OJPathology> Vol.3 No.1, January 2013

OPEN ACCESS

Lack of MICA Expression Predicts a Worse Prognosis in Patients with Bladder Cancer

PDF (Size:3290KB) PP. 41-50 DOI: 10.4236/ojpathology.2013.31008

Author(s)

Mauricio Orozco-Levi, Alba Ramírez-Sarmiento, Michael Borchers, Cristiane Murta-Nascimento, Francesc Macià, Beatriz Casado, Maeba Polo, Andrea Caballero-Benitez, Fredy Diaz-Quijano, Antoni Gelabert

ABSTRACT

Background: Bladder and lung cancer are among the ten most common cancers in both genders. The NKG2D receptor and one of its ligands, MICA, are associated with smoking and susceptibility to both chronic obstructive pulmonary disease and lung cancer. Objective: We hypothesized that NKG2D-MICA system was associated with other smoking-related epithelial cancers such as bladder cancer. Design, Setting, and Participants: 70 cases of primary non-muscle invasive bladder cancer were screened for the MICA expression and CD8+, CD4+ and NK cell infiltration. Most patients (n = 55, 78.6%) were current or former smokers. Measurements: Tissue microarray (TMA) technology was chosen to evaluate MICA and tumor infiltrating lymphocytes in samples with confirmed bladder cancer. Kaplan-Meier curves and univariate Cox analysis was used to assess relapse, all-cancer mortality and specific bladder cancer mortality. Results and Limitations: MICA was expressed in most cancer specimens examined (*i.e.*, 70%). Relapse of bladder cancer was not associated with the status of MICA expression (log rank p = 0.1123). Nevertheless, a significant association existed between high MICA expression and bladder cancer mortality (HR = 0.25; $CI_{95\%}$ = 0.06 - 0.97). Tumor infiltrating CD4+ and CD8+ lymphocytes were found in the majority (64%) of samples. Cells expressing the NKG2D receptor were found in only 3% of the samples. There was no linear function between NKG2D+ cells and number or ratio of CD4+ and CD8+ TIL. Conclusions: MICA is expressed in a significant proportion of bladder carcinomas. MICA expression associates with significant survival advantages in the face of both all-cancer and bladder cancer. The NKG2D-MICA system could represent a common mechanism involved in the immunopathology and natural history of bladder neoplasms.

KEYWORDS

Bladder Cancer; NKG2D Ligands; MICA; Survival; Prognosis

Cite this paper

M. Orozco-Levi, A. Ramírez-Sarmiento, M. Borchers, C. Murta-Nascimento, F. Macià, B. Casado, M. Polo, A. Caballero-Benitez, F. Diaz-Quijano and A. Gelabert, "Lack of MICA Expression Predicts a Worse Prognosis in Patients with Bladder Cancer," *Open Journal of Pathology*, Vol. 3 No. 1, 2013, pp. 41-50. doi: 10.4236/ojpathology.2013.31008.

References

[1] J. Ferlay, H. R. Shin, F. Bray, D. Forman, C. Mathers and D. M. Parkin, "GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]," International Agency for Research on Cancer, Lyon, 2010. http://globocan. iarc. fr

[2] T. Skov, P. Sprogel, G. Engholm and C. Frolund, "Cancer of the Lung and Urinary Bladder in Denmark, 1943-87: A Cohort Analysis," Cancer Causes Control, Vol. 2, No. 6, 1991, pp. 365-369. doi:10.1007/BF00054296

[3] R. J. Black, F. Bray, J. Ferlay and D. M. Parkin, "Cancer Incidence and Mortality in the European Union: Cancer Registry Data and Estimates of National Incidence for 1990," European Journal of Cancer, Vol. 33, No. 7, 1997, pp. 1075-1107. doi:10.1016/S0959-8049(96)00492-3

[4] A. F. Kantor and J. K. McLaughlin, "Second Cancer Following Cancer of the Urinary System in Connecticut, 1935-82," National Cancer Institute Monograph, Vol. 68, 1985, pp. 149-159.

[5] R. Doll and R. Peto, "The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today," Journal of the National Cancer Institute, Vol. 66, No. 6, 1981, pp. 1191-1308.

[6] H. Kuper, P. Boffeta and H. O. Adami, "Tobacco Use and Cancer Causation: Association by Tumour Type," Journal of Internal Medicine, Vol. 252, No. 3, 2002, pp. 206-224. doi:10.1046/j.1365-2796.2002.01022.x

[7] A. W. Hitchings, M. Kumar, S. Jordan, V. Nargund, J. Martin, D. M. Berney, et al., "Prediction of Progression in pTa and pT1 Bladder Carcinomas with p53, p16, pRb," British Journal of Cancer, Vol. 91, No. 3, 2004, pp. 552-557. doi:10.1038/sj.bjc.6601954

[8] J. H. Mydlo, J. A. Agins, J. Donohoe and B. M. Grob, "A Review of Urologic Cancer Patients with Multiple Primary Malignancies," World Journal of Urology, Vol. 19, No. 4, 2001, pp. 240-243. doi:10.1007/s003450100210

[9] J. H. Mydlo and M. Gerstein, "Patients with Urologic Cancer and Other Nonurologic Malignancies: Analysis of a Sample and Review of the Literature," Urology, Vol. 58, No. 6, 2001, pp. 864-869. doi:10.1016/S0090-4295(01)01394-2

[10] A. El-Hakim, A. D. Smith and G. Weiss, "Patients with Bladder and Lung Cancer: A Long-Term Outcome Analysis," British Journal of Urology International, Vol. 93, No. 9, 2004, pp. 1225-1227. doi:10.1111/j.1464-410X.2004.04842.x

[11] E. Salminen, E. Pukkala and L. Teppo, "Bladder Cancer and the Risk of Smoking-Related Cancers during Follow-Up," Journal of Urology, Vol. 152, Pt. 1, 1994, pp. 1420-1423.

[12] A. M. Jamieson, A. Diefenbach, C. W. McMahon, N. Xiong, J. R. Carlyle and D. H. Raulet, "The Role of the NKG2D Immunoreceptor in Immune Cell Activation and Natural Killing," Immunity, Vol. 17, No. 1, 2002, pp. 19-29. doi:10.1016/S1074-7613(02)00333-3

[13] A. Robert, "Eagle and John Trowsdale. Promiscuity and the Single Receptor: NKG2D. Nature Reviews," Immunology, Vol. 7, No. 9, 2007, pp. 737-744. doi:10.1038/nri2144

[14] M. T. Borchers, S. C. Wesselkamper, V. Curull, A. Ramirez-Sarmiento, A. Sánchez-Font, J. Garcia-Aymerich, C. Coronell, J. Lloreta, A. G. Agusti, J. Gea, J. A. Howington, M. F. Reed, S. L. Starnes, N. L. Harris, M. Vitucci, B. L. Eppert, G. T. Motz, K. Fogel, D. W. McGraw, J. W. Tichelaar and M. Orozco-Levi, "Sustained CTL Activation by Murine Pulmonary Epithelial Cells Promotes the Development of COPD-Like Disease," Journal of Clinical Investigation, Vol. 119, No. 3, 2009, pp. 636-649. doi:10.1172/JCI34462

[15] S. Bahram, M. Bresnahan, D. E. Geraghty and T. Spies, "A Second Lineage of Mammalian Major Histocompatibility Complex Class I Genes," Proceedings of the National Academy of Sciences of the United States, Vol. 91, No. 14, 1994, pp. 6259-6263. doi:10.1073/pnas.91.14.6259

[16] World Medical Association Declaration of Helsinki, "Ethical Principles for Medical Research Involving Human Subjects," Adopted by the 18th WMA General Assembly Helsinki, June 1964 and Amended by the 52nd WMA General Assembly, Edinburgh, October 2000. http://ohsr. od. nih. gov/guidelines/helsinki. html

[17] L. F. R. Vallmanya, R. A. Laborda, T. J. Lloreta, A. R. Cortadellas, S. J. Placer and G. A. Mas, "Immunohisto-chemical Expression of p53, p21, p16 and Ciclin D1 in Superficial Bladder Cancer. A Tissue Microarray Study," Actas Urologicas Espanolas, Vol. 30, No. 8, 2006, pp. 754-762.

[18] A. L. Rodriguez, F. V. Llena, R. C. Angel, J. L. Trull and A. G. Mas, "Histopatological Validation of Tissue-Microarray Technology in Urotelial Cancer. Our Experience," Actas Urologicas Espanolas, Vol. 28, No. 3, 2004, pp. 215-220.

[19] A. M. Dancau, R. Simon, M. Mirlacher and G. Sauter, "Tissue Microarrays," Methods in Molecular Biology, Vol. 576, 2010, pp. 49-60. doi:10.1007/978-1-59745-545-9_4

[20] S. F. Shariat, H. Tokunga, J. H. Zhou, J. H. Kim, G. E. Ayala, W. F. Benedict, et al., "p53, p21, pRB and p16 Expression Predict Clinical Outcome in Cystectomy with Bladder Cancer," Journal of Clinical Oncology, Vol. 22, No. 6, 2004, pp. 1014-1023. doi:10.1200/JCO.2004.03.118

[21] H. P. Cathro, M. E. Smolkin, D. Theodorescu, V. Y. Jo, S. Ferrone and H. F. Frierson Jr., "Relationship between HLA Class I Antigen Processing Machinery Component Expression and the Clinicopathologic

Characteristics of Bladder Carcinomas," Cancer Immunology, Immunotherapy, Vol. 59, No. 3, 2010, pp. 465-472. doi:10.1007/s00262-009-0765-9

[22] V. Groh, S. Bahram, S. Bauer, A. Herman and M. Beauchamp, "Spies T. Cell-Stress Regulated Human Major Histocompatibility Complex Class I Gene Expressed in Gastrointestinal Epithelium," Proceedings of the National Academy of Sciences of the United States, Vol. 93, No. 22, 1996, pp. 12445-12450. doi:10.1073/pnas.93.22.12445

[23] D. Cosman, J. Mullberg, C. L. Sutherland, et al., "ULBPs, Novel MHC Class I-Related Molecules, Bind to CMV Glycoprotein UL16 and Stimulate NK Cytotoxicity through the NKG2D Receptor," Immunity, Vol. 14, No. 2, 2001, pp. 123-133. doi:10.1016/S1074-7613(01)00095-4

[24] P. Xiao, L. Xue, L.-H. Che, J.-J. Peng, H.-X. Wu, Y. Li and H. Qiao, "Expression and Roles of MICA in Human Osteosarcoma," Histopathology, Vol. 52, No. 5, 2008, pp. 631-656. doi:10.1111/j.1365-2559.2008.02989.x

[25] H. Wang, D. Yang, W. Xu, Y. Wang, Z. Ruan, T. Zhao, J. Han and Y. Wu, "Tumor-Derived Soluble MICs Impair CD3(+) NKT. Like Cell Cytotxicity in Cancer Patients," Immunology Letters, Vol. 120, No. 1-2, 2008, pp. 65-71. doi:10.1016/j.imlet.2008.07.001

[26] A. I. Roberts, L. Lee, E. Schwarz, V. Groh, T. Spies, E. C. Ebert and B. Jabri, "NKG2D Receptors Induced by IL-15 Costimulate CD28-Negative Effector CTL in the Tissue Microenvironment," The Journal of Immunology, Vol. 167, 2001, pp. 5527-5530.

[27] HV Herr and A Morales, "History of Bacillus Calmett-Guerin and bladder Cancer: An Immunotherapy Succes Story," Journal of Urology, Vol. 179, No. 1, 2008, pp. 53-56. doi:10.1016/j.juro.2007.08.122

[28] Alexandro AB, Jackson AM, O'Donell MA and James K, "BCG Immunotherapy of Bladder Cancer: 20 Years on," Lancet, Vol. 353, No. 9165, 1999, pp. 1689-1694. doi:10.1016/S0140-6736(98)07422-4

[29] A. Bohle and S. Brandau, "Immune Mechanisms in Bacillus Calmette-Guerin Immunotherapy for Superficial Bladder Cancer," Journal of Urology, Vol. 170, No. 3, 2003, pp. 964-969. doi:10.1097/01.ju.0000073852.24341.4a

[30] A. Bohle, J. Gerdes, A. J. Ulmer, A. G. Hotstetter and H. D. Flad, "Effects of Local Bacillus Calmette-Guerin Therapy in Patients with Bladder Carcinoma on Immunocompetent Cells of the Bladder Cancer," Journal of Urology, Vol. 144, No. 1, 1990, pp. 53-58.

[31] A. Martino, R. Casetti, A. Sacchi and F. Poccia, "Central Memory Gammadelta T Lymphocytes Primed and Expanded by Bacillus Calmette-Guerin Infected Dendritic Cells Kill Mycobacterial-Infected Monocytes," The Journal of Immunology, Vol. 179, No. 5, 2007, pp. 3057-3064.

[32] J. Lee, K. Choi, M. R. Olin, S. N. Cho and T. W. Molitor, "Gammadelta T Cells in Immunity Induced by Mycobacterium Bovis Bacillus Calmette-Guerin Vaccination," Infection and Immunity, Vol. 72, No. 3, 2004, pp. 1504-1511. doi:10.1128/IAI.72.3.1504-1511.2004

[33] A. M. Jackson, A. B. Alexandro, R. W. Kelly, A. Skibinska, K. Esuvaranthan, S. Prescott, G. D. Chisholm and K. James, "Changes in Urinary Cytokines and Soluble Intercellular Adhesion Molecule-1 (ICAM) in Bladder Cancer after Bacillus Calmette-Guerin (BCG) Immunotherapy," Clinical & Experimental Immunology, Vol. 99, No. 3, 1995, pp. 369-375. doi:10.1111/j.1365-2249.1995.tb05560.x

[34] G. N. Thalman, A. Sermir, C. Rentch, K. Mohrle, M. G. Cecchini and U. E. Studer, "Urinary Interleukin-8 and 18 Predict the Response of Superficial Bladder Cancer to Intravesical Therapy with Bacillus Clamette-Guerin," Journal of Urology, Vol. 164, No. 6, 2000, pp. 2129-2133. doi:10.1016/S0022-5347(05)66983-2