemia, abdominal wall defects, and visceromegaly.[1] It has an estimated incidence of 1 in 10,000–15,000 live births.[2] Diagnosis is primarily clinical and based on major and minor criteria; the presence of three major criteria or two major and one minor criterion supports the diagnosis, with macroglossia being the most frequent feature, reported in up to 97% of cases.[1–3] Several risk factors have been associated with Beckwith–Wiedemann syndrome (BWS), including higher concordance among monozygotic twins, female sex, and the use of assisted reproductive technologies. From a clinical perspective, an adequate differential diagnosis is essential and should include other pathogenic entities characterized by overgrowth or dysmorphic features, such as Sotos syndrome, Costello syndrome, and Perlman syndrome, as well as metabolic and storage disorders, including congenital hypothyroidism, mucopolysaccharidoses, gangliosidoses, and Pompe disease.[1–3]

Received date 20 December 2025
Accepted for publication 19 February 2026
Published online 21 August 2026

*Corresponding Author: Miguel Angel Arrabal-Polo.
Email: arrabalp29@gmail.com

BWS results from a variety of genetic and epigenetic alterations affecting the regulation of imprinted genes located at the chromosomal region 11p15.5, which leads to marked heterogeneity in clinical presentation and disease expression. In up to 90% of cases, the syndrome is caused by dysregulation of genes involved in cell cycle progression and somatic growth control, providing a molecular basis for the wide spectrum of phenotypic manifestations observed in affected patients.[4] This genetic and clinical heterogeneity largely explains the variability in both the severity and combination of clinical features.

Hypomethylation of imprinting center 2 (IC2), occurring in approximately 50–60% of cases, is typically associated with the development of macroglossia and omphalocele. Mosaic paternal uniparental disomy (accounting for 20–25% of cases) is most commonly associated with hemihypertrophy and a significantly increased risk of tumor development. CDKN1C mutations (present in 5–10% of cases) are linked to omphalocele and cleft palate, usually with a comparatively lower tumor risk.[2,4,5] Finally, hypermethylation of imprinting center 1 (IC1), observed in 5–10% of patients, is associated with macrosomia and omphalocele.[1,3,6]

BWS has been associated with several renal abnormalities, including hydronephrosis, nephrolithiasis, calyceal diverticula, and medullary sponge kidney (MSK), historically referred to as Cacchi–Ricci disease. MSK is characterized by dilation of the collecting ducts within the inner portions of the medullary pyramids. Although its etiology remains unclear, its clinical relevance lies in its association with nephrocalcinosis, renal stone formation, and metabolic abnormalities such as hypercalciuria, hypocitraturia, and incomplete distal renal tubular acidosis, reported in up to 40% of cases.[7,8]

Renal involvement in Beckwith–Wiedemann syndrome has traditionally been considered within the context of pediatric surveillance, primarily due to the increased risk of embryonal tumors such as Wilms tumor. Consequently, most clinical follow-up protocols are focused on early childhood, with particular emphasis on oncological screening. However, growing evidence suggests that non-malignant renal abnormalities may persist or become clinically relevant beyond the pediatric period, underscoring the need for a broader, long-term perspective on renal health in patients with BWS.[2]

Medullary sponge kidney represents a paradigmatic example of a benign but clinically significant renal anomaly that may remain underdiagnosed, particularly in asymptomatic or minimally symptomatic individuals. Advances in imaging techniques, including contrast-enhanced computed tomography and CT urography, have improved the recognition of characteristic medullary collecting duct abnormalities, yet the diagnosis of MSK is still frequently delayed or incidental. In patients with underlying genetic syndromes such as BWS, subtle imaging findings may be initially overlooked or attributed to nonspecific renal changes, further contributing to underrecognition.[9]

In addition, the clinical presentation of MSK is heterogeneous, ranging from incidental radiological findings to recurrent nephrolithiasis, nephrocalcinosis, metabolic disturbances, and chronic flank pain. This variability complicates the establishment of standardized diagnostic and follow-up strategies, particularly in adult patients with congenital syndromes traditionally managed in pediatric settings. As a result, the transition from pediatric to adult care represents a critical period during which renal manifestations may emerge or evolve.[10,11]

Against this background, detailed case reports remain valuable tools for expanding current knowledge on rare associations such as BWS and MSK. By providing comprehensive clinical, radiological, and metabolic characterization, case-based evidence can help refine clinical suspicion, inform follow-up strategies, and guide individualized management in scenarios where large prospective studies are unlikely to be feasible.

We report this case to highlight the occurrence of medullary sponge kidney as a late-onset benign renal manifestation in Beckwith–Wiedemann syndrome and to emphasize the importance of appropriate imaging and metabolic evaluation beyond childhood.

According to Spanish regulations, formal approval by an institutional ethics committee was not required for this study, as it represents a single anonymized clinical case report without experimental intervention. Written informed consent for publication was obtained from the patient.

This case report was prepared in accordance with the CARE (CAse REport) guidelines,[12] and the completed CARE checklist is provided as Supplementary Material S1.

Case Report

A 20-year-old woman presented at birth (2005) with macroglossia and omphalocele, requiring neonatal surgical repair of the abdominal wall in Jaén, University Hospital Complex, Spain. Due to clinical suspicion of BWS, genetic testing performed in 2008

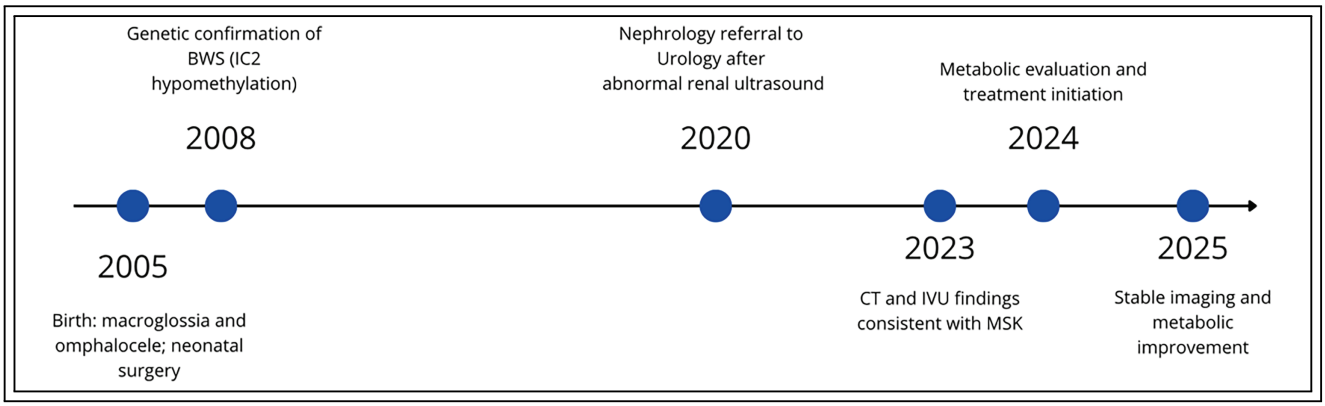

FIGURE 1. Clinical timeline of a patient with Beckwith–Wiedemann syndrome showing key diagnostic, radiological, and therapeutic milestones leading to the diagnosis and management of medullary sponge kidney

confirmed abnormal hypomethylation of the imprinting control region 2 (IC2) on chromosome 11p.

The patient remained under pediatric follow-up and was referred to nephrology in 2020 because of ultrasound findings suggestive of bilateral medullary abnormalities with suspected nephrocalcinosis. Genetic testing for polycystic kidney disease was negative, and she was subsequently referred to urology for follow-up in San Cecilio University Hospital, Granada. Spain. The clinical timeline is shown in Figure 1.

At the time of urological evaluation, the patient was asymptomatic, with no history of renal colic, hematuria, urinary tract infections, or flank pain. Physical examination was unremarkable.

Computed tomography performed in 2023 revealed calcifications within the excretory system associated with diffuse medullary dilation during the excretory phase (Figure 2, blue arrows). Intravenous urography demonstrated multiple punctate calcifications in a "bouquet of flowers" pattern on non-contrast images (orange arrows) and the characteristic "paintbrush" or "sunburst" appearance of the calyces during the excretory phase, without evidence of obstructive uropathy (purple arrows) (Figure 3). These findings were consistent with MSK.

Metabolic evaluation in 2024 revealed significant hypercalciuria (358 mg/24 h; normal <260 mg) and hypocitraturia (145 mg/24 h; normal >320 mg), with normal calcium–phosphate metabolism parameters. Complete distal renal tubular acidosis was excluded by arterial blood gas analysis. Serum creatinine was 0.69 mg/dL with an estimated glomerular filtration rate (eGFR) of 98 mL/min/1.73 m².

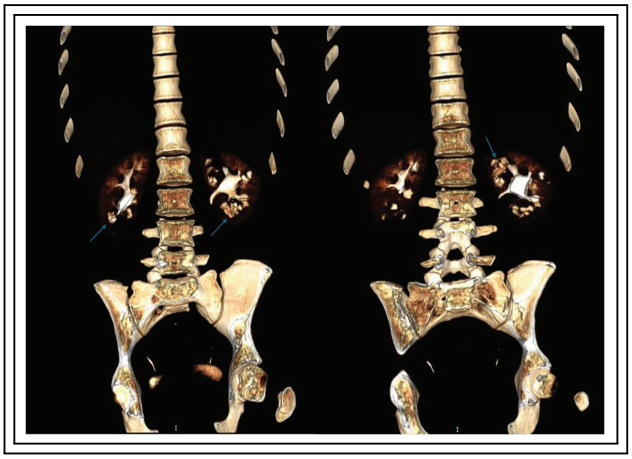

FIGURE 2. CT reconstruction showing dilated medullary collecting ducts (blue arrows)

Treatment with hydrochlorothiazide (25 mg/day) and potassium citrate (40 mEq/day) resulted in improvement of hypercalciuria (280 mg/24 h) and hypocitraturia (330 mg/24 h). Follow-up imaging in 2025 demonstrated stable medullary calcifications without urinary tract lithiasis.

During follow-up, the patient showed a favorable clinical and metabolic response to medical therapy. Twenty-four–hour urine analysis demonstrated improvement of hypercalciuria and hypocitraturia, and renal function remained preserved. Follow-up imaging performed in 2025 revealed stable medullary nephrocalcinosis without evidence of urinary tract lithiasis or obstruction. No treatment-related adverse effects were observed, and the patient remained asymptomatic throughout follow-up.

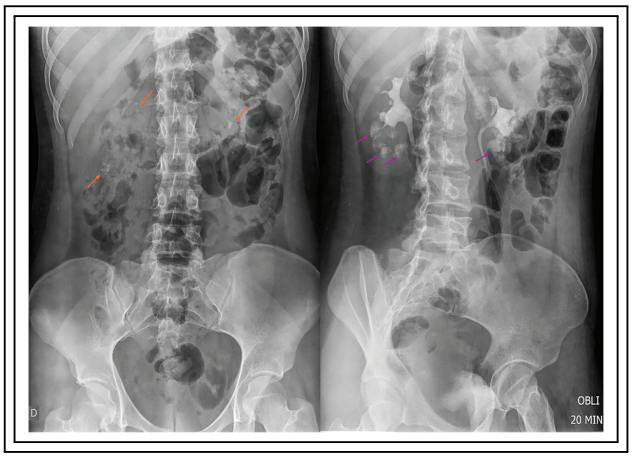

FIGURE 3. Urography is showing multiple punctate calcifications in a "bouquet of flowers" pattern on non-contrast images (orange arrows) and the characteristic "paintbrush" or "sunburst" appearance of the calyces during the excretory phase (purple arrows)

Discussion

In 1998, Choyke et al. reported renal abnormalities in patients with BWS; among 152 patients, 13% exhibited medullary collecting duct dilation consistent with MSK and 12% had hydronephrosis.[8] While the association between BWS and embryonal tumors such as Wilms tumor is well established in childhood, benign renal abnormalities predominate during adolescence and adulthood, as confirmed by Elliot et al.[13] These observations support the relevance of renal surveillance beyond pediatric age in patients with BWS.

The exact mechanism underlying the association between medullary sponge kidney and BWS remains unclear. Nevertheless, MSK should be suspected in patients with BWS who exhibit medullary collecting duct dilatation with dependent calcifications on ultrasound imaging. MSK is characterized by intramedullary calcifications within dilated collecting ducts, which may extend toward the renal papillae and predispose to nephrolithiasis.[14] Systematically evaluated case series have reported nephrolithiasis prevalence rates of up to 60–70% in patients with medullary sponge kidney.[15] Conversely, the prevalence of MSK among patients with nephrolithiasis is likely underestimated in many reports and has been shown to range from approximately 2% to 20%,[1,2,9] depending on study design, imaging techniques, and whether MSK is systematically sought and characterized.

The pathogenesis of MSK appears to be multifactorial, encompassing developmental, genetic, and potentially acquired mechanisms. Developmental hypotheses include altered interactions between the metanephric mesenchyme and the ureteric bud, with disruptions in the GDNF signaling pathway proposed as a contributing mechanism.[16] In addition, intratubular obstruction by calcium salt deposition has been suggested as a secondary process that may promote ductal dilatation and stone formation.[14,16] From an anatomical standpoint, MSK-related abnormalities are bilateral in up to 70% of cases and occur with similar frequency in both sexes.[14,16]

Anatomical abnormalities are frequently associated with metabolic disturbances, particularly hypercalciuria, hypocitraturia, and incomplete distal renal tubular acidosis, collectively conferring a high risk of nephrocalcinosis and nephrolithiasis. The kidney stones most commonly observed are composed of calcium oxalate and/or calcium phosphate.[17,18] Although hypercalciuria represents the most prevalent metabolic abnormality, other alterations, such as hyperuricosuria and hypomagnesuria, may further contribute to calcium crystal precipitation. In the present case, typical anatomical and metabolic features of medullary sponge kidney were observed, including medullary nephrocalcinosis associated with hypercalciuria and hypocitraturia. Notably, despite these characteristic findings and the well-established high risk of stone formation in MSK, the patient did not present overt nephrolithiasis, and medullary calcifications remained stable during follow-up. This clinical course illustrates the heterogeneity of MSK presentation and underscores the importance of early metabolic evaluation and targeted medical management, even in the absence of active stone disease.

Beyond nephrolithiasis and metabolic abnormalities, patients with MSK may experience a chronic flank pain syndrome that is often poorly understood and can be significantly debilitating, even in the absence of active stone disease. This pain may substantially impair quality of life and does not always correlate with imaging findings or stone burden. Recognition of this clinical entity is important, as it frequently represents a major driver of healthcare utilization and therapeutic interventions in this patient population.[2,19]

Management of MSK is multifactorial and includes dietary measures such as adequate hydration, a normocalcemic diet, and oxalate restriction, together with pharmacological therapy aimed at correcting underlying metabolic

abnormalities.[1] Thiazide diuretics are commonly used to control hypercalciuria, frequently in combination with potassium citrate to correct associated hypocitraturia and increase urinary citrate excretion. Long-term thiazide therapy, however, may itself induce hypocitraturia secondary to hypokalemia, an effect that can be effectively prevented by appropriate potassium supplementation, most commonly with potassium citrate.[10] Other metabolic or systemic adverse effects may also occur and should be actively monitored during follow-up.

Follow-up of patients with MSK should be structured and individualized, particularly in those who have developed nephrolithiasis and/or nephrocalcinosis. The primary objectives of surveillance are monitoring stone activity, metabolic abnormalities, and symptom burden, rather than anticipating significant deterioration of renal function, as MSK is generally associated with preserved renal function or only mild chronic kidney disease.

At our center, an initial follow-up is performed every three months, including imaging studies and a comprehensive metabolic evaluation. Once the disease is considered clinically stable and lithogenic risk factors are adequately controlled, follow-up is extended to two evaluations per year. These follow-up visits consist of renal ultrasonography and/or plain abdominal radiography, together with repeat metabolic assessment, in order to ensure sustained disease control and early identification of new risk factors.

From a broader clinical standpoint, the association between BWS and MSK raises important considerations regarding long-term renal surveillance and transitional care. While pediatric follow-up in BWS is well established and largely centered on tumor risk,[2,16] less attention has traditionally been paid to benign renal manifestations that may become clinically relevant later in life.[8] This gap may contribute to delayed diagnosis or fragmented care once patients transition to adult services. In this context, the present case illustrates how renal abnormalities initially identified through nonspecific imaging findings may ultimately reveal a defined congenital renal condition with relevant metabolic implications, emphasizing that MSK should not be regarded merely as an incidental radiological diagnosis, but rather as a condition requiring structured metabolic assessment and individualized follow-up.[20]

Moreover, this case highlights the importance of multidisciplinary collaboration involving pediatric specialists, nephrologists, urologists, and radiologists. Such an approach facilitates continuity of care and ensures that subtle but clinically meaningful findings are appropriately investigated. In rare genetic syndromes such as BWS, where phenotypic expression may evolve over time, this coordinated strategy is particularly relevant.

Although formal guidelines for adult renal follow-up in BWS are lacking, accumulating case-based evidence may help inform future recommendations. Until such data are available, a risk-adapted approach based on imaging findings, metabolic abnormalities, and clinical symptoms appears justified. The present report contributes to this evolving framework by illustrating the potential benefits of systematic evaluation and proactive management in a rare but clinically relevant setting.

From a clinical management perspective, this report illustrates a structured and multidisciplinary approach to a rare association between BWS and MSK. The diagnosis of MSK was established using a combination of contrast-enhanced computed tomography and intravenous urography, allowing accurate characterization of medullary collecting duct dilatation and nephrocalcinosis. Although intravenous urography is currently less frequently used, it remains a valuable diagnostic tool in selected cases, particularly when classical radiological patterns such as the “paintbrush” or “sunburst” appearance are sought.[14,18] Metabolic evaluation was systematically performed, identifying hypercalciuria and hypocitraturia, which guided targeted medical therapy with thiazide diuretics and potassium citrate, in accordance with current recommendations for MSK management.[10,17]

A major strength of this case lies in the comprehensive longitudinal evaluation, integrating genetic confirmation of BWS, multimodal imaging, metabolic assessment, and structured follow-up into adulthood. This approach allowed not only an accurate diagnosis but also effective metabolic control and radiological stability over time. In addition, this case highlights the importance of extending renal surveillance beyond childhood in patients with BWS, as benign but clinically relevant renal abnormalities may manifest later in life.[8,13] The favorable response to medical therapy further supports the role of early identification and correction of metabolic risk factors in preventing stone formation and disease progression.

Nevertheless, several limitations inherent to case reports must be acknowledged. First, causality between BWS and MSK cannot be inferred from a single observation, and the underlying

pathophysiological mechanisms linking imprinting defects at chromosome 11p15 to medullary collecting duct malformations remain speculative. Second, the absence of long-term outcomes beyond early adulthood precludes conclusions regarding lifetime stone risk or renal function trajectory. Finally, genetic analyses were not directed specifically toward genes implicated in nephrolithiasis or tubular development beyond standard testing, which may limit mechanistic insights.

Despite these limitations, this case contributes to the limited body of literature describing renal medullary anomalies in BWS and reinforces the need for awareness of MSK as a potential late manifestation. Careful imaging selection, systematic metabolic evaluation, and individualized follow-up represent key elements of optimal management in this rare clinical context.

A formal patient perspective was not obtained for this case report.

Acknowledgement

None.

Funding Statement

The authors received no specific funding.

Author Contributions

Alberto Zambudio-Munuera and Maria del Carmen Cano-Garcia: conception and write manuscript; Africa Navarro-Garcia: figure and data collection; Jose Luis Martin-Rodriguez: bibliography review; Miguel Ángel Arrabal-Polo: revision and final approval. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

Data supporting the findings of this study are available from the corresponding author upon reasonable request, in accordance with institutional and data protection regulations.

Ethics Approval

According to Spanish regulations, formal approval by an institutional ethics committee was not required for this study, as it represents a single anonymized clinical case report without experimental intervention. Written informed consent for publication was obtained from the patient.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Materials

The supplementary material is available online at https://www.techscience.com/doi/10.32604/cju.2026.077945/s1.

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