Expression of Stem Cell Marker ALDH1 in Cervical Intraepithelial Neoplasia

Ping Gong, Juan Palazzo

Department of Pathology, Thomas Jefferson University Hospital, Philadelphia, PA

ABSTRACT

BACKGROUND

Cervical cancer is the second most common type of cancer in women worldwide. The human papilloma virus (HPV) has recently been shown to specifically target cervical cancer stem cell (CSC) s. The ability to identify and characterize CSCs is crucial for understanding cervical cancer. Aldehyde degydrogenase (ALDH) 1, a detoxifying enzyme responsible for the oxidation of intracellular aldehydes, has been shown to be a stem cell marker in several tissue types and tumors. We investigated the expression pattern of ALDH1 in cervical intraepithelial neoplasia (CIN) and its possible role in carcinogenesis.

DESIGN

Fifty-six cervical biopsy specimens with the diagnoses of normal cervical mucosa, koilocytosis, CIN1, CIN2, and CIN3 were collected from the pathology files at Thomas Jefferson University Hospital. All diagnoses were confirmed by at least two experienced pathologists. Immunohistochemical staining for ALDH1 was performed following a previously published protocol. Any cytoplasmic staining of ALDH1 in the epithelial cells was considered positive. Positive and negative controls were used in each study.

RESULTS

Normal cervical mucosa had no ALDH1 expression. In koilocytosis, 2 of 7 cases showed ALDH1+ cells limited to the basal layer. In CIN1, 11 of 20 cases showed ALDH1+ cells limited to the lower 1/3 of epithelium and the other 9 cases were negative for ALDH1. In CIN2, 7 of the 13 cases showed positive cells limited to the basal layer, 4 cases showed positive cells extending to the mid and upper 1/3 of the mucosa. Two cases were negative for ALDH1. All CIN3/carcinoma in situ (CIS) cases were positive for ALDH1. Three of 6 cases show positive cells extending up to mid 1/3 of mucosa and the other three cases show positive cells extending up to the upper 1/3 of mucosa.

CONCLUSION

Cervical dysplasias show positive staining for ALDH1 compared to normal cervical mucosa. ALDH1 expression and distribution parallels the degree of cervical dysplasia. CSC, as detected by ALDH1 expression, may play a role in the progression of cervical intraepithelial neoplasia and carcinogenesis.

INTRODUCTION

- Cervical cancer is the second most common type of cancer in women worldwide. The relationship between the development of cervical cancer and infection with certain types of Human Papilloma Viruses (High risk HPV) is well established
- The human papilloma virus (HPV) has recently been shown to specifically target cervical cancer stem cell (CSC) s. The ability to identify and characterize CSCs is crucial for understanding cervical cancer.
- Aldehyde degydrogenase (ALDH) 1, a detoxifying enzyme responsible for the oxidation of intracellular aldehydes, has been shown to be a stem cell marker in several tissue types and tumors.
- We investigated the expression pattern of ALDH1 in cervical intraepithelial neoplasia (CIN) and its possible role in carcinogenesis.

METHODS

- Fifty-six cervical biopsy specimens including 10 normal cervical mucosa, 7 koilocytosis, 20 CIN1, 13 CIN2, and 6 CIN3/carcinoma in situ (CIS) were collected from the pathology files at Thomas Jefferson University Hospital.
- All diagnoses were confirmed by at least two experienced pathologists.
- Immunohistochemical staining for ALDH1 was performed following a previously published protocol. Any cytoplasmic staining of ALDH1 in the epithelial cells was considered positive. Positive and negative controls were used in each study.

Diagnosis	Distribution of ALDH1 in squamous epithelia				Total
	negative	lower 1/3	mid 1/3	upper 1/3	
Normal	10	0	0	0	**10**
Koilocytosis	5	2	0	0	**7**
CIN1	9	11	0	0	**20**
CIN2	2	7	2	2	**13**
CIN3/CIS	0	0	3	3	**6**

Table 1: The summary of the expression and distribution of ALDH1 in normal and cervical intraepithelial neoplasm

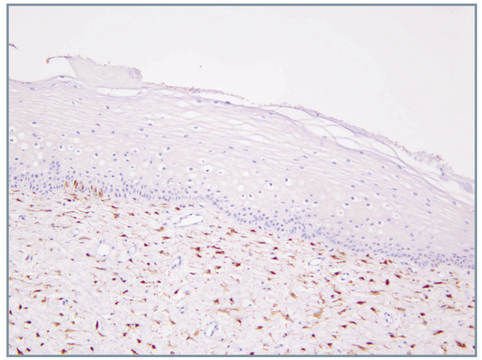

Figure 1: Negative ALDH1 expression in normal cervical mucosa

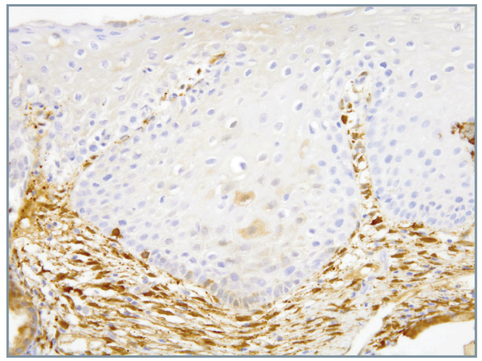

Figure 2: ALDH1 expression is limited to the basal cell layer in Koilocytosis

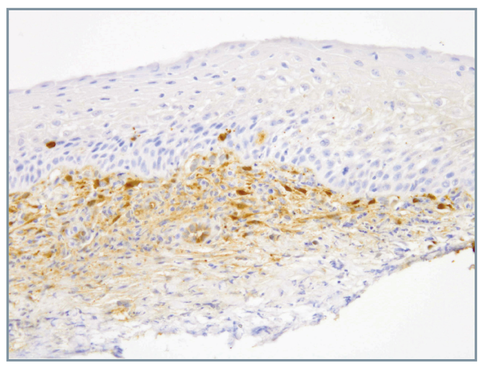

Figure 3: ALDH1 expression cells are limited to the lower third portion of the squamous epithelium in CIN1

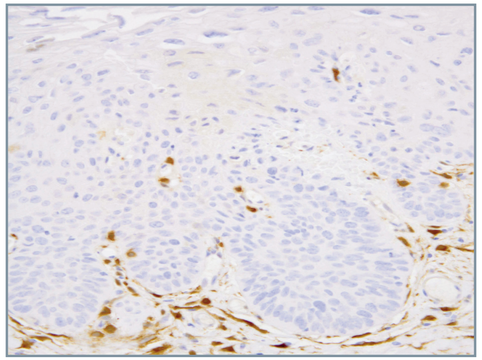

Figure 4: ALDH1 expression cells extend to the mid third of the squamous epithelium in CIN2

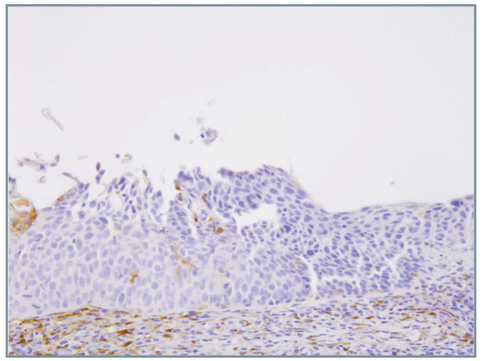

Figure 5: ALDH1 positive cells extend to the upper third of the squmaous epithelium in CIN3

CONCLUSIONS

- Cervical dysplasia show positive staining for ALDH1 compared to normal cervical mucosa.
- ALDH1 positive cells distribution paralells the dysplastic cells in cervical dysplasia.
- CSC, as detected by ALDH1 expression, may play a role in the progression of cervical intraepithelial neoplasia and carcinogenesis.