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*Neurol Neuroimmunol
Neuroinflammation*
2014;1:e31; doi: 10.1212/
NXI.0000000000000031

EARLY CERVICAL MYELITIS AFTER HUMAN PAPILLOMA VIRUS VACCINATION

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In 2006, an adjuvant vaccine against 4 human papillomavirus (HPV) types was licensed. By 2012, 45 countries had introduced HPV vaccination.¹ HPV encompasses a group of more than 100 viruses, of which at least 13 are high-risk types, responsible for cervical and other anogenital cancers.² There are currently 2 vaccines that prevent HPV 16 and 18 infection (known to cause 70% of cervical cancers) and development of subsequent cervical precancerous lesions.¹

Case report. A 14-year-old immunocompetent girl noticed her left hand felt weak and numb. These symptoms spread over 5 days to the rest of her arm and ipsilateral thoracic region, abdomen, and leg. Three days earlier she had received a first dose of quadrivalent HPV recombinant vaccine (qHPV, Gardasil). She had not had fever or previous symptoms suggestive of infection. On examination, she had bilateral diminished sensation to light touch, pain, and vibration below C5 level; muscle weakness of her left arm and leg, being able to move joints against resistance (grade 4 according to the Medical Research Council scale for muscle strength); and hyperreflexia bilaterally with nonsustained clonus and a left extensor plantar response. Neurologic examination was otherwise normal.

Brain and cervical spine MRI revealed an isolated C1-C2 hyperintense lesion in T2-weighted images (figure). CSF analysis showed normal glucose (0.49 mg/dL) and protein levels without cells, an increased myelin basic protein (6.4 ng/mL), an increased nonspecific immunoglobulin M ratio, and the presence of oligoclonal bands. Serology and PCR ruled out infectious etiologies, with negative testing for *Borrelia*, *Treponema*, *Listeria*, herpesviruses 1, 2, and 6, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, and HIV. Laboratory screening showed normal angiotensin-converting enzyme, vitamin B₁₂, and folate levels and was negative for antinuclear and antitransglutaminase antibodies.

Cervical transverse myelitis was diagnosed. Treatment with 1 g IV methylprednisolone was given for 5 days and clinical improvement ensued. Six months later, only mild left hand hypoesthesia and lower

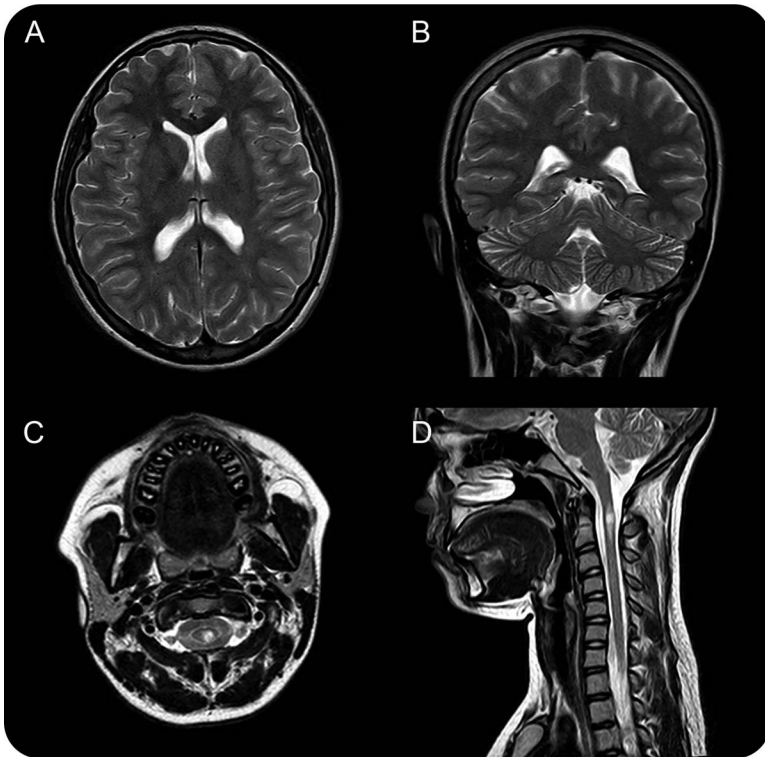
extremity hyperreflexia persisted. Follow-up brain and spinal MRI revealed an improvement of the cervical lesion without development of new lesions.

Discussion. HPV infection is transmitted mainly through sexual contact and it is a necessary step in the pathogenesis of cervical cancers. Cervical cancer is the second most common cancer in women and causes more than 270,000 deaths per year, mostly in low- and middle-income countries.¹ In the United States, there are an estimated 11,000 newly diagnosed cases of HPV-associated cervical cancer and 4,000 resulting deaths annually.³ The World Health Organization recommends vaccination for girls aged 9–13 years as “the most cost-effective public health measure against cervical cancer.”¹ However, there are safety concerns regarding HPV vaccines.

The relationship between HPV vaccination and subsequent CNS inflammation remains unclear. A recent review summarizes 9 published cases of CNS demyelination following HPV vaccination; clinical syndromes vary and include myelitis, optic neuritis, and encephalitis.⁴ In the genesis of CNS inflammatory disorders post-HPV vaccination, both molecular mimicry between vaccine antigen and myelin proteins and toxic materials in vaccine components are seen as potential causative factors.⁵ There are previous reports of CNS inflammatory syndromes following HPV vaccination describing a 10-day to 5-month time lapse from vaccination to symptom onset, with a minimum of a 21-day interval in cases developing myelitis. Recent reviews on this topic did not find an increased rate of subsequent autoimmune diseases; nevertheless, they acknowledge limitations regarding statistical power⁶ and data concerning specific populations.⁷

We present a case of transverse myelitis 3 days after HPV immunization. To our knowledge, this is the earliest case of CNS inflammation following HPV immunization, with a less than 7-day interval from vaccination to symptom onset. Regarding etiology, the patient was immunocompetent and there were no systemic signs of infection. The absence of cells in CSF analysis and the presence of oligoclonal bands with an increased nonspecific immunoglobulin M ratio suggested a background of a CNS inflammatory condition; however, the mechanism of disease, whether viral-induced or immune-mediated, remains to be determined.

Figure Brain and cervical spine MRIs showing an isolated C1-C2 lesion



Brain MRI T2-weighted images: axial (A) and coronal (B) images showing absence of brain lesions. Cervical MRI T2-weighted images: axial (C) and sagittal (D) images showing an isolated C1-C2 hyperintense lesion.

In conclusion, the probable benefits of mass vaccination with HPV seem to outweigh the potential risks. However, we must continue to report and investigate cases of inflammatory disorders of the CNS associated with qHPV vaccination, both for safety reasons and because it may help comprehend the pathogenesis of subsequent CNS demyelination.

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Author contributions: Dr. Fernández-Fournier: conceptualization and manuscript drafting. Dr. Díaz de Terán: manuscript drafting. Dr. Tallón Barranco: manuscript revision. Dr. Puertas: manuscript revision.

Acknowledgement: The authors thank the Neurology Department at La Paz University Hospital, especially Dr. Olga Trabajos, MD, who provided careful patient care and assistance during the patient's hospitalization.

Study funding: No targeted funding reported.

Disclosure: The authors report no disclosures. Go to Neurology.org/nn for full disclosures. The Article Processing Charge was paid by Fundación Investigación Biomédica del Hospital La Paz.

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Received June 20, 2014. Accepted in final form August 6, 2014.

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