Cervical Dysplasia and Carcinoma After Quadrivalent Vaccination Against The Human Papillomavirus

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OBJECTIVES:

- Though highly effective, the vaccine against the human papillomavirus (HPV) does not completely eradicate the risk of cervical dysplasia and subsequent malignancy.
- The objective of this study was to identify and describe the population of patients who develop cervical dysplasia or malignancy despite prior HPV vaccination.

METHODS:

- We identified 35 patients treated between 2007 and 2017 for cervical intraepithelial neoplasia II/III, adenocarcinoma in situ and invasive carcinoma of the cervix after immunization with at least 2 doses of the quadrivalent HPV vaccine.
- HPV status was unknown to the authors prior to vaccination.
- Demographic, pathologic and clinical data were retrospectively collected.
- Descriptive statistics were used to summarize patient and disease characteristics.

Table 1: Summary of Patient Characteristics		
	n	%
Number of vaccine doses		
2 doses	4	11.4
3 doses	22	62.9
not reported	9	25.7
Stage		
CIN I-II	2	5.7
CIN III or ACIS	13	37.1
IA1	5	14.3
IA2	1	2.9
IB1	12	34.3
IB2	2	5.7
Number of risk factors for cervical cancer*		
0	5	14.3
1	25	71.4
2	5	14.3
Histology		
Squamous	18	51.4
Adenocarcinoma	17	48.6
Lymphovascular Space Invasion†		
Yes	10	50
No	8	40
Not reported	2	10

* Risk Factors include: Smoking, immunosuppression, history of sexually transmitted infection

† Among patients with invasive carcinoma (n=20)

RESULTS:

- Median follow-up was 17.1 months.
- The median age at diagnosis was 27.8 years (range, 18.2-36.1), and the median age at completion of HPV vaccination was 21.0 years (range, 13-30). Age at diagnosis is summarized in Figure 1.
- HPV infection was documented in 26 patients (74.3%). Only one patient was immunocompromised (2.9%). Fifteen patients (42.9%) had cervical dysplasia and 20 (57.1%) had invasive carcinoma.
- All patients with invasive carcinoma had stage I disease; 6 (33.3%) had stage IA and 12 (66.7%) stage IB disease.
- Fifty percent of cases with carcinoma had lymphovascular space involvement (n=10).
- Patient’s management is summarized in Figure 2. Thirty patients (85.7%) had fertility-sparing surgery and 32 (91.4%) were treated with surgery alone.
- At the time of their last follow-up, 32 patients (91.4%) had no evidence of disease. Two patients had evidence of cervical dysplasia and/or persistent HPV infection following treatment; 1 patient had recurrent malignancy and was treated with pelvic exenteration.

CONCLUSIONS:

- Cervical dysplasia and carcinoma after HPV vaccination can occur, and a majority of cases are HPV associated, suggesting incomplete coverage of the vaccine or vaccination after HPV exposure.
- In our series, all vaccinations occurred after the CDC recommended age of 11-12 years old, which highlights the need to complete vaccination prior to HPV exposure, in addition to continued screening for cervical cancer per guidelines.

Figure 2: Management of Cervical Dysplasia and Invasive Carcinoma