

A, B, O(H) Blood Group Antigen Distribution in Normal Skin and Squamous Cell Carcinoma of the Penis

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Summary. The distribution of A, B, O(H) blood group antigens was studied in paraffin sections of 4 and 11 specimens, respectively, of normal skin and squamous cell carcinoma of the penis using specific red cell adherence (SRCA) test. In the normal skin of the penis the antigens appeared on the uppermost cornifying layers, while basal and malpighian layers were devoid of antigens. In squamous cell carcinoma of the penis the antigens were either absent or confined only to the epithelial pearl formations. Each of the 4 normal skins and 3 of the 11 carcinomas were antigen positive. As the blood group antigens were frequently absent in patients with carcinoma of the penis regardless of the tumor grade and stage as well as patient's condition, they lack the power to discriminate invasive potential.

Key words: Blood group antigens, Carcinoma of the penis, SRCA test.

Introduction

Cell surface antigens identical to those that designate the A, B, and O blood groups are normally present in various human tissues [1, 2]. A partial or complete loss of the blood group antigens has been reported to occur in carcinomas arising from epithelium of different organs including the skin [1–3]. The specific red cell adherence (SRCA) test of Kovarik et al. [1] has been currently used for localization of these antigens. Whilst the loss of blood group antigens has been shown to have useful prognostic value in urothelial tumors [4–7], no attempt has been made to investigate the value of these antigens in the lesions of the penis. However, blood group antigens could be helpful in predicting aggressive potential of carcinoma of the penis and therefore perhaps in selecting appropriate treatment.

As a preliminary study the distribution of blood group antigens in normal skin and squamous cell carcinoma of the penis has been studied.

Material and Method

Clinical records of patients with lesions of the penis treated at our hospital since 1970 were reviewed. There were 11 patients with histologically proven squamous cell carcinoma of the penis. The lesions were staged according to Jackson's classification [8]. Stage I tumors are limited to the glans penis and/or foreskin. Stage II tumors invade into the shaft or corpora without nodal or distant metastases. Stage III tumors are confined to the shaft of the penis with regional lymph node metastases. Stage IV tumors demonstrate metastases in distant organs. Hematoxylin and eosin stained sections of the lesions were reviewed to verify the grades. Tumors were graded as well, moderately and poorly differentiated for grades I, II, and III respectively. Questionnaires were mailed to assess the patient's status. In addition, we studied 4 specimens of normal skin of the penis to serve as a base line in determining the possible value of the blood group antigens in the carcinoma of the penis.

A specific red cell adherence test was performed according to the method of Kovarik et al. [1] with few modifications to permit the preparation of permanent hematoxylin and eosin stained sections. Briefly, 4 μ sections were deparaffinized in changes of xylol and rehydrated in graded alcohol to distilled water. The slides were washed in tris-buffered saline (TBS) pH 7.4 for 15 min and transferred to a moist chamber. The slides were covered with the appropriate antisera (anti-A, anti-B) for 15 min, Ulex extract for blood group O patients for 60 min. The slides were then washed in 3 changes of TBS for 15 min each and covered with a few drops of TBS containing 7 g/dl bovine serum albumin (BSA) fraction V for 15 min. This step served to reduce non-specific binding of the erythrocytes to the tissue sections. The slides were then incubated with a 1% erythrocyte suspension in 7% BSA in TBS for 15 min and were inverted on wooden applicators in a dish filled with TBS for 15 min. After the excess erythrocytes were settled out, while inverted, the slides were transferred onto wooden applicators in another dish filled with a 2% solution of glutaraldehyde in 0.067 M phosphate buffer pH 7.4 with 5.4 g/dl of dextrose and left for 30 min. This step served to fix specifically attached indicator erythrocytes to the tissue sections. Then the slides were slowly rinsed in distilled water and stained with hematoxylin and eosin. At least 2 preparations from each specimen were examined.

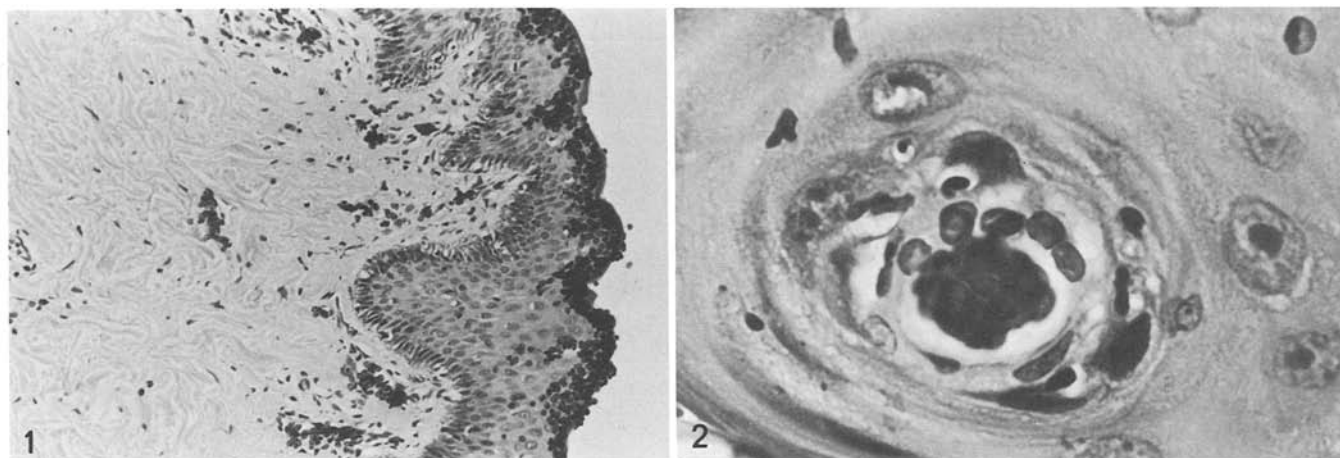


Fig. 1. Normal skin of the penis. Note positive antigen reaction limited to the uppermost cornifying layers of epidermis

Fig. 2. Squamous cell carcinoma of the penis. Note positive antigen reaction confined to the epithelial pearl formation

Table 1. SRCA test results from patients with squamous cell carcinoma of the penis

Pt. — Age — Blood type	Grade	Stage	SRCA	Last Known Status
1 — 63 — A	I	II	—	Well at 11 yrs.
2 — 66 — A	I	II	—	Well at 12 yrs.
3 — 67 — B	III	I	—	Died, CVA at 5 yrs.
4 — 45 — A	III	I	—	Well at 11 yrs.
5 — 54 — A	II	III	+	Died, lung metastasis at 3 yrs.
6 — 44 — A	I	I	—	Well at 8 yrs.
7 — 46 — O	I	I	—	Well at 4 yrs.
8 — 44 — A	I	I	—	Well at 7 yrs.
9 — 85 — O	II	I	—	Well at 2 yrs.
10 — 63 — B	II	I	+	Well at 1 1/2 yrs.
11 — 55 — A	I	I	+	Short follow-up, well

Controls included omission or substitution of antisera or Ulex extract, and the presence of positive reaction in the endothelium of the vessels and negative reaction in the stroma.

Results

In the normal skin of the penis the antigens appeared on the uppermost cornifying layers of the epidermis, while basal and malpighian layers devoided antigens (Fig. 1).

In the squamous cell carcinoma of the penis the antigens were either absent or confined only to the epithelial pearl formations (Fig. 2).

Positive results were defined as >30% of the cornifying epidermis in the normal skin or alternatively of the epithelial pearls in carcinoma of the penis showing red cell adherence.

Each of the 4 normal skins and 3 of the 11 squamous cell carcinomas were antigen positive (Table 1). Correlation could not be found between the results and tumor grade and stage as well as the patient's status.

Discussion

Detection of blood group antigens on the epithelial cell surface has been shown to be useful in predicting malignant potential of urothelial tumors [4–7]. This usefulness relies on the fact that normal epithelium contains surface antigens similar to those of the A, B and O blood groups, while these antigens are usually lost in tumors with aggressive potential.

In this study the distribution of blood group antigens in normal skin and squamous cell carcinoma of the penis has been assessed. In the normal skin, blood group antigens appeared on the uppermost cornifying layers of the epidermis, while basal and malpighian layers devoided antigens.

Using an immunofluorescent method to determine blood group antigens in human tissues, Szulman [9] found that the antigens were more consistently and uniformly detectable in the skin of fetuses than in that of 1 and 5-year old babies. It was also shown that immunofluorescent stainings for the antigens were much more diffuse and intense

in non-cornifying squamous epithelia (cervix, esophagus, tongue) than in cornifying squamous epithelium (skin) [10]. Therefore, the antigens in the skin may be low in quantity, perhaps due to its exposed situation. The blood group antigen reactivity in normal skin of the penis should serve as a base line in determining the possible value of these antigens in cases of malignancy.

In squamous cell carcinoma of the penis, blood group antigens were either absent or confined to the epithelial pearl formations, as well as uppermost cornifying layers of the normal epidermis associated with malignancy. Each of the 4 normal skins and 3 of the 11 squamous cell carcinomas examined were antigen positive. Correlation was not seen between the results and tumor grade and stage as well as the patient's condition, as most of the patients had low grade, low stage tumors and a favorable prognosis (Table 1).

Kovarik et al. [1] using a mixed cell agglutination test found that the blood group antigens were present in 3 of the 14 squamous cell carcinomas of the skin. Similarly, they noted that the antigens appeared on the epithelial pearl formations. Furthermore, variable patterns of blood group antigens despite invasive disease have also been found in squamous cell carcinoma of the bladder. Richie et al. [7] examined 9 squamous cell carcinomas of the bladder by the SRCA test. Two patients had positive antigens and survived 5 years, while 6 patients had negative antigens, of whom 3 died of cancer. In addition, some factors influencing blood group antigen reactivity including methodologic factors, blood group O and non-secretor status of the patient could be responsible for negative observations [11].

As the blood group antigens, under the condition of this study, were frequently absent in carcinomas of the penis regardless of the tumor grade and stage as well as the patient's status, they lack the power to discriminate invasive potential.

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