Brachial neuritis following quadrivalent human papilloma virus (HPV) vaccination

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Introduction

Brachial neuritis, originally described as neuralgic amyotrophy by Maurice Parsonage and John Turner [7] in 1948, known as “Parsonage Turner Syndrome”, is a condition that causes pain and weakness of the shoulder girdle and/or upper extremity. While brachial neuritis is a rare condition, it is the most common cause of nontraumatic brachial plexopathy [6]. This condition has been misinterpreted or misdiagnosed as rotator cuff pathology, adhesive capsulitis, tendonitis, cervical radiculopathy, compression neuropathy, tumor of the spine or brachial plexus, amyotrophic lateral sclerosis, herpes zoster, and acute poliomyelitis. The etiology of this condition remains a mystery. Surgery, viral disease, infection, autoimmune mechanism, and immunization have been reported as precipitating factors of brachial neuritis. Debeer et al. reported that in 30–85% of the cases, an antecedent event can be found 3–14 days before the initial onset of pain [2].

The typical presentation of brachial neuritis is one of an otherwise healthy individual who experiences the sudden onset of intense pain in the affected upper extremity without a history of trauma. Typically, the pain is localized to the shoulder girdle and can last from a few days to a few weeks. The pain is followed shortly thereafter by weakness, which may manifest in any of the major peripheral motor nerves of the upper extremity. We present the case of a young woman with a median nerve distribution palsy that affected the muscles of both the anterior interosseous nerve (AIN) distribution and the motor branch to the thenar intrinsic muscles.

Case Report

A 25-year-old, right-hand-dominant female was referred by her primary care physician with a presumptive diagnosis of left carpal tunnel syndrome of 5 months duration. The patient’s chief complaint was loss of hand dexterity due to the inability to flex her left thumb interphalangeal (IP) joint. The patient had received two of the series of three recommended Gardasil® (Merck & Co., Whitehouse Station, NJ, USA) vaccinations for human papilloma virus (HPV) prophylaxis into the left deltoid of the affected upper extremity. Three days after the second injection, she noted intense burning pain in her entire left upper arm. After the pain subsided over the next 24 to 48 h, the patient noted that she was unable to grip a glass due to lack of thumb flexion while washing dishes. Other than the initial pain, she denied febrile illness, night sweats, chills, or any dermatologic-type rash. At the time of the second injection, the patient denied having viral or flu-like symptoms. There were no neurological symptoms, numbness, tingling, or

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paresthesias at the time of the injection to suggest an intraneural injury.

Initial electromyographic (EMG) and nerve conduction velocity studies performed 3 months after the onset of symptoms were interpreted as normal; however, electrodiagnostic motor testing of the flexor pollicis longus (FPL), pronator quadratus, and flexor digitorum profundus (FDP) to the index finger was not performed. Serologic testing for rheumatoid and other autoimmune or inflammatory disorders was normal. She denied hereditary familial neuritis or neuralgic amyotrophy.

On physical examination, the patient had full active and passive range of motion of her cervical spine, shoulder, elbow, forearm, and wrist. Left thumb IP joint active range of motion was absent with passive range of motion from 0° to 60° (Fig. 1). She did demonstrate active flexion against gravity with her index finger FDP; however, she was unable to flex it against minimal resistance, indicating grade 3/5 motor strength. Grip strength measured 55 lb on the right and 45 lb on the left. Sensation was intact and symmetric with Semmes–Weinstein monofilament testing and 128 Hz vibratory sensation. Tinel's signs were negative over the brachial plexus, cubital tunnel, radial tunnel, pronator quadratus, Guyon's canal, carpal tunnel, and dorsal radial sensory nerve.

Repeat EMG and nerve conduction studies were performed 5 months after the inciting event. This study demonstrated increased insertional activity in the AIN innervated FPL and index finger FDP as well as the median nerve innervated palmaris longus and abductor pollicis brevis. This study was consistent with a high median nerve distribution palsy.

We recommended treatment by observation. By 8 months, the patient began to experience increasing

strength in her index finger FDP. At 1 year after the onset of symptoms, she had largely regained her index FDP strength but still had complete loss of function of her FPL muscle with a persistent loss of manual dexterity. Fortunately, at 16 months following the initial insult, the patient experienced return of FPL function with improved dexterity, obviating the need for tendon transfer.

Discussion

Human papilloma virus is the most common sexually transmitted disease in the USA with an estimated 6.2 million new infections per year [5]. Genotypes 16 and 18 of the virus have been linked to approximately 70% of cervical cancers and precancerous lesions worldwide, and genotypes 6 and 11 are linked to 90% of genital warts [5]. Gardasil® and Cervarix®, the quadrivalent HPV vaccines, (GlaxoSmithKline, London, UK) have shown efficacy in the prevention of HPV-related disease. The current recommendations for the administration of Gardasil® are to girls aged 11 to 12 years, prior to sexual activity, but vaccinations are offered in females up to age 26 [5]. The injections are given as a series of three vaccinations at 0, 2, and 6 months. Typically, the injections are administered in the nondominant deltoid.

The adverse effects of the Gardasil® vaccine generally have been reported as being similar to those of other vaccinations including local irritation and inflammatory reactions as well as general symptoms such as fever, nausea, and dizziness [5]. The Center for Disease Control and Prevention (CDC) as well as the package insert for Gardasil® do not mention brachial neuritis or any serious long-term side effects of the vaccine. By 2009, 40 million doses of Gardasil® had been administered.

Reports of brachial plexus neuritis can be found in the literature after other vaccinations. Brachial neuritis after vaccination administration is a well-described phenomenon although the exact etiology is unknown [10]. Cases of neuritis after tetanus vaccination, an immune-mediated, local demyelinating response to the tetanus toxoid is believed to be the cause of the neuritis. The CDC considers brachial neuritis occurring 2 to 28 days after tetanus vaccination a reportable event with presumed vaccine causation [4]; however, this relationship has not been defined for brachial neuritis after HPV vaccination. The HPV vaccine, however, does not contain a toxoid so the exact mechanism leading to neuritis of the brachial plexus remains unclear [2].

To our knowledge, this is the second case of brachial neuritis after an HPV vaccine reported in the English literature [2]. In our search of the Vaccine Adverse Event Reporting System (VAERS) data of reportable events [9], 17

Fig. 1 On physical examination, the patient's left thumb IP joint active range of motion was 0° of flexion and passive range of motion was from 0° to 60° of flexion

cases of the HPV vaccine causing side effects listed as “brachial plexus injury,” “brachial plexopathy,” and “brachial radiculitis” were identified, including 16 from Gardasil® and 1 from Cervarix®. Approximately 30,000 VAERS reports are filed annually, with 10–15% classified as serious; however, limited clinical information is available using this database.

This disorder is easily mistaken for other pathology or injuries around the shoulder or upper extremity. When considering this diagnosis, physicians should remember to ask specifically about recent illness or vaccination as a possible inciting event. In addition, since shoulder muscles are more commonly affected, less common presentations such as was seen in this case make definitive diagnosis even more challenging. While less common, the AIN territory has been involved in reported cases of brachial neuritis [3, 8, 11].

Treatment of brachial neuritis is typically supportive. Analgesics and immobilization should be prescribed in the acute phase, and active rehabilitation is recommended once the affected muscles begin to recover. Prognosis is generally good; however, some patients have some long-term residual weakness of the affected extremity [1]. We caution against performing tendon transfers in similar cases, as this case illustrates late recovery possible 16 months after the inciting event.

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