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Costello Syndrome and Transitional Cell Carcinoma of Bladder

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Abstract

Costello syndrome is a rare neurodevelopmental disorder (RASopathy) caused by activating germline mutation in HRAS. Due to ubiquitous HRAS gene expression, Costello Syndrome affects multiple organ systems and individuals are predisposed to cancer. A male patient, at 13 years of age, had a suspicion of two small findings in the bladder after he had a history of dysuria and microscopic hematuria by two urine analyses. Both were completely resected and the pathology revealed Fibroepithelial polyps. The patient was followed up by an ultrasound of the bladder every six months.

Keywords

Costello, Pediatric, Children, Transitional Cell Carcinoma

1. Introduction

Costello syndrome is typically characterized by failure to thrive in infancy, developmental delays, short stature, coarse fascial features, intellectual disability, diffuse hypotonia and joint laxity, and many other features.

Besides, patients with Costello syndrome have an approximately 15% lifetime risk for malignant tumors, including rhabdomyosarcoma, neuroblastoma, and transitional cell carcinoma of the bladder in adolescents and young adults [1] [2].

A male 13-year-old patient, in our case, had two bladders found by an ultrasound after he had a urological symptom.

2. Case

The patient presented to my clinic at the age of 13 years for the first time, complaining of dysuria and with two urine analysis tests of microscopic hematuria, with no clinical finding by physical examination, but short stature, curly fine hair,

and coarse fascial features.

The examination was followed by an ultrasound of the kidneys and bladder which demonstrated suspicion of two small findings in the left wall of the bladder, each one about 5 mm.

In February 2023, both findings were completely resected by a pediatric resectoscope.

Pathology demonstrated Fibroepithelial polyps with subepithelial stroma cells and few blood vessels.

My patient was followed by an ultrasound every 6 months with no pathological findings and with non-urological symptoms.

As the findings in pathology were not cancerous, the patient will be followed by cystoscopy every two years and an ultrasound every 6 months.

3. Discussion

Costello syndrome is typically characterized by failure to thrive in infancy because of severe postnatal feeding difficulties, developmental delay, short stature, coarse fascial features, curly, fine or spare hair, intellectual disabilities, loose soft skin with deep palmar and plantar creases, diffuse hypotonia and joint laxity with ulnar deviation of the wrists and fingers.

Costello syndrome is a RASopthy caused by activating germline mutation in HRAS. Costello syndrome affects multiple organ systems and individuals are predisposed to cancer.

In a review published in April 2022, 13 patients above 10 years of age had bladder lesions detected in 11/13 patients.

Histological analysis documented premalignant lesions in 90% of cystoscopies performed, epithelial dysplasia in 71% and papillary urothelial neoplasm of low malignant potential in 19%, bladder Cancer G1/Low Grade (Ta), was removed in 10% [1].

The occurrence of bladder carcinoma in adolescents is distinctly unusual as this is typically a neoplasm of older adults and is not seen with increased frequency in other tumor predisposition syndromes. The increased tumor frequency in CS led to the proposal of a screening protocol, consisting of abdominal and pelvic ultrasounds, and urine studies for catecholamine metabolites and hematuria.

Registry-based studies of patients with Costello syndrome and related disorders diagnosed with molecular genetics and a high-quality long-term follow-up are necessary to further estimate the incidence of malignancy.

Our 13-year-old male patient had a fibroepithelial polyp in a pathologic specimen after it was resected completely on the bladder [3].

The dilemma was how to continue follow-up with the patient, considering his health condition and the need for clinical follow-up of other clinical findings from which he suffers, so after going through many works and articles and a detailed explanation to the patient and his parents [4] [5], it was decided to follow-up with a urinary tract ultrasound test once every six months and a diagnostic cystoscopy

test Once every two years and depending on the findings that are discovered, we will decide on changing the nature of the follow-up.

Screening for microscopic hematuria as a marker for bladder carcinoma may be indicated, although this requires further evaluation.

Because there is not a consensus guideline as these guidelines are based on expert opinion and do not represent evidence-based guidelines due to the lack of data for this condition (Figure 1, Figure 2).

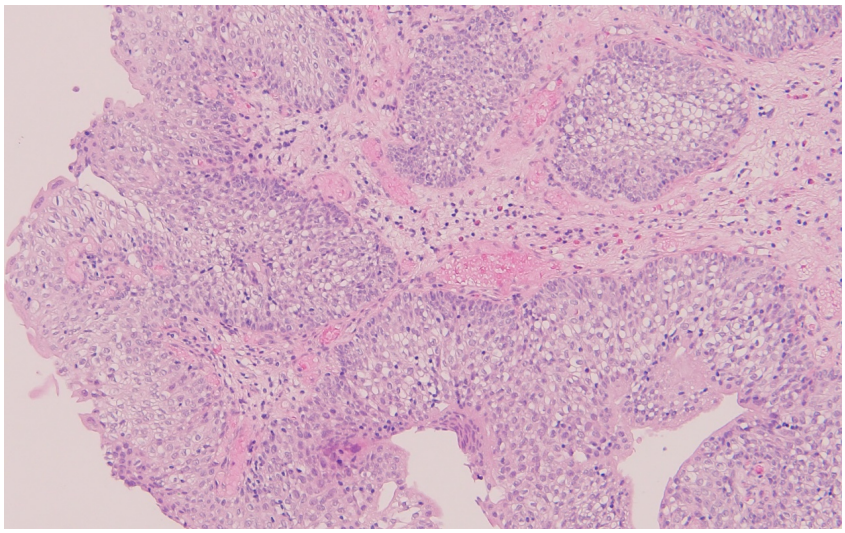

Figure 1. Fibroepithelial polyps in Costello syndrome.

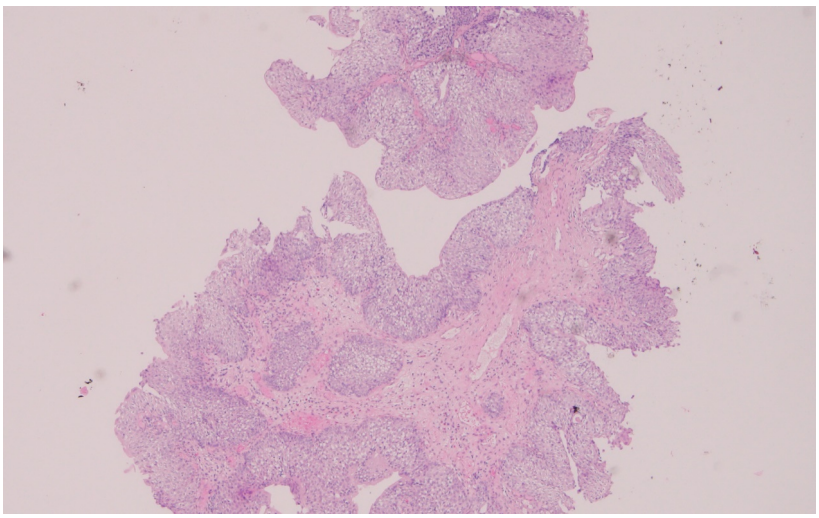

Figure 2. Fibroepithelial polyps with underlying stromal cells with few blood vessels.

4. Conclusion

Costello syndromes have an approximately 15% lifetime risk for malignant tumors, with bladder cancer caused in adolescents and young adults. Our patient had a benign finding in his pathologic specimen, but he has the potential to have a malignant tumor, so he has to be in follow up as we recommend doing an

ultrasound every 6 months with urine analysis with cystoscopy every 2 years [4].

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Leoni, C., Paradiso, F.V., Foschi, N., *et al.* (2022) Prevalence of Bladder Cancer in Costello Syndrome: New Insights to Drive Clinical Decision-Making. *Clinical Genetics*, **101**, 454-458. https://doi.org/10.1111/cge.14111

[2] Beukers, W., Hercegovac, A. and Zwarthoff, E.C. (2014) HRAS Mutations in Bladder Cancer at an Early Age and the Possible Association with the Costello Syndrome. *European Journal of Human Genetics*, **22**, 837-839. https://doi.org/10.1038/ejhg.2013.251

[3] Schmetz, A., Ballesta-Martínez, M.J., Isidor, B., Sousa, A.B., Wieczorek, D. and Bramswig, N.C. (2024) Adult Syndromology: Challenges, Opportunities and Perspectives: Illustrated by the Description of Four Adults with COSTELLO Syndrome. *Journal of Medical Genetics*, **36**, 95-102. https://doi.org/10.1515/medgen-2024-2023

[4] Urakami, S., Igawa, M., Shiina, H., Shigeno, K., Kikuno, N. and Yoshino, T. (2002) Recurrent Transitional Cell Carcinoma in a Child with the Costello Syndrome. *Journal of Urology*, **168**, 1133-1134. https://doi.org/10.1016/S0022-5347(05)64609-5

[5] Gripp, K.W., Scott Jr, C.I., Nicholson, L., McDonald-McGinn, D.M., Ozeran, J.D., Jones, M.C., Lin, A.E. and Zackai, E.H. (2002) Five Additional Costello Syndrome Patients with Rhabdomyosarcoma: Proposal for a Tumor Screening Protocol. *American Journal of Medical Genetics*, **108**, 80-87. https://doi.org/10.1002/ajmg.10241