World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 7.409

PRUNE BELLY SYNDROME ASSOCIATED WITH TRISOMY 21 AND MULTIPLE MALFORMATIONS: A CASE REPORT OF A COMPLEX MOROCCAN PEDIATRIC PATIENT

H. Ed-Dukar*[1], R. Abilkassem[2]

[1]4th Junior Resident, Department of Pediatric, Children's Hospital, Ibn Sina University Hospital, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco.
[2]Head of Department, Professor, Department of Pediatrics, Mohammed V Military Hospital, Faculty of Medicine and Pharmacy, Rabat, Morocco.

***Corresponding Author: H. Ed-Dukar**
4th Junior Resident, Department of Pediatric, Children's Hospital, Ibn Sina University Hospital, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco.

Article Received on 21/07/2025 **Article Revised on 12/08/2025** **Article Accepted on 01/09/2025**

ABSTRACT
Prune Belly Syndrome (PBS) is a rare congenital disorder characterized by abdominal wall hypoplasia, bilateral cryptorchidism, and obstructive uropathy. Its association with trisomy 21 is exceptionally rare. We report a 3-year-old Moroccan boy with syndromic PBS and confirmed trisomy 21, presenting with multiple visceral and neurological malformations. The patient had abdominal muscle hypoplasia, bilateral undescended testes, megaureters, and polycystic kidneys. Cardiac anomalies included partial atrioventricular canal defect and atrial septal defects. Neurological evaluation revealed schizencephaly, while audiometry demonstrated severe bilateral deafness. Despite recurrent urinary infections, renal function was preserved under prophylactic management. This case illustrates a rare syndromic association and emphasizes the importance of multidisciplinary care and genetic evaluation in complex presentations.

KEYWORDS: Prune Belly Syndrome, Trisomy 21, Congenital Malformations, Uropathy, Schizencephaly, Multiple Malformations.

INTRODUCTION
Prune Belly Syndrome (PBS), or triad syndrome, is a rare congenital disorder that predominantly affects males, with an estimated incidence of 1 in 30,000 live births.[1] It is classically defined by a triad of abdominal wall hypoplasia, bilateral cryptorchidism, and obstructive urinary tract anomalies. The etiology remains debated, with theories ranging from early fetal obstruction to primary mesodermal developmental anomalies.

Trisomy 21 (Down syndrome) is the most common chromosomal disorder, responsible for global developmental delays and a wide malformation spectrum, notably cardiac and gastrointestinal. Its association with PBS is exceedingly rare, raising questions about potential developmental and genetic interactions.

We present a clinical case highlighting this rare association, marked by multiple visceral and neurological malformations, contributing to the characterization of complex syndromic forms.

MATERIALS AND METHODS
This is a single-case observational study reporting a 3-year-old boy diagnosed with Prune Belly Syndrome (PBS) associated with trisomy 21. Data were collected from medical records, imaging studies, laboratory results, and clinical examinations conducted from birth until the current follow-up at 3 years of age.

RESULTS
Clinical Presentation
We report the case of a 3-year-old boy diagnosed with Prune Belly Syndrome associated with trisomy 21, within a context of complex polymalformative syndrome.

The pregnancy was full-term and the delivery was vaginal. Birth weight was 3500 g. In the neonatal period, the patient developed severe respiratory distress requiring mechanical ventilation for 24 days in intensive care.

From birth, dysmorphic features were suggestive of Down syndrome, with generalized axial hypotonia, flat facial profile, upslanting palpebral fissures, broad flat

neck, and a single transverse palmar crease. Karyotype confirmed a free and homogeneous trisomy 21.

Neurodevelopmental delay was noted, discordant with chronological age: at 3 years, the child had not yet acquired walking, exhibited absent speech, and did not respond to auditory stimuli. Clinical examination also revealed a pectus carinatum. Growth was delayed, with weight, height, and head circumference all below −2 standard deviations.

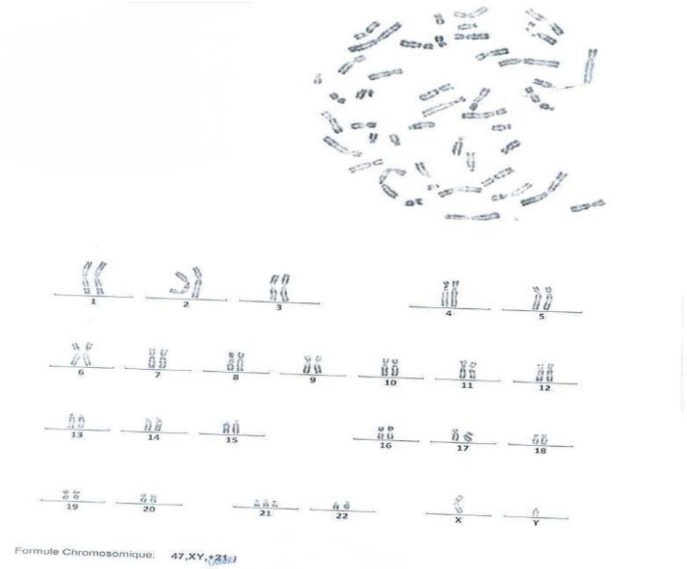

Figure 1: Karyotype analysis of the patient showing a free and homogeneous trisomy 21 (47,XX+21), confirming the diagnosis of Down syndrome.

PBS was evident through marked abdominal wall hypotonia, significant abdominal distension, and bilateral undescended testes. Associated urinary tract malformations included bilateral megaureters, polycystic kidneys, congenital urethral stenosis, balanitic hypospadias, and ectopic ureteral orifices, complicated by recurrent urinary tract infections. Bilateral ureterostomy was performed at 14 months, followed by two meatoplasties. DMSA renal scintigraphy revealed hypertrophic kidneys with heterogeneous uptake, consistent with polycystic disease and recurrent pyelonephritis, but with preserved renal function (right kidney: 60%, left: 40%). Long-term antibiotic prophylaxis was initiated.

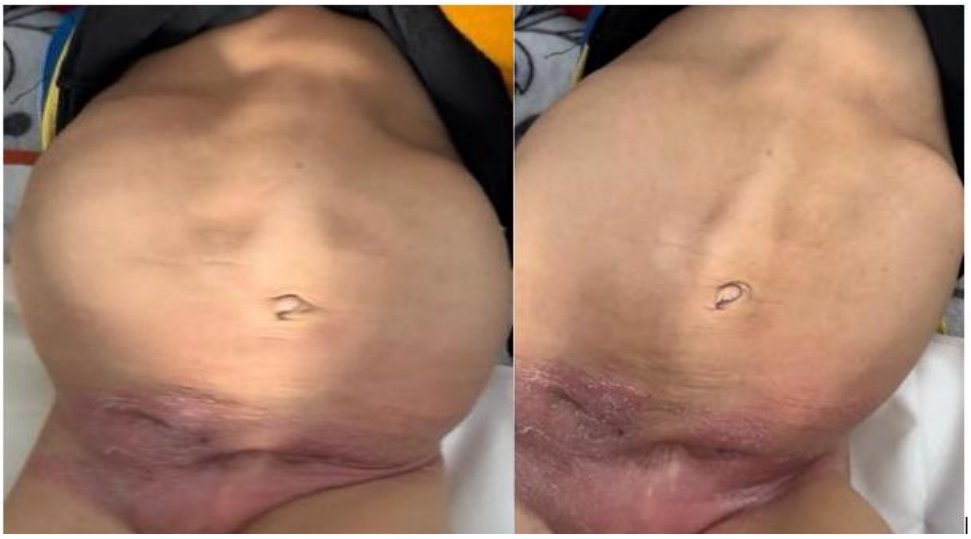

Figure 2: clinical image showing marked abdominal distension with hypotonia and hypotrophy of the abdominal wall muscles, characteristic of prune belly syndrome.

Cardiac evaluation revealed a partial atrioventricular canal defect with a closed ventricular septal defect (VSD), an ostium secundum atrial septal defect (11 mm), and an ostium primum defect (8 mm), without pulmonary hypertension or urgent surgical indication.

Audiometric evaluation demonstrated bilateral severe sensorineural hearing loss, with unmeasurable auditory thresholds in both ears (right and left). The patient was undergoing physiotherapy, speech-language therapy, and pediatric audiologic follow-up. Cerebral MRI revealed a left parietal schizencephaly without ventricular communication.

This case illustrates a rare syndromic form of PBS associated with trisomy 21, combining urological, cardiac, neurological, and auditory malformations and global developmental delay, underscoring the need for close multidisciplinary follow-up involving nephrology, urology, cardiology, neurology, ENT, and developmental pediatrics.

DISCUSSION

This case illustrates a rare and complex form of PBS associated with trisomy 21, complicated by multiple visceral, neurological, and auditory malformations. This syndromic association is exceptional, with few reported cases, raising significant etiopathogenic, clinical, and prognostic questions.

Clinical and etiopathogenic features of Prune Belly Syndrome

PBS, first described by Fröhlich in 1839, is defined by a classic triad: abdominal muscle hypoplasia, bilateral cryptorchidism, and obstructive uropathy.[1] However, complete triad presentation occurs in only 60% of cases, with variable phenotypes including syndromic forms.[2]
Its pathogenesis remains debated. One theory suggests early fetal urinary tract obstruction leads to massive distension, preventing abdominal muscle development.[3] Another theory proposes a primary mesodermal defect affecting musculature, kidneys, and genital organs[4], supported by embryological and molecular studies implicating WNT and Notch signaling pathway disruptions.[5]

Our patient exhibited the full triad of PBS, with additional findings of polycystic kidneys, urethral stenosis, and preserved renal function an encouraging prognostic factor. Urinary prophylaxis is essential to prevent recurrent infections and progression to chronic kidney disease.[6]

Genetic studies of Prune Belly Syndrome: toward molecular clarification

While the etiology of Prune Belly Syndrome remains largely idiopathic, recent advances in molecular genetics have shed light on potential underlying mechanisms. Genetic studies in familial or syndromic cases have identified candidate genes involved in mesodermal differentiation, urinary tract development, and abdominal wall formation. Mutations in the CHRM3 gene, encoding the M3 muscarinic receptor implicated in bladder contractility, have been reported in a few familial PBS cases, suggesting a monogenic autosomal recessive form.[17] Similarly, variants in HNF1β, a transcription factor involved in renal development, have been associated with genitourinary anomalies resembling PBS, particularly when renal cystic dysplasia is present.[18]

Whole-exome sequencing in sporadic cases has also uncovered mutations in genes involved in the BMP, WNT, and Notch signaling pathways, which are crucial for early urogenital embryogenesis.[5,9] However, no recurrent mutations have been consistently identified across studies, underscoring the syndrome's genetic heterogeneity. In our case, no genetic testing specifically targeting PBS-related genes was performed, but the presence of a confirmed constitutional trisomy 21 does not exclude the possibility of concurrent monogenic variants contributing to the complex phenotype. The consideration of genome-wide studies (e.g., CGH-array or exome sequencing) is increasingly recommended in atypical or syndromic PBS presentations to better delineate underlying genetic contributors.[14, 19]

Rare association with trisomy 21: genetic and developmental insights

Trisomy 21 is the most frequent chromosomal abnormality, often associated with congenital heart disease (50% of cases), gastrointestinal anomalies, and developmental delay.[7] Its association with PBS is exceedingly rare, with fewer than ten cases reported.[8]

No direct genetic link has been established, suggesting either chance association or additive developmental disruptions. However, trisomy 21 is known to dysregulate key developmental pathways (SHH, BMP, WNT), potentially increasing susceptibility to urogenital malformations.[9] A study by Lyle et al. noted overrepresentation of regulatory gene anomalies in trisomic patients with rare malformations.[10]

The homogeneous, free trisomy 21 in this case rules out mosaicism or translocation, suggesting a straightforward constitutional anomaly.

Associated polymalformations: syndromic extension and functional impact

In addition to PBS and trisomy 21, the patient exhibited complex congenital heart disease (partial AV canal, ASD, VSD), a rare cerebral malformation (parietal cleft akin to schizencephaly), severe bilateral deafness, and global developmental delay.

Congenital heart defects are common and serious in Down syndrome, contributing to morbidity and mortality.[11] Schizencephaly, defined by a CSF-filled cortical cleft, is exceptionally rare in trisomic patients.[12] Its coexistence with PBS is unprecedented, raising the possibility of an expanded syndromic phenotype or multifactorial origin.

The profound bilateral deafness, with unidentifiable auditory thresholds, significantly worsens developmental

prognosis and necessitates specialized care.[13] Together, these features may suggest an unrecognized genetic syndrome, warranting advanced genetic testing (e.g., CGH-array, exome sequencing).[14]

Multidisciplinary management and prognosis

Managing PBS associated with trisomy 21 presents a multidisciplinary challenge involving nephrology, urology, cardiology, neurology, ENT, and rehabilitation. Preserving renal function through long-term antibioprophylaxis and conservative surgery is a key priority.[15] Urogenital malformation correction must be individualized based on neurological and cardiac prognosis.

In this case, normal renal function is a positive prognostic factor. However, the severe neurodevelopmental delay and profound hearing loss limit functional rehabilitation potential. Prognosis depends on the severity of malformations and infection or cardiac complication control. Woodard et al. reported a 30% neonatal mortality rate in severe PBS cases.[16]

Long-term follow-up should focus on early detection of chronic kidney disease, cardiac monitoring, and developmental support.

CONCLUSION

This case highlights a rare syndromic form of PBS associated with trisomy 21 and multiple visceral and neurological malformations. It underscores the importance of early diagnosis, multidisciplinary management, and genetic evaluation. Reporting such cases may contribute to better understanding of pathogenesis and therapeutic strategies.

ACKNOWLEDGEMENTS

The authors thank the pediatric and genetics teams of Mohammed V Military Hospital for their support in patient management.

FUNDING

No funding was received for this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Routh JC, Huang L, Retik AB, Nelson CP. Contemporary epidemiology and characterization of newborns with Prune Belly syndrome. Urology, 2010; 76(1): 44–8.
2. Woodhouse CRJ. Prospects for fertility in boys with prune belly syndrome. J Urol, 2004; 172(4): 1420–2.
3. Yiee JH, Johnson EK, Gonzales ET. Management of end-stage renal disease in prune belly syndrome. Urol Clin North Am, 2010; 37(2): 349–57.
4. Farikullah J, Keith R, Stewart RJ, Kenny SE, Ransley PG. Prune belly anomaly: associated anomalies, management and outcome. J Pediatr Urol, 2010; 6(1): 11–5.
5. Goetz SC, Anderson KV. The primary cilium: a signalling centre during vertebrate development. Nat Rev Genet, 2010; 11(5): 331–44.
6. Sobral Filho DC, Dos Santos DR, Toledo AP, et al. Long-term follow-up of patients with prune belly syndrome: urinary tract infection and renal function. Int Braz J Urol, 2019; 45(6): 1206–13.
7. Freeman SB, Bean LH, Allen EG, et al. Ethnicity, sex, and the incidence of congenital heart defects: a report from the National Down Syndrome Project. Genet Med, 2008; 10(3): 173–80.
8. Velasquez MP, Meza JL, Portilla J, et al. Prune belly syndrome associated with Down syndrome: a rare association. Urol Case Rep, 2018; 19: 62–4.
9. Antonarakis SE. Down syndrome and the complexity of genome dosage imbalance. Nat Rev Genet, 2017; 18(4): 147–63.
10. Lyle R, Béna F, Gagos S, et al. Genomic deletions and duplications in patients with Down syndrome. Hum Mol Genet, 2009; 18(19): 3718–29.
11. Brodsky MC, Patel BC. Congenital heart defects in Down syndrome: implications for vision and development. Ophthalmology, 2013; 120(7): 1573–5.
12. Barkovich AJ, Kjos BO, Jackson DE Jr, Norman D. Normal and abnormal development of the cerebral cortex: MR imaging and histopathology. Radiology, 1988; 168(1): 223–9.
13. Shearer AE, Hildebrand MS, Smith RJ. Hereditary hearing loss and deafness overview. GeneReviews® [Internet]. 1999 Jul 26 [updated 2021 Mar 18]. Available from: https: //www.ncbi.nlm.nih.gov/books/NBK1434/
14. Cooper GM, Shendure J. Needles in stacks of needles: finding disease-causal variants in a wealth of genomic data. Nat Rev Genet, 2011; 12(9): 628–40.
15. Bomalaski MD, Baskin LS. Prune belly syndrome. Urol Clin North Am, 2004; 31(4): 497–509.
16. Woodard JR, Hendren WH, Jeffs RD. Prune belly syndrome: A proposed classification. J Urol, 1979; 121(2): 148–50.
17. Weber S, Thiele H, Mir S, Toliat MR, Sozeri B, Horst J, et al. Muscarinic acetylcholine receptor M3 mutation causes urinary bladder disease and a Prune-Belly-like syndrome. Am J Hum Genet, 2011; 89(5): 668–74.
18. Clissold RL, Hamilton AJ, Hattersley AT, Bingham C, Carr IM, Sheridan E, et al. HNF1B-associated renal and extra-renal disease—an expanding clinical spectrum. Nat Rev Nephrol, 2015; 11(2): 102–12.
19. Caruana G, Wong MN, Walker A, Heloury Y, Dickinson JE, Peat RA, et al. Copy-number variation analysis in Prune Belly Syndrome implicates multiple developmental pathways. PLoS One, 2014; 9(2): e88765.