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Blood Group Isoantigens and Bladder Cancer

An Overview

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Key Words

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Abstract

The role of blood group ABO(H) surface isoantigen measurement in bladder cancer is discussed. The basis for this test is examined and an attempt is made to place the current status of this test in proper perspective.

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Bladder cancer is a world-wide problem and accounts annually for approximately 10,000 deaths in the United States. Although bladder cancer may represent a wide variety of diseases with different causes, it is felt that bladder carcinogenesis may be a multistage process of initiating and promoting factors. Initiation is regarded as irreversible, but promotion may be prevented or inhibited before the development of an autonomous tumor [1].

The tendency for urothelial tumors to be multicentric in time and space has long been recognized and is reflected in the increasing use of random biopsies of apparently normal-appearing bladder wall in an effort to define early neoplastic or pre-neoplastic changes.

70% of all superficial bladder tumors recur and, in roughly a third of these cases, the tumor ultimately becomes more aggressive and invasive. At present radical surgery is deferred until muscle invasion occurs accounting for the low survival rates since widespread micrometastasis invariably occurs during the interval from initial diagnosis to muscle invasion.

Identification of bladder cancer patients with initially superficial tumors, who later will suffer invasive or meta-static disease, is a major problem confronting urologists. If the invasive potential of superficial bladder tumors could be predicted, then the criteria for initial aggressive therapy in selected cases could be established. Such predictive capabilities currently do not exist, but the role of blood group ABO(H) surface isoantigens in bladder tumors is being widely investigated relative to this problem.

The ABH blood group substances are glycoproteins with a molecular weight ranging from 300,000 to 1,000,000. These substances are composed of about 85% carbohydrates and 15% amino acids. The carbohydrate

moiety is composed of five sugars arranged in a large number of fairly short chains attached by a covalent linkage to a peptide backbone composed of 15 amino acids of which threonine, serine,

proline and alanine compose two thirds. Most epithelial and endothelial cell surfaces contain ABO(H) substances which in these locations are referred to as isoantigens [2].

In 1968 the Specific Red Cell Adherence Test (SRCA) was used to test blood group isoantigens in tissue sections from carcinoma of the cervix where it was found that the cells lose their isoantigen as they undergo changes from cellular atypia to anaplasia [3].

The principle of this test is that epithelial cells possessing the respective isoantigen should absorb the appropriate antisera (antibody) and consequently, after being washed, possess free extending 'receptors' with affinity for the respective antigen. Red blood cells of the same blood group added at this stage should combine with the extending antibody receptors on the treated epithelial cells and give rise to red cell adherence (fig. 1). Conversely if the epithelial cells have lost their isoantigen, red cell adherence will not occur.

Reports utilizing the SRCA test for bladder tumors began appearing in the urological literature in 1975 and since then numerous retrospective studies have been carried out on paraffin-embedded tissue blocks from patients with bladder tumors who have had 5-year follow-ups. The initial results with the test were encouraging showing that, in over 80% of superficial bladder tumors that ultimately became invasive, the isoantigens were absent at the time of initial diagnosis, while the tumor was still superficial. On the other hand only 10–15% of the superficial tumors that remained superficial lost their

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Bladder epithelial cell with surface antigen

Red cell with surface antigen

Antisera (antibody)

Attachment of antibody to surface antigen

Agglutination reaction

Fig. 1. Principle of the SRC A test.

surface isoantigen. Most high grade, invasive tumors were antigen negative [4]. Thus, it was concluded that cell surface antigens, normally expressed on epithelial cells, were not expressed on cells of most bladder tumors that have a high malignant potential, even those that were histologically well differentiated and superficial initially. Based on these early reports many investigators felt that the SRCA test would be a useful parameter in predicting tumor invasiveness and that it would have a tremendous clinical application. However, once this test was used more widely, the inherent problems associated with tissue sections such as antigen variability attributable to different fixation techniques and difficulty in interpreting the results due to lack of standardization became apparent [5]. Techniques to improve the test by using

single cell suspensions [6] or immunoperoxidase stains [7] are now being utilized in an attempt to overcome the previous problems and to standardize the test [8].

Attempts are also being made to correlate DNA profile, as measured by flow cytometry, and blood group isoantigens in the same specimens to see whether these two tests complement each other and to assess their value in predicting the invasive potential of superficial bladder tumors. These techniques show a good correlation between antigen counts and bladder histology and provide the basis for evaluating the test further on a prospective basis [9, 10].

A standardized prospective study should be carried out at this stage and this might help in defining the role of blood group isoantigen measurement in the overall management of patients with bladder cancer. Until such time as a definite answer is obtained, blood group isoantigen measurement should be confined to the research laboratory and, at present, clinical therapy of patients should not be influenced by this test.

References

- Whitmore, W.F., Jr.: Management of bladder cancer: current problems in cancer, vol. 4 (Year Book Medical Publishers, Chicago 1979).
- Erskine, A.G.; Socha, W.W.: The principles and practice of blood grouping; 2nd ed., p. 64 (Mosby, St. Louis 1978).
- Kovarik, S.; Davidsohn, I.; Stejskal, R.: ABO antigens in cancer. Detection with mixed cell agglutination reaction. Archs Path. 86: 12(1968).
- Newman, A.J., Jr.; Carlton, C.E., Jr.; Johnson, S.: Cell surface A, B or O(H) blood group antigens as an indicator of malignant potential in stage A bladder carcinoma. J. Urol. 124: 27 (1980).
- Bishop, M.C.: Blood group antigens and bladder cancer. Br. med. J. 284: 1426 (1982).
- Srinivas, V.; Hansen, P.A.; Kiruluta, H.G.: Single cell suspension of human bladder mucosa: possible use in quantitating ABO(H) isoantigens in transitional cell carcinoma of bladder. Urology 20: 608 (1982).
- Wiley, E.L.; Mendelsohn, G.; Droller, M.G.; Eggleston, J.C.: Immunoperoxidase detection of carcinoembryonic antigen and blood group substances in papillary transitional cell carcinoma of the bladder. J. Urol. 128: 276 (1982).
- Srinivas, V.; Kiruluta, H.G.: ABO(H) isoantigens in bladder tumors: a new technique of quantitative analysis. J. Urol. 131: 245 (1984).
- Orihuela, E.; Srinivas, V.; Stainano-Coico, L.; Old, L.J.; Me-lamed, M.; Whitmore, W.F., Jr.: Prognostic value of DNA profile and ABO(H) antigen reactivity in superficial bladder cancer (Abstract). J. Urol. 131: 276a (1984).
- 10 Srinivas, V.; Orihuela, E.; Lloyd, K.O.; Old, L.J.; Whitmore, W.F., Jr.: Quantitative estimation of ABO(H) isoantigens in bladder tumors (Abstract). J. Urol. 131: 266a (1984).