

CASE REPORT

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## Herpes zoster vaccine (Zostavax®): Cellulitic injection site reaction or bacterial cellulitis?

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### ABSTRACT

A 70 y old woman presented with a cellulitic reaction following Zostavax® injection. This reaction could be differentiated from bacterial cellulitis on the basis of the temporal relationship between vaccination and onset of the reaction, its non progression and unresponsiveness to antibiotic therapy. Alerting health care providers to this type of reaction, also seen with pneumococcal and pertussis containing vaccines, should avoid the inappropriate use of antibiotics.

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bacterial cellulitis; cellulitic reaction; healthcare providers; Zostavax®

### Introduction

Herpes zoster or shingles, the cutaneous dermatomal eruption of reactivated varicella zoster virus (VZV) is a growing global public health issue, particularly in those over 50 y of age.<sup>1</sup> Vaccines have been trialled<sup>2</sup> to reduce its incidence, severity and its most common and debilitating complication, post-herpetic neuralgia.<sup>3</sup>

Zostavax®, the most studied and only approved zoster vaccine, was demonstrated<sup>4</sup> to have an efficacy of 63.9% and 37.6% and 65.7% and 66.8% for 60–69 y old and ≥70 year old patients for prevention of herpes zoster and post-herpetic neuralgia respectively.

Injection site reactions satisfying the Brighton Collaboration Local Reaction Working Group Level 2 of diagnostic certainty for bacterial cellulitis<sup>5</sup> (at least 3 of the following signs/symptoms: localized pain or tenderness [pain to touch], erythema, induration or swelling and warmth, and reaction at the injection site.) have been reported to occur in 0.7% to 1.2% of Zostavax® vaccine recipients.<sup>6</sup>

In this case report differentiation between a cellulitic injection site reaction and bacterial cellulitis following Zostavax® administration is reviewed in the context of other vaccines in which this clinical dilemma has been reported.

### Patient presentation

A fit 70 y old woman sought Zostavax® vaccination as her husband, who had splenectomy 8 y previously for lymphoma, had severe herpes zoster complicated by post-herpetic neuralgia for 10 months.

Zostavax® (Batch AK000265) was administered by subcutaneous injection into the left deltoid. She reported that she had no fever but a red, painful, tender swelling of almost the entire left upper arm on the evening after injection. She sought care

one day after vaccination from another general practitioner who diagnosed bacterial cellulitis and prescribed Cephalexin 500mg 6 hourly and recommended hospital admission if her condition worsened.

Review by the author 7 d after the vaccination resulted in the antibiotics being ceased due to lack of efficacy. The reaction resolved spontaneously 3 weeks post vaccination without any treatment.

### Discussion

Bacterial cellulitis is a pauci bacillary syndrome,<sup>7</sup> defined by the Brighton Collaboration Local Reaction Working Group post vaccination<sup>5</sup> as “an acute infectious and expanding inflammatory condition of the skin” with

Level 1a of diagnostic certainty – includes at least 3 of the following signs/symptoms – localized pain or tenderness (pain to touch), erythema, induration or swelling and warmth and reaction at the injection site and laboratory confirmation by culture.

Level 2 of diagnostic certainty – at least 3 of the signs/symptoms for level 1a and reaction at the injection site and diagnosed by a qualified healthcare provider.

Thirty five cases of a reaction listed as cellulitis, satisfying the level 2 of diagnostic criteria, were retrieved from the Vaccine Adverse Event Reporting System (VAERS) database as at April 2016 for Zostavax®, all treated with antibiotics.

If these cases were due to bacterial cellulitis, pathogenic bacteria could be introduced during vaccine administration from contaminated needles/syringes, infected vaccinator or from contaminated skin.<sup>8</sup>

With contaminated diphtheria, tetanus toxoid and pertussis vaccine localized infection has been shown<sup>9</sup> to occur from 1 to 8 d (median 5 days) after injection.

However these reactions may be due to a cellulitic reaction, also satisfying the level 2 of diagnostic certainty, which resolves spontaneously without antibiotic therapy.

This reaction forms a subset of extensive limb swelling (ELS) reported by Woo et al.<sup>10</sup> within 1 day after vaccination in approximately 75% of cases in an analysis of VAERS data. Although this reaction was seen with a broad spectrum of vaccines, including varicella vaccine, the most studied of these were diphtheria, tetanus and pertussis containing vaccines<sup>11,12</sup> with “fever and injection pain observed most frequently on the first evening, whereas redness and swelling were observed most frequently on the second evening.”<sup>11</sup>

An acute, febrile, cellulitic reaction, unresponsive to antibiotics has been reported for pneumococcal vaccines; Nelson et al.,<sup>13</sup> 10 valent pneumococcal polysaccharide vaccine (PPV10), F/31, onset 8 hours post vaccination, maximal 24 hours, resolved by day 5 and 23 valent pneumococcal polysaccharide (PPV23). Hasan et al.,<sup>14</sup> M/38, onset 4 hours post vaccination, maximal day 4, resolved by day 17. Huong et al.<sup>15</sup> 17 children (9M, 8F), 24–138 months old, onset average 9 hours post vaccination and Yousef & Mannan<sup>16</sup> M/5, onset 24 hours post vaccination.

Differentiation between cellulitic reaction at the injection site and bacterial cellulitis is based on the temporal relationship between onset of the reaction and vaccination, progression of the reaction and response to antibiotic treatment.

In the adverse event following Zostavax<sup>®</sup> administration reported here the reaction occurred on the day of vaccination, did not progress and was unresponsive to antibiotic therapy, thus being a cellulitic reaction at the injection site rather than cellulitis of bacterial origin.

Educating health care providers about this not uncommon adverse event should decrease the over-diagnosis of bacterial cellulitis and the inappropriate use of antibiotics following Zostavax<sup>®</sup> administration – a vaccine increasingly promoted<sup>17</sup> for the prevention of herpes zoster.

## Abbreviations

ELS	Extensive Limb Swelling
PPV10	10 valent pneumococcal polysaccharide vaccine
PPV23	23 valent pneumococcal polysaccharide vaccine
VAERS	Vaccine Adverse Event Reporting System

## Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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