UROLOGICAL ASSOCIATION OF KERALA
NEWS LETTER FEBRUARY 2024

Changing paradigm of High-Risk NMIBC management: What's New?

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Bladder cancer is a significant global health concern, ranking as the tenth most common cancer worldwide with nearly half a million new cases annually. Non-muscle invasive bladder cancer (NMIBC) accounts for 75% of these cases, primarily urothelial carcinoma. NMIBC encompasses a spectrum of disease stages, including Ta, T1, and carcinoma in situ (CIS), and is typically managed with transurethral resection followed by immunotherapy with Bacillus Calmette-Guerin (BCG) and surveillance.

High-risk NMIBC, particularly high-grade T1 tumors, presents challenges due to its high recurrence rate (approximately 50%) and potential for progression to muscle invasion within two years of diagnosis. To address these complexities, risk stratification systems have been established to categorize NMIBC into low, intermediate, and high-risk groups based on various factors, including stage, grade, size, presence of CIS, and response to treatment. This article enumerates the recent developments under diagnosis and management subheadings with short descriptions.

Recent advancements in the diagnosis of high-risk NMIBC have focused on enhancing visualization techniques beyond standard white light cystoscopy and transurethral resection. Emerging technologies include:

1. Photo-dynamic Diagnosis (PDD): This technique uses violet light after instilling 5-aminolaevulinic acid (ALA) or hexaminolaevulinic acid (HAL) to improve the sensitivity of detecting malignant tumors, especially CIS.

2. Narrow-band Imaging (NBI): NBI enhances the contrast between normal urothelium and cancer tissue, improving tumor detection

3. Confocal Laser Micro-endoscopy: Offers high-resolution, real-time histological grading but requires further validation.

4. IMAGE1 S System: An image enhancement system that uses different light spectra modalities to potentially improve diagnostic accuracy.

5. Optical Coherence Tomography (OCT): Offers the capability to provide real-time bladder cancer staging by imaging below the mucosal surface.

Recent developments in the treatment of high-risk NMIBC include:

1. Optimal timing of Re-TURBT? : Recommended by guidelines for eligible cases within six weeks of the initial transurethral resection.

2. Transurethral Laser Resection of Bladder Tumour: Perioperative complications like obturator nerve reflex are less in laser resection with Holmium (HOLRBT) group compared to the TURBT

3. Radical Cystectomy: Immediate radical cystectomy is suggested for very high-risk NMIBC (New risk class from EAU guidelines) cases to prevent disease progression.

4. Management of BCG Failure: Various scenarios where BCG treatment is unsuccessful require different approaches, including radical cystectomy.

5. Intravesical Chemotherapy: Strategies involve the use of gemcitabine, docetaxel, and multidrug platinum-based regimens for BCG-unresponsive disease.

6. Device-Assisted Intravesical Chemotherapy: TAR-200 is an intravesical drug delivery system that releases gemcitabine in a controlled continuous manner.

7. Conductive Chemohyperthermia: This technique combines hyperthermia with chemotherapy to enhance drug penetration and immune activation.

8. Electromotive Drug Administration (EMDA): Uses electrical current to improve the penetration of chemotherapeutic agents into the bladder wall.

Immunotherapy is also emerging as a promising treatment for high-risk NMIBC, particularly the use of immune checkpoint inhibitors like PD-1/PD-L1 inhibitors. Pembrolizumab (following KEYNOTE 057trial) has received FDA approval for BCG-unresponsive NMIBC with CIS. To address the ongoing global shortages of intravesical BCG, strategies including expanding the use of chemotherapy and combination approaches with BCG has been suggested. Nadofaragene Firadenovec is a FDA spproved option in BCG unresponsive NMIBC.

Additionally, genomic markers and urinary biomarkers are being investigated for their potential in diagnosing and surveilling high-risk NMIBC. Several tests, such as CXbladder, Xpert Monitor, and UroMonitor, have shown promise in detecting recurrence and progression with high sensitivity and specificity.

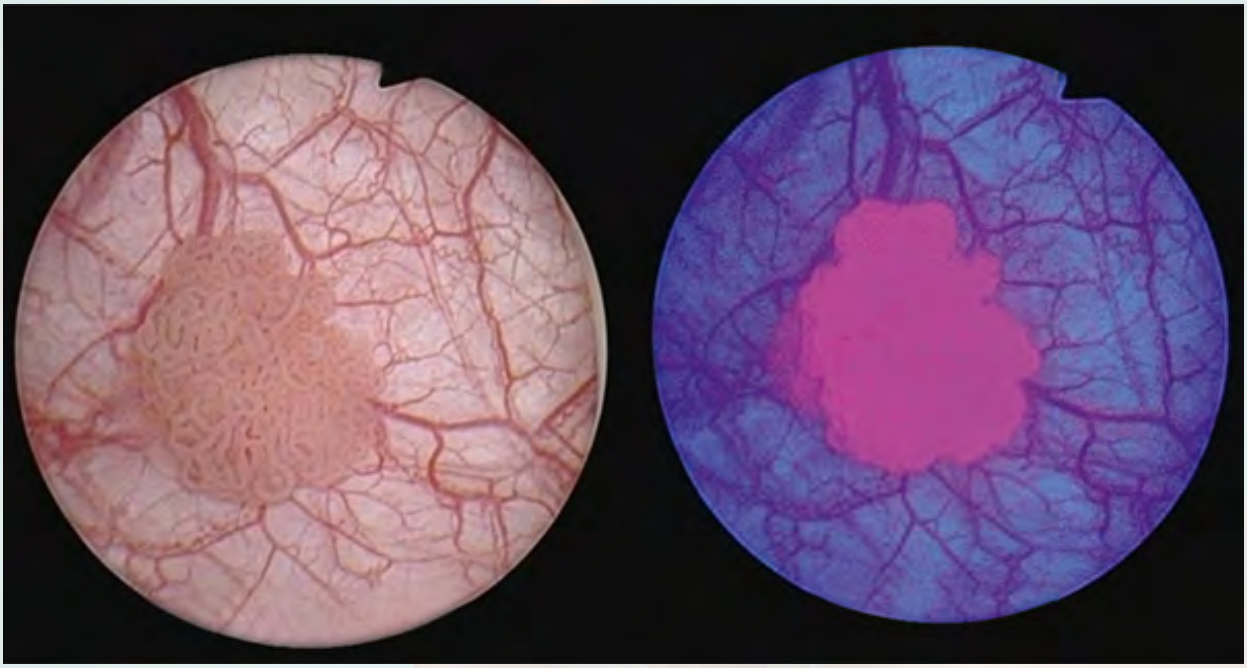
Artificial intelligence (AI) is playing an increasing role in predicting disease recurrence and progression. AI-based models using radiomics, histopathological markers, and genomic markers have shown superior accuracy compared to traditional statistical methods.

In conclusion, the management of high-risk NMIBC is evolving with the introduction of new diagnostic techniques, treatment options, and surveillance methods.

Intravesical therapies, immunotherapy, and AI-based tools are expanding the armamentarium for clinicians managing this challenging disease. As clinical trials continue to explore these options, the landscape of NMIBC management is likely to undergo further transformation, potentially reducing the need for radical cystectomy in high-risk cases.

Images:

1. Photodynamic diagnosis



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