Letters

RESEARCH LETTER

Reports of Injection Site Necrosis After 23-Valent Pneumococcal Vaccine Use

Although clinical trials typically identify common adverse events associated with vaccines, they are usually underpowered to detect rare adverse events. Once the vaccine has been administered to a larger, more diverse population after approval by the US Food and Drug Administration (FDA), rare adverse events may emerge. Postmarketing safety surveillance is critical to further characterize the safety profile of licensed vaccines.[1]

Supplemental content

The FDA and the Centers for Disease Control and Prevention monitor postmarketing safety of US-licensed vaccines using the Vaccine Adverse Event Reporting System (VAERS), a passive surveillance system that relies on individuals to report adverse events.[2] In 2020, the FDA detected a safety signal of injection site necrosis after 23-valent pneumococcal vaccine (Pneumovax 23; Merck). Herein we describe the evaluation and outcomes of this safety signal.

Methods | Our evaluation included a case series review, calculation of reporting rate, and a PubMed search for similar reports. Under statutory authority pursuant to public health, no approval from institutional review boards or informed consent was required for this case series analysis.

We queried the VAERS database on May 15, 2020, using Medical Dictionary for Regulatory Activities preferred terms for injection site necrosis. We reviewed reports, including submitted medical records (eg, clinician notes and pathology reports), and defined a case using adapted criteria for a local reaction at or near the injection site.[3] We calculated a reporting rate using vaccine distribution data from the manufacturer.

Results | Of 104 identified VAERS reports, 48 met our case definition. Of these cases, most were for skin necrosis (n = 43), 5 of which also included fat necrosis. The remaining cases were necrosis of fascia (n = 2); fat and fascia (n = 1); fat, fascia, and muscle (n = 1); and muscle (n = 1). One-half of the 48 cases were reported from foreign countries and one-half were from the US. In 23 cases (47.9%), the reactions were serious, including 1 fatality (unrelated to vaccination). Seventeen patients (35.4%) required hospitalization, and 26 (54.2%) required surgical intervention, most commonly debridement. Eight patients (16.7%) underwent multiple surgical procedures, and 3 (6.3%) required a skin graft.

For patients with skin necrosis (n = 43), median (range) age was 67 (18-96) years, and most patients were female (n = 36). Twelve patients were immunocompromised. Concomitant vaccinations were reported in 10 patients, 5 of whom were injected in the same arm as the 23-valent pneumococcal vaccine. Concurrent diagnoses of cellulitis and abscess were reported in 16 and 3 patients, respectively. There were too few cases of fat, fascia, or muscle necrosis to draw meaningful conclusions.

The injection site necrosis reporting rate was less than 0.2 cases per million vaccine doses distributed. Literature search revealed 2 cases of injection site necrosis after the 23-valent pneumococcal vaccine.[4,5]

Discussion | Assessment of VAERS reports confirmed the occurrence of injection site necrosis after 23-valent pneumococcal vaccine administration. Often, skin necrosis developed after a progression of typical local symptoms (eg, redness, swelling, and pain). These reports are consistent with published descriptions of injection site necrosis, which has been reported as a rare complication for many vaccines and injectable drugs.[6]

This study is limited by use of passive surveillance data; we were unable to establish causality using VAERS reports alone. However, the timing and the location of reactions at the injection site suggest a possible causal association with the vaccine. Patient-related factors (eg, comorbidities) and mechanical factors (eg, improper injection technique) may also contribute.[4,5] Although not equivalent to an incidence rate, the reporting rate suggests this condition is rare. A similar safety signal has not been detected for the more recently approved 15-valent and 20-valent pneumococcal conjugate vaccines. Other study limitations include differences in time since approval and variations in the exposed populations, which preclude direct comparison among vaccines.

The Pneumovax 23 US package insert has been updated to include injection site necrosis in section 6.2, Post-Marketing Experience. The overall benefit-risk balance for this vaccine remains favorable.

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Concept and design: Day, Thompson, Alimchandani.
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