



Short communication

Brachial plexus neuritis following HPV vaccination

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ABSTRACT

We present a 19-year-old girl who developed a left brachial plexus neuritis following vaccination with a quadrivalent human papillomavirus (HPV) vaccine. Post-vaccination brachial plexus neuritis is a rare event. Nevertheless, this first case warrants careful attention in view of the large vaccination campaigns in young adolescents being launched all over the world.

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1. Introduction

Genital human papillomavirus (HPV) is the most common sexually transmitted infection in Europe and the United States, with an estimated 20 million new infections every year [1]. In June 2006, the quadrivalent HPV vaccine type 6, 11, 16, 18 (Gardasil[®], MSD, Whitehouse Station, New Jersey) was approved by the FDA for use in humans. Large placebo-controlled studies have shown its efficacy in the prevention of HPV related disease [2–4]. In Belgium, recommendations for the use of HPV vaccines have been written for the ‘Hoge Gezondheidsraad’ by a working group presided by Hoppenbrouwers (full text available at <http://www.logopraam.be/images/baarmoederhalskanker/8204%20HPV%20NL.pdf>). So far, complications reported with its use mainly include local irritation and inflammatory reactions at the injection site as well as mild general symptoms including fever, urticaria, nausea and vomiting. As large vaccination campaigns are being launched in many countries in the western world, and are being considered in developing countries, more severe local and general complications need to be monitored closely. To the best of our knowledge, we present the first case of plexus brachialis neuritis following HPV vaccination.

2. Case report

A 19-year-old student was referred to the Orthopaedic Department with a 3-month history of severe shoulder pain heavily interfering with normal daily activities. She had no known allergies and her BMI was 17.9. There was no trauma in the history and no (viral) illness was reported. A first Gardasil[®] injection was given in the left deltoid muscle on 10/03/2007. On 06/04/2007 surgery on the right wrist was performed. A second injection of Gardasil[®] was given in the left deltoid muscle on 10/05/2007 and 1 month later she woke up with severe pain in the left shoulder. The pain interfered heavily with her daily activities and worsened during the following weeks. Because of severe pain two corticosteroid injections were given, one in the subacromial space and one in the acromioclavicular joint but none of these relieved the pain. When she attended our Orthopaedic Outpatient Clinic, 10 weeks after the initial onset of the pain, she had severe pain in the entire left shoulder region radiating across the back of the scapula, to the upper arm, the left elbow and the left breast. Active and passive mobility of the left shoulder was normal but painful. Strength was diminished in the left infra- and supraspinatus muscle but there was no visible muscle wasting. There was no neurological deficit. Clinical examination of the cervical spine was normal. Standard radiographs, ultrasound and MRI of the left shoulder were normal. Nuclear imaging showed no abnormalities.

A needle electromyography (EMG) examination, performed on 07/09/2007, 3 months after the onset of the pain showed neurogenic abnormalities consistent with brachial plexitis (Parsonage Turner syndrome). There was no familial history of neuralgia

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amyotrophy or hereditary familial neuritis with brachial plexus predilection. Conservative treatment, consisting of adequate analgesia was initiated and resulted in gradual pain relief. The last Gardasil® injection was given into upper outer quadrant of the right gluteus maximus muscle without any complications. Eight months after the onset of the pain, there was marked improvement of strength and mobility of the left shoulder but pain remained present requiring high doses of analgetics.

3. Discussion

Gardasil® is commercially available in Belgium since 2006 and is reimbursed by the social security system for girls aged between 12 and 16 years at the time of the first administration.

The federal authorities are currently considering vaccination for girls through the compulsory medical school examination system. In other countries, including the United States and the European Union, compulsory vaccination for HPV has recently been in the heat of the debate [5].

In accordance to the manufacturer's recommendation, the injection was performed in the left deltoid muscle in this right-handed female student. The dominant side is avoided, in order to minimize the local irritation and stiffness often reported following intramuscular (IM) vaccination. In this case, however, the patient experienced progressive pain and muscle weakness while EMG unequivocally demonstrated plexus brachialis neuritis (Parsonage Turner syndrome). Interestingly, the involved muscles demonstrated no signs of active denervation. The absence of denervation potentials was probably related to the time delay (3 months) between the onset of the symptoms and the EMG.

Parsonage Turner syndrome, or brachial neuritis, is a clinically defined syndrome that consists of sudden severe pain around the shoulder girdle. After days or weeks the pain becomes less severe but muscle weakness and even muscle wasting may become obvious. The aetiology of the syndrome remains an enigma. Surgery, viral diseases, infections, autoimmune mechanisms and immunizations have been reported to be precipitating factors associated with the occurrence of Parsonage Turner syndrome. In 30–85% of the cases such a precipitating factor can be found 3–14 days before the initial onset of the pain.

The disorder is often mistaken for other disorders affecting the shoulder region, including cervical radiculopathy, adhesive capsulitis, shoulder arthritis, calcifying tendonitis or other rotator cuff problems, Herpes Zoster. Disorders causing muscle wasting or weakness, especially nerve root compression, spinal cord or brachial plexus tumours, anterior poliomyelitis or amyotrophic lateral sclerosis, should also be considered in the differential diagnosis. A history of sudden intense shoulder pain without trauma and with normal clinical findings in the shoulder and neck region, should allow the clinician to differentiate between brachial plexus neuritis and the other above-mentioned disorders. As soon as the pain subsides and weakness develops, the diagnosis will become obvious and can be confirmed by electromyography. The prognosis of brachial plexus neuritis is usually good but recovery can be quite prolonged with recovery of strength and function within 5–8 years.

Post-surgical brachial plexus neuritis has been described in the literatures [6–8]. Typically acute shoulder pain develops within a few hours or days after the surgery. The described patient was operated on the contralateral wrist 2 months prior to the onset of the pain, but she only developed shoulder pain 2 months after surgery. A common predisposing factor in the cause of brachial plexus neuritis seems to be a decrease in physical resistance, usually seen some days or weeks before the onset of the pain. It is possible that in this case the surgery might have been a factor contribut-

ing to the decrease in physical resistance making this patient more susceptible for post-vaccination neuritis.

Reports of brachial plexus neuritis can be found in the literature after small pox vaccination [9], tetanus toxoid immunization [10–13], immunizations for diphtheria, tetanus and pertussis (DTP) [13–15], influenza vaccination [16], and after recombinant hepatitis B vaccination [17].

The exact etiology of post-vaccination brachial plexus neuritis is unknown. Direct injury to the nerve is unlikely because often the not-injected limb can be involved. Moreover, an injection in the deltoid muscle can lead to an axillary nerve injury, but, as in this case, larger parts of the brachial plexus are usually involved. In cases of neuritis after tetanus vaccination, an immune-mediated response to the tetanus toxoid is believed to be the cause of the neuritis. The HPV vaccine, however does not contain a toxoid so it remains unclear how it could have given rise to a neuritis of the brachial plexus. It seems strange that in this particular case, the neuritis only occurred one month after the second Gardasil® injection, but, a similar delay in appearance of clinical symptoms after a DTP vaccination has been previously described by Hamati-Haddad and Fenichel [14].

To the best of our knowledge this case represents the first report of brachial plexus neuritis after HPV vaccination. A search in the VAERS database (Vaccine Adverse Event Reporting Database)

Table 1

Overview of the number of brachial nervous conditions reported as vaccine adverse effects in VAERS

Vaccine	Number of brachial nervous events reported in VAERS
Anthrax (Biothrax)	1
Anthrax (no brand name)	1
HIB + HEP B (Comvax)	1
DTAP (Acel-Imune)	1
DTAP (Infanrix)	2
DT adsorbed (no brand name)	3
HIB (Acthib)	1
HEP A (Havrix)	2
HEP A (VAQTA)	3
HEP B (Engerix-B)	3
HEP B (Recombivax HB)	1
HPV (Gardasil)	4
Influenza (Fluarix)	4
Influenza (Flushield)	2
Influenza (Fluvirin)	11
Influenza (Fluzone)	17
Influenza (no brand name)	5
Lyme (Lymerix)	3
Measles + Mumps + Rubella (MMR II)	2
Meningococcal (Menactra)	1
Pneumo (Pneumovax)	6
Pneumo (Prenvar)	1
Polio virus, inact. (IPOL)	2
Polio virus, inact. (Poliovax)	1
Smallpox (Dryvax)	1
TDAP (Adacel)	12
TD adsorbed (no brand name)	3
TD adsorbed (no brand name)	3
TD adsorbed (no brand name)	2
Tetanus diphtheria (no brand name)	7
Tetanus toxoid (no brand name)	2
Tetanus toxoid (no brand name)	2
Tetanus toxoid, adsorbed (no brand name)	2
Typhoid live oral TY21A (Vivotif)	1
Typhoid VI polysaccharide (no brand name)	1
Typhoid VI polysaccharide (TYPHIM VI)	2
Varicella (Varivax)	2
Yellow fever (YF-VAX)	1
Vaccine not specified (no brand name)	1
Total	120

revealed another 120 cases classified as 'brachial plexopathy', 'brachial plexus injury' or 'brachial radiculitis' (Table 1). Interestingly four cases were reported after a Gardasil® injection. Unfortunately, we do not have any additional information on the clinical presentation, physical findings or electromyographic data.

So far, over 20 million doses of Gardasil® have been administered. Even if we keep in mind that health complaints in adolescents in a cohort eligible for HPV vaccinations might be coincidental and should not be considered as adverse effects [18], it can be extrapolated that the post-vaccination event described in this patient is one of extreme rarity. However, in view of the number of countries currently undertaking systematic vaccination, careful monitoring of unusual complications like this is important. Since the HPV vaccination comprises three consecutive injections, clinicians should be aware that consecutive injections may theoretically potentiate the neurological complications observed after the first or second injection.

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