Fatal disseminated varicella zoster infection following zoster vaccination in an immunocompromised patient

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In November 2014, a 79 year-old gentleman was admitted to a Scottish hospital with a widespread vesicular rash consistent with varicella zoster virus (VZV) infection. He was diagnosed with chronic lymphocytic leukaemia in January 2012 and finished six cycles of fludarabine, cyclophosphamide and rituximab in April 2014. Five weeks prior to admission he received the zoster vaccine as part of the immunisation programme against shingles. Afterwards, he gradually developed malaise and, four weeks after vaccination, some vesicles appeared at the injection site. On admission, he was pyrexial at 41ºC and presented a vesicular rash on his right upper arm, torso and extremities. He showed no respiratory distress and a chest X-ray was unremarkable. He was pancytopenic with haemoglobin 109 g/L, white cell count $1.3x10^9$/L (lymphocytes $0.6x10^9$/L) and platelets $55x10^9$/L. Intravenous (iv) antimicrobial therapy was started with piperacilin/tazobactam, gentamicin and high dose iv aciclovir (10 mg/kg tds). Human normal immunoglobulin (HNIG) was added on day three (400 mg/kg every other day for a total of five doses). The patient continued to develop new vesicular lesions yet remained stable with neither clinical nor radiological evidence of systemic involvement. On day six, he suffered an abrupt clinical deterioration and was transferred to the Intensive Care Unit (ITU) for mechanical ventilation, inotropic support and acute renal failure management. A chest X-ray revealed patchy consolidation throughout both lungs. Aciclovir was increased (iv 20 mg/kg tds) and ganciclovir (iv 5 mg/kg bd) was added in case of possible cytomegalovirus (CMV) superadded pneumonititis. Ganciclovir was stopped 24 hours later as CMV testing was negative. Bronchoalvelar lavage (BAL), vesicle fluid and plasma were positive by polymerase chain reaction (PCR) for VZV. BAL was negative for respiratory viruses and culture for bacteria and fungi were also negative. After four days in the ITU, no further vesicles had developed. Although the patient was extubated and VZV became negative in plasma and BAL by day 12 in ITU, he subsequently deteriorated developing multi-organ failure and dying 25 days after admission. VZV Oka vaccine strain (vOka) was detected in vesicle fluid using PCR.

VZV is an ubiquitous alphaherpesvirus which causes vesicular rash. Herpes zoster (HZ) or shingles results from reactivation of latent VZV in nerve-root ganglia, usually many years after the primary VZV infection (varicella or chicken pox). HZ is typically restricted to one or two contiguous dermatomes, but can be extensive in elderly and immunocompromised individuals. HZ complications include postherpetic neuralgia, HZ ophthalmicus, stroke and meningoencephalitis[1]. Life threatening disseminated disease can occur in severely immunosuppressed patients. The zoster vaccine has been shown to be effective in preventing both zoster and postherpetci neuralgia, whith the result that immunisation programmes were introduced in the United States in 2006[2] and subsequently in other

European countries . Zoster vaccine contains the same VZV Oka live, attenuated strain in the varicella vaccine, formulated with a significantly higher dose. The vaccine is well tolerated and safe[2,3] however, a single death following the zoster vaccination has been reported in an immunosuppressed patient rted[3]. The UK zoster immunisation programme started in September 2013, initially targeting people aged 70 (routine programme) and 78 or 79 (catch up programme) and coverage rates of around 60% have been reached in the target age groups. While varicella vaccine is licensed in some immunocompromised populations, recommendations for the use of zoster vaccine in the immunocompromised is mixed[2,4,5]. Even where limited use in the immunocompromised is recommended, zoster vaccine is contraindicated for individuals with haematological malignancies[4]. Confusingly, current recommendations also suggest that zoster vaccine can be given six months after the end of chemotherapy or radiotherapy[4], as was the case for this patient.

PCR results demonstrate the possibility of the zoster vaccine causing widespread lethal infection in the immunocompromised. If a varicella rash develops after inadvertent zoster vaccination, aciclovir should be instigated urgently. To our knowledge, this is the first lethal case following zoster vaccination in Europe and reinforces existing advice not to immunise individuals with haematological malignancies .

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