Increased complications with Atopic Dermatitis and Varicella-Zoster virus

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Abstract

A retrospective case note analysis and telephone consultation of 79 children, discharged from our teaching hospital with varicella zoster virus infection between 2003 and 2010, was performed. The hypothesis was that children with atopic dermatitis were more at risk of skin complications than children without.

It was found that children with atopic dermatitis were significantly more likely to have varicella zoster virus infection complicated by cellulitis (21% versus 6%; p=0.05), haemorrhagic varicella (14% versus 2%; p=0.04) and superimposed 'skin and soft tissue infection' (61% versus 34%; p=0.008). Subjective severity of scarring was scored significantly higher in children with atopic dermatitis compared to those without (p = 0.006).

In conclusion, skin related complications of varicella zoster virus infection are significantly more common in children with atopic dermatitis. Inclusion of atopic dermatitis as a "special case" in childhood vaccination programmes may prevent these complications. This warrants further more objective evaluation in a prospective study.

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Background

Varicella Zoster Virus (VZV) is a highly transmissible airborne illness causing a vesicular exanthem, with fever, myalgia, and malaise. It has a population incidence of 13-16 cases per 1000 and in non-vaccinated populations is most prevalent in 1-4 year olds. Skin related complications such as scarring are common. In Atopic Dermatitis (AD) several factors such as defective skin barrier function and impaired innate immunity contribute to increased susceptibility to cutaneous infections. The hypothesis was that these children have an increased rate of complications and post infection scarring. This study establishes "proof of concept".

Methods

Permission was obtained from the Guy's and St Thomas' ethics committee. Using hospital clinical coding to identify patients, we performed a retrospective case note analysis of children, less than 16 years of age, discharged from the teaching hospital, with VZV infection from January 2003 to December 2010. Patients with VZV infections are not routinely admitted to hospital, so these were patients with complications such as fever, infections or dehydration, for example. Other patients admitted were to specialist departments, such as the renal ward, where patients were immunosuppressed and required monitoring when infected.

Paper and electronic case notes were reviewed to confirm diagnoses, from the medical history and the clinical details of the admission. The parents or carers of all living patients were then contacted by telephone, where possible. Guardians were asked to verify the clinical details and to answer a questionnaire, with a subjective grading system of 1-10, to evaluate the severity of scarring. Data analysis was conducted using Excel and SPSS (version 18) statistical software, with significance tests by Student's T-Test for parametric data and Chi Squared and Mann-Whitney U tests for non-parametric data.

Results

Seventy nine patients were identified from hospital coding, 78 of them had sufficiently complete data to be included. Of this study group, the families of 48 (62%) patients were contacted to complete the short, subjective questionnaire. Of these

telephone consultations, 21 (44%) had AD and 27 (56%) did not. Any patients noted to have doctor-diagnosed AD by medical notes and with the diagnosis verified by parent or carer, by telephone, were included in the AD group for analysis. As not all families were contactable, several diagnoses of AD in the notes, which could not be verified by the families, were left. Seven such patients, in whom the diagnosis of AD had been recorded by a doctor in the case notes, were included in the analysis. Therefore, of 78 children with VZV infection: 28 (36%) were assigned to the AD group and 50 (64%) were not.

The average age of children was 3.4 ±3.3 years and 3 ±2.7 years, with and without AD, respectively. The median interval between hospital admission and telephone survey was over three years in each group (1100 days in AD group and 1561 days in non AD group). Thirteen patients were either admitted to the paediatric intensive care unit (PICU), or were transferred in to the PICU from other hospitals. The majority were admitted due to complications to VZV such as fever, dehydration or sepsis, but certain renal patients were admitted due to their immunosuppression from medication. The demographic and clinical details are summarised in Table I. (*See next page*)

Comparing skin related complications, significant differences were found. Those with AD were significantly more likely to have VZV complicated by cellulitis (21% with AD, 6% without AD, p=0.05) or haemorrhagic varicella (14% with AD, 2% without AD, p=0.04). Superimposed skin and soft tissue infection (SSTI) complicated the course of 34% of non AD patients and 61% of AD patients (p=0.01). There were no statistically significant differences in other separate recorded complications, including mortality rates - where 3 deaths occurred in the group without AD (p=0.18). The incidence of parental reporting of subsequent shingles was higher in the AD group although not statistically significant (4 (19%) vs. 1 (4%), p=0.07). There was no difference in the rate of post VZV infection scarring between the groups, (15(71%) with AD versus 18(67%) without AD, p=0.72,) however, the subjective severity of scarring on a scale of 1-10 was scored significantly higher by the families of children with AD, compared to those without (5.7 ± 2.9 versus 2.8 ± 2.1, p = 0.006). The majority of families from both groups wished their child had received the varicella vaccine (67% and 78%, with and without AD).

Discussion

This study reports that children with AD and VZV infection are more likely to develop skin related complications such as haemorrhagic varicella, and are at significantly increased risk of superimposed bacterial SSTI. This is in interesting contrast to some evidence which suggests that VZV in early life protests against the development of AD.[1]

Families score the severity of scarring significantly higher in children with AD. The rate of shingles following VZV infection may be higher in those with AD. Though this study did not show a higher rate of systemic complications in children with AD, it should be noted that these complications did occur in the non-AD group. Also, whilst there were no fatalities in the AD group (possibly due to small numbers), there was a 3% mortality rate in children with varicella zoster infection, but no atopic dermatitis. The fact that children are dying from varicella infections must weigh heavily in any future decision on vaccination schedules.

Despite the limitations of this study - parental assessment of residual scarring rather than an objective review and the lack of severity scoring data for those patients with AD - these study findings may nevertheless be somewhat representative of children in the UK who require hospitalisation or transfer to a tertiary hospital for VZV related complications.

Hospitalisation rates, in the United Kingdom for VZV, are reported as 16.7 per 100 000 children aged 0-14;[2] in one 13-month period there were 112 admissions for severe VZV. There is some evidence[3] that these patients have reduced virus specific effector cells, which may contribute to their susceptibility to severe viral infections such as varicella. In the UK, varicella vaccine is not included in the routine immunisation schedule, but is recommended for susceptible health care workers, and susceptible close contacts of immunocompromised patients.[4,5]

There are two vaccines licensed for use in the UK, both of which have comparable efficacy.[6] The efficacy of the vaccine after two doses is 98.3%, with this efficacy lasting consistently at 10-year follow up.[7] Break through and significantly milder infections, with fewer complications, do occur in up to 15% of vaccinated patients.[8] The morbidity, and even mortality, associated with varicella has led to some countries including varicella vaccination in the routine childhood immunisation schedule.[9] Permanent sequelae seen in 10% of children in the US, were most often due to severe skin scarring or cerebellar ataxia.[10] It should be noted that varicella dramatically increases the risk of acquiring lesions infected with Group A Streptococcus (GAS).[11]

While there are public health arguments[6] supporting the current UK decision not to include varicella vaccine in the routine childhood schedule, the availability of a safe, effective vaccine provides the opportunity to minimise the morbidity of varicella in particularly vulnerable patient groups. In Germany, after the introduction of VZV immunisation for all children, VZV-related hospital admissions fell by 63% and incidence of complications by 81%, with the greatest reductions in skin related complications.[12] There is evidence that a universal varicella vaccine could potentially prevent up to 15% of all paediatric invasive GAS disease.[11] Seven European countries now recommend varicella vaccination for 'high risk patients'.[9] These findings suggest that children with AD are at significantly higher risk of post varicella skin complications.

Table 1: Data from analysis of paient records and telephone survey follow-up

	Atopic Dermatitis N= 28	Without - Atopic Dermatitis N= 50	P	95% CI
Age	3.4±3.3	3.0±2.7	0.52	-0.94,1.83
Mortality (N)	0	3	0.18	
Transfer from peripheral hospital (N)	6 (21)	7 (14)	0.45	
Length of stay (days)	6.6±10.0	5.7±5.7	0.63	-2.8,4.5
PICU admissions (N)	5 (18)	8 (16)	0.87	
PICU length of stay (days)	4.2±2.8	8.3±8.5	0.33	-13.0,4.8
Complications				
Superficial and/or soft tissue infection (SSTI)	17 (61)	15 (34)	0.008	
Cellulitis	6 (21)	3 (6)	0.05	
Haemorrhagic Chicken Pox	4 (14)	1 (2)	0.04	
Necrotising Fasciitis	1 (4)	1 (2)	0.71	
Superadded infection	6 (21)	6 (12)	0.32	
Preseptal/orbital cellulitis	2 (7)	1 (2)	0.28	
Abscess	0 (0)	4 (8)	0.11	
Eczema herpeticum	1 (4)	0 (0)	0.19	
Encephalitis	1 (4)	4 (8)	0.41	
Sepsis (positive blood culture)	2 (7)	1 (2)	0.28	
Pneumonia/pneumonitis	2 (7)	6 (12)	0.44	
Immunosuppresion	2 (7)	4 (8)	0.83	
Surgical interventions (N)	2 (7)	5 (10)	0.76	
Telephone consultation (N)	**21**	**27**		
Ethnicity				
White	11 (52)	12 (44)	0.59	
Black	3 (14)	3 (11)	0.74	
Asian	3 (14)	4 (15)	0.96	
White/Black	2 (10)	6 (22)	0.24	
White/Asian	0 (0)	1 (4)	0.37	
Chinese	1 (5)	0 (0)	0.25	
Other	1 (5)	1 (4)	0.86	
Shingles (N)	4 (19)	1 (4)	0.07	
Retrospectively would have wished for the varicella vaccine (N)	14 (67)	21 (78)	0.81	
Have chicken pox scars (N)	15 (71)	18 (67)	0.72	
Scar rating	5.7±2.9	2.8±2.1	0.006	

Data presented are N±SD (%). PICU: Paediatric Intensive Care Unit

A multi-centre prospective study of children with AD and chickenpox could help establish the magnitude of the problem, and whether the designation of AD, as an indication for varicella vaccination, can be justified in European countries, where vaccination is not included in the routine childhood immunisation schedule.

Conflict of interests:

The authors state that they have no conflict of interests or any financial interests

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