

Inflammatory cloacogenic polyp with low grade mucinous dysplasia in orthotopic neobladder: expect the unexpected

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Dear Editor,

Radical cystectomy for non-neoplastic conditions, like congenital defects, entails reconstructing urinary transit through various diversion surgeries. Among these, orthotopic neobladder is a surgical procedure suitable for low-risk patients with extended life expectancy, involving the creation of a pouch using an iso-peristaltic ileal or colonic segment to replace the native bladder ¹. Urinary diversions involving intestinal segments may present with different types of complications, with malignancy being the rarest ^{2,3}, with an estimated prevalence of 0.2% ³ and an 8.5- to 10.5-fold increased risk of colon-type adenocarcinoma compared to the general population. In particular, orthotopic colonic neo-bladders bear a significantly higher risk (25-fold) of neoplastic transformation compared to ileal neo-bladders ³. Neoplasms within the intestinal component of urinary diversions may be represented by either benign (mostly colonic adenomas) or malignant lesions (mostly colonic adenocarcinoma), with a latency ranging from 6 to 33 years ^{3,4}. The exact mechanism underlying the carcinogenesis in these instances is still unclear, although endogenous production of nitrosamines by bacterially reduced nitrate may play a putative role ³.

We report a unique case of a polypoid lesion arising with a 31-year latency in a colonic neo-bladder performed for a non-neoplastic condition. In July 2023, a 48-year-old male patient presented at our center to follow-up a neobladder biopsy diagnosis of urothelial carcinoma in situ performed in another center. A computed tomography scan revealed a 46 mm polypoid lesion involving the left lateral side of the neobladder, partially involving the homolateral ureteral meatus. According to the urologist of the afferent hospital, an accurate resection of the lesion was not amenable due to the altered patient's anatomy. The patient had previously undergone surgical treatment for bladder exstrophy in 1992 at the age of 17 years, involving a ureterosigmoidostomy and perineal colostomy according to the Gersuny technique, followed by urethroplasty and mons pubis reconstruction. Bladder exstrophy is one of the manifestations of the Exstrophy-Epispadias Complex, comprising different

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lower abdominal midline malformations, like epispiadias, bladder exstrophy, and cloacal exstrophy, which require surgical correction within the first years of life ⁵. In the suspicion of malignancy, supported by the results of the previous biopsy, the patient underwent a cystectomy and cutaneous uretero-ileostomy. Macroscopically, the neobladder measured 13x7x6 cm and presented a 6 cm pedunculated polyp located on the left lateral wall, close to the homolateral ureteral meatus. Histological examination revealed a non-invasive polypoid lesion with an admixture of colorectal and transitional epithelium, featuring thickened muscularis mucosa and scant lymphoid-plasmacytoid infiltrate. These findings were consistent with an inflammatory cloacogenic polyp, an entity commonly arising in the anal transitional zone ⁶. However, the colorectal mucosa presented marked glandular hyperplasia with enlarged columnar cells showing nuclear pseudostratification, focal low-grade dysplasia, and abundant extracellular mucin pools, with mucus focally dissecting the lamina propria. These features partially resembled those of mucinous low-grade neoplasms involving the appendix (so-called LAMNs) ⁷. Immunohistochemical staining confirmed the presence of cytokeratin 7, p63, and GATA3 in the transitional epithelium and cytokeratin 5/6 in the basal layer, while the colorectal epithelium exhibited cytokeratin 20 positivity. Both urothelial and colorectal epithelia displayed intense cytoplasmic-membranous staining for β -catenin. The proliferative index, assessed with the Mib1/Ki-67 antibody, was inhomogeneous, with higher percentages in the colorectal epithelium and an average value of 6%. NGS analysis performed on both DNA and RNA with the Oncomine Comprehensive Assay revealed a pathogenetic *MYC* exon 2 mutation (VAF 5%), and variants of uncertain significance (VUS) of the genes *SLX4* and *NBN*, but no mutations in *KRAS* or *GNAS* genes that are typical of appendiceal LAMNs.

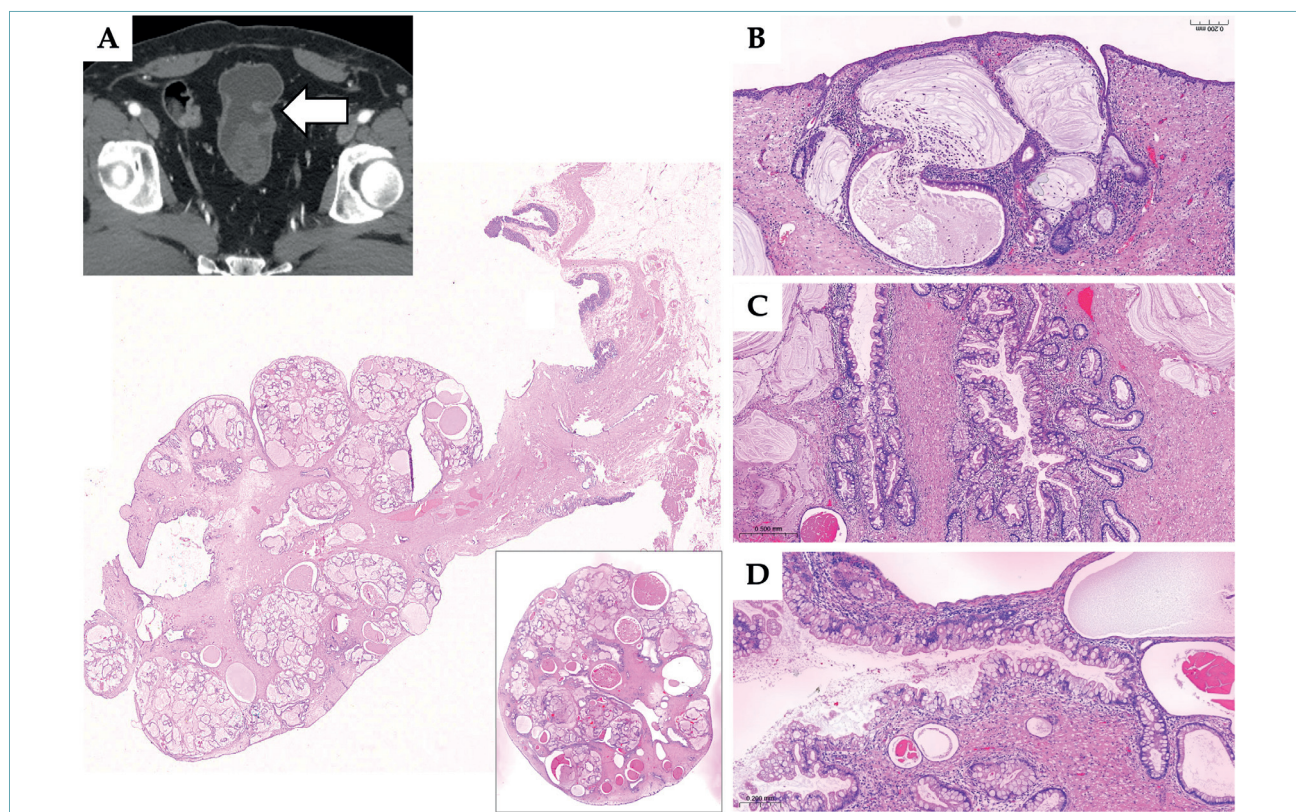


Figure 1. The neo-bladder polypoid lesion (A, with an upper left inset showing the CT scan and a lower right inset showing a cross-section of the polyp, HE, 2x magnification) exhibited an admixture of transitional and colorectal epithelia. The first represents the superficial layer of the polyp while the latter is associated with mucin pools focally dissecting the hyperplastic muscularis mucosae (B, HE, 10x magnification) and showing features of mild nuclear enlargement and pseudostratification consistent with low-grade dysplasia (C, D, HE, 20x magnification). A scant inflammatory infiltrate is present (B-D). Abbreviations: HE, hematoxylin-eosin stain.

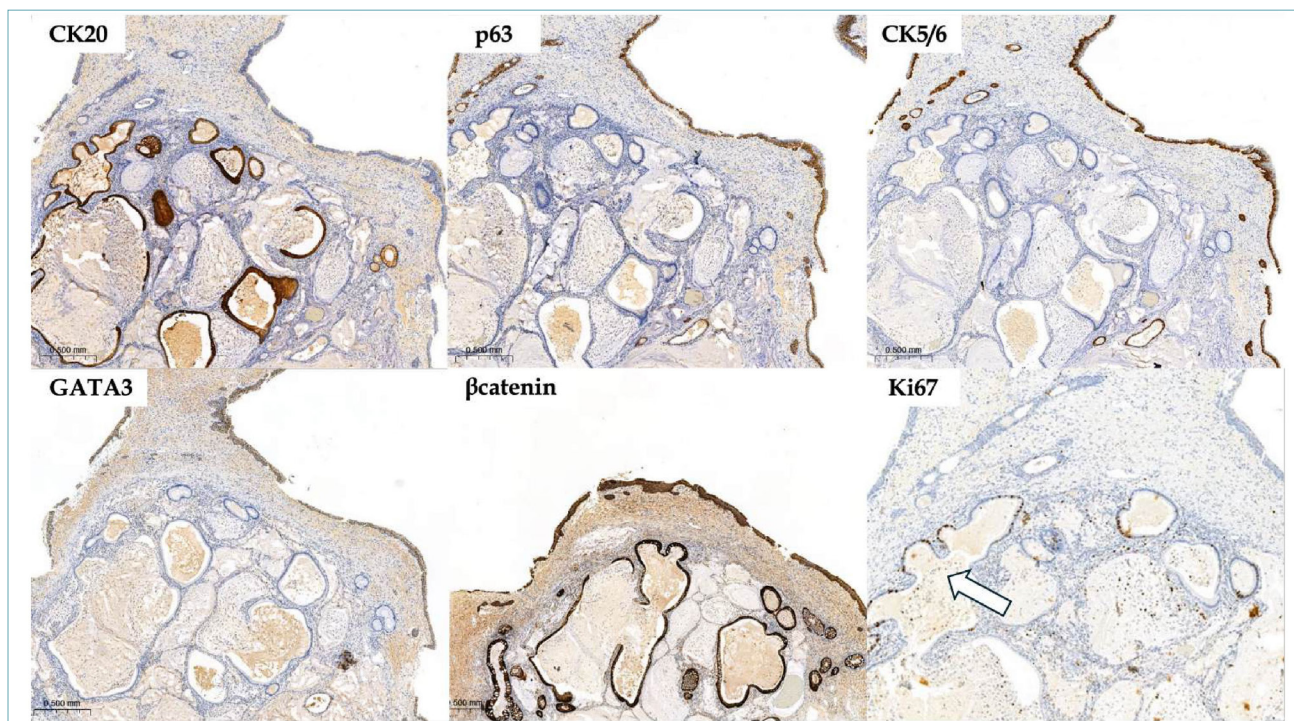


Figure 2. Immunohistochemistry showed CK20 positivity in the colorectal component, and p63, GATA3, and CK5/6 positivity in the transitional epithelium covering the surface of the polyp. Both the colorectal and transitional epithelia showed consistent cytoplasmic-membranous staining for β -catenin. The proliferative index (Ki-67) median value was around 6%, with higher percentages in the colorectal component (arrow).

Resection margins were negative, and the remaining bladder and ureteral mucosa did not show features of urothelial carcinoma *in situ* or other remarkable alterations. To the best of our knowledge, this case represents the first report of an inflammatory cloacogenic polyp in an orthotopic neobladder, with additional features of what we can call a low grade “mucinous dysplasia.” Urinary diversions involving intestinal segments can present interesting diagnostic challenges such as in this case, where urothelial carcinoma *in situ* was diagnosed at first. In this case, we propose that changes in the local environment experienced by the colorectal mucosa within the neo-bladder contributed to the emergence of an inflammatory cloacogenic polyp, followed by the subsequent occurrence of low-grade dysplasia with mucinous characteristics. The evolutive potential of this non-invasive lesion is presumably extremely low, and the patient is healthy with no major complications after five months from surgery. In conclusion, we emphasize the need for a nuanced approach and careful consideration in addressing lesions arising in urinary diversions.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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AUTHORS CONTRIBUTION

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by CP, AB, MDE, EO, NF and GR. The first draft of the manuscript was written by Carlo Pescia and Nicola Fusco and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

ETHICAL CONSIDERATION

Informed consent was obtained from the patient.

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