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Expression of Tryptophanyl-tRNA Synthetase (WARS) and Indoleamine 2,3-Dioxygenase-1 (IDO1) in Predicting Bladder Cancer Staging

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INTRODUCTION & AIM

Bladder cancer (BC) is one of the most common malignancies worldwide. Like other cancers, BC can produce the enzyme indoleamine 2,3-dioxygenase-1 (IDO1), which, by modulating the immune system, protects the tumor and promotes its progression. When IDO1 is present, it depletes tryptophan from the microenvironment, producing kynurenine metabolites. This situation blocks the local immune response, but does not affect the IDO1-producing cell itself. The mechanisms behind this resistance remain unclear, although there is evidence that stores are generated by the enzyme tryptophanyl-tRNA synthetase (WARS), which carries tRNA with the amino acid, ensuring protein synthesis and cell cycle progression.

The aim of this study was to investigate whether the expression of IDO1 and WARS is associated with BC staging.

METHOD

For this study, bladder cancer (BC) samples from 165 patients were analyzed, including 88 with non-muscle invasive bladder cancer (NMIBC) and 77 with muscle-invasive bladder cancer (MIBC). The expression of IDO1 and WARS was assessed by immunohistochemistry in tumor and inflammatory cells. For this, anti-IDO1 and anti-WARS antibodies were standardized in our laboratory using placental tissue as a positive control. After determining the optimal dilution and nonspecific blocking, a score of 0 to 2 was adopted: 0 for no positivity, 1 for staining in less than 50% of the tissue, and 2 for staining above 50%. Based on the scores, correlation and chi-square analyses will be performed, comparing the expression of the enzymes with staging.

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RESULTS & DISCUSSION

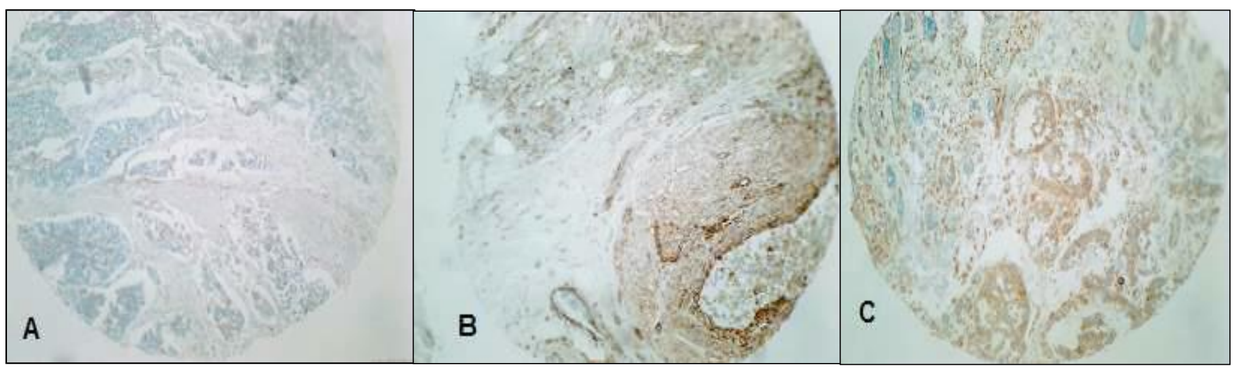

Figure: Score on TMA slide markings, immunohistochemistry with the Anti-WARS antibody. A Score 0 for tumor cells and Score 0 for inflammatory cells. B Score 1 for tumor cells and Score 1 for inflammatory cells. C Score 2 for tumor cells and Score 2 for inflammatory cells.

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IDO1 (Score)	0	39 (40 %)	12 (18 %)	*p<0.05*
	1	55 (56 %)	45 (67 %)	
	2	4 (4 %)	10 (15 %)	
WARS (Score)	0	1 (1 %)	0 (0 %)	*p<0.05*
	1	24 (25 %)	33 (49 %)	
	2	73 (75 %)	34 (51 %)	

Table: Expression of IDO1 and WARS in NMIBC and MIBC. Qui-square demonstrated significant association

Main result: The high expression of IDO1 predicts MIBC, whereas high expression of WARS predicts NMIBC. The association of IDO1 and WARS with bladder cancer suggests that these enzymes play complementary roles in the disease's pathophysiology. While IDO1 promotes immunosuppression, WARS appears to act as an adaptation mechanism for tumor cells to ensure their survival and proliferation. Thus, these enzymes may represent promising targets for therapeutic strategies, especially in the early stages of the disease.

CONCLUSION

It is possible that the enzymes IDO1 and WARS play a role in the pathophysiology of BC and have predictive value in the staging of the disease. The study is ongoing for further clarification.

FUTURE WORK / REFERENCES

1. Munn DH, Zhou M, Attwood JT, Bondarev I, Conway SJ, Marshall B, Brown C, Mellor AL. Prevention of allogeneic fetal rejection by tryptophan catabolism. Science. 1998 Aug 21;281(5380):1191-3.
2. Platten M, Wick W, Van den Eynde BJ. Tryptophan catabolism in cancer: beyond IDO and tryptophan depletion. Platten Cancer Res. 2012 Nov 1;72(21):5435-40.
3. Adam I, Dewi DL, Mooiweer J, Sadik A, Mohapatra SR, Berdel B, Keil M, Sonner JK, Thedieck K, Rose AJ, Platten M, Heiland I, Trump S, Opitz CA. Upregulation of tryptophanyl-tRNA synthethase adapts human cancer cells to nutritional stress caused by tryptophan degradation. Oncoimmunology. 2018 Sep 5;7(12):e1486353.