



The Impacts of Gianotti-Crosti Syndrome (Papular Acrodermatitis of Childhood) on the Quality of Life of Children

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Background: Gianotti-Crosti syndrome (GCS) is a self-remitting eruption related to viral infections. Ribavirin has been reported to be effective in treating severe GCS. Before clinical trials on antiviral agents, the magnitude of GCS affecting the quality of life in children should be ascertained.

Aim: To investigate the impact of GCS on the QOL of children.

Methods: Our setting was a teaching clinic. We validly translated the Children Dermatology Life Quality Index into Chinese. We recruited all children aged five to 16 years diagnosed with GCS over two years. For each child with GCS, we recruited the next age-and-sex pair-matched child consulting us for atopic dermatitis (AD), and the next age-and-sex pair-matched child brought to consult us for problems unrelated to the skin as controls. All study and control subjects completed the CDLQI.

Results: 23 children were GCS and 46 children as controls were recruited. The impacts of GCS on children were significantly higher than children brought to consult us for problems unrelated to the skin ($P < 0.05$), with the parameters *symptoms and feelings, leisure, school or holidays, and treatment* mostly affected. However, the scores were low. Four (17%) study subjects and none (0%) in the second control had total CDLQI higher than 30%. The difference is insignificant (RR: inapplicable; $P = 0.11$).

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Impacts of AD on children were significantly higher than such for GCS ($P < 0.001$). Twelve (52%) children with AD and four (17%) children with GCS had total scores higher than 30% (RR: 3.00, 95% CI: 1.13 – 7.94; $P < 0.05$).

When compared to a similar study on children with pityriasis rosea, the impacts of GCS were very similar to those of pityriasis rosea.

Conclusion: GCS casts relatively low impacts on the QOL of children. These impacts were much lower than such of AD.

Keywords: Children dermatology life quality index; Chinese children dermatology life quality index; paraviral exanthema; Chuh and Zavar's classification of Gianotti-Crosti syndrome; Chuh and Zavar's diagnostic criteria of Gianotti-Crosti syndrome.

1. BACKGROUND

Gianotti-Crosti syndrome (GCS, also known as *papular acrodermatitis of childhood*) is a skin eruption previously reported to be related to hepatitis B virus infection [1,2], but is now closely related to Epstein Barr virus [3,4] and other viral infections [5,6]. Applying polymerase chain reaction to detect human herpesvirus 6 and 7 DNA and reverse transcriptase polymerase chain reaction to detect human herpesvirus 6 U91 messenger-RNA transcripts in the plasma and peripheral blood mononuclear cells of children with GCS, we have reported that GCS in our locality might be associated with primary infection of human herpesvirus 6B [7].

Many clinical trials have been reported over the past decade on the active treatment of exanthems which might be caused by viruses, such as the use of acyclovir on pityriasis rosea (PR) [8,9]. In one of these studies [10], children with PR were recruited. However, we have found that PR does not exert significant impact on the quality of life (QOL) of most children [11]. For these children, the use of active antiviral treatments is still controversial.

To our best knowledge, no study has been reported on the impact of GCS on the QOL of children. We believe that such a study is necessary so that further interventional studies might have a baseline outcome measure to refer to.

2. AIM

Our aim is to investigate the impact of GCS on the QOL of children.

3. METHODS

3.1 Children Dermatology Life Quality Index

The Children Dermatology Life Quality Index (CDLQI) [12] is a vigorously validated tool to

assess impacts of skin diseases on QOL of children. It has been applied to children with a wide range of skin diseases internationally [13-16].

It consists of ten questions, and is designed for use in children aged five to 16 years. It is categorised in six parameters: *symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment*.

3.2 Translation

We obtained permission from the copyright holders of CDLQI to translate this index into Chinese, and to be applied in this study. Two professional translators translated the English version of CDLQI (E_1) into Chinese independently (C_1 and C_2). They then compared C_1 and C_2 , made adjustments, and agreed on the third version (C_3). Two other translators then back-translated C_3 into English (E_2 and E_3). They disclosed their translation, made adjustments, and agreed on the fourth version (E_4). All translators then compared E_1 and E_4 , made final adjustments, and produced C_4 [17].

3.3 Establishing the Validity and Reliability

We requested 30 children with and 30 children without skin diseases to complete C_4 , and assessed the severities of the skin problems. Several children attended again seven days later for medical care. We requested them to complete C_4 again.

3.4 Recruitment

Our setting is a teaching clinic attached to a university teaching hospital. Over a two-year period (24 calendar months), we requested each child aged five to 16 years who was brought to consult us with the final diagnosis being GCS to

participate in our study. For each study subject, we requested the next child of the same sex and similar age (within one year) who was brought to consult us for atopic dermatitis (AD) as the first group of controls. We also requested the next child of the same sex and similar age (within one year) who consulted us for diseases unrelated to the skin as the second group of controls. Our diagnoses of GCS was made according to a set of validated diagnostic criteria [18,19]. We diagnosed AD according to the criteria of the United Kingdom Working Party [20-22].

4. RESULTS

4.1 Establishing Validity and Reliability

The 60 children completed C_4 with ease. All items were found to be unambiguous and relevant to our local context. The scores were positively correlated with physician-rated disease severities. The results for C_4 and E_1 were very similar for similar diseases. C_4 is therefore valid.

Nine children with skin problems and seven with no skin problem attended us again seven days later, and were requested to complete C_4 again. Test-retest correlation was strong ($\gamma_s = 0.958$; P less than 0.01). Cronbach's α was 0.83 for all the test parameters. C_4 is therefore reliable, and becomes Chinese CDLQI.

4.2 Patient-control Study

During the two-year period, we diagnosed a total of 23 children aged five to 16 years with GCS. All had parental agreement to participate. The response rate was thus 100%. All children with GCS completed the CDLQI satisfactorily. The completion rate was thus 100%.

Out of the 23 children, 15 were males and eight were females. They aged from five to 14 (mean: 7.8 years). The two control groups were sex-matched. The first group of controls with AD aged six to 16 years (mean: 8.2 years). The second group of controls consulting us for problems unrelated to the skin aged seven to 14 years (mean: 7.2 years).

The outcomes for CDLQI are depicted in Table 1. The total CDLQI scores of children with GCS were significantly higher than such of controls not consulting us for skin diseases (P less than 0.05). For the individual parameters, the scores of children with GCS were significantly higher than

such of controls for the parameters *symptoms and feelings*, *leisure*, *school or holidays*, and *treatment*. However, the total CDLQI score for children with GCS was 4.91, which was 16.4% out of the full score of 30 only.

The highest parameter affected was *symptoms and feeling* (39.8%). The second top parameter affected was *leisure* (16.9%). This parameters were covered by three questions, regarding *swimming or sports*, *going out and playing*, and *choice of clothes*. As the lesions in GCS are prominently affecting the face and the distal aspect of the limbs, it is expected that the children would not be allowed to attend these activities.

Two other parameters contended to be the third highest parameters – *school or holidays*, and *sleep*, at 8.7% for both. *School or holidays* covers either *schoolwork* or *enjoyment in holiday* over the previous week. *Sleep* was covered by one question directly asking for whether sleep was affected. Having such subacute and pruritic rash, the children were actually very adjustable with less than 10% of the top scores for these parameters.

Four (17%) children with GCS and none (0%) in the second control group had total CDLQI higher than 30%. The difference is insignificant (RR: inapplicable; $P = 0.11$).

The impacts of AD on children were significantly higher than such for GCS (P less than 0.001). 12 (52%) children with AD had total scores of CDLQI more than 30%. Such was significantly more than four (17%) children with GCS with total score over 30% (RR: 3.00, 95% CI: 1.13 – 7.94; P less than 0.05), and also significantly more than no (0%) child consulting us not for skin problems (RR: inapplicable; P less than 0.0001).

Table 2 shows the results of this study as compared to results of a previous study on ten children with PR [11]. Both groups demonstrated no significant difference in total scores and in scores for all the parameters. The scores for children with GCS were insignificantly higher than such for children with PR, particularly for the parameter of *symptoms and feelings*. This may be related to pruritus being commoner and more severe for children with GCS than those for children with PR, which was substantiated by clinical studies in these paraviral exanthems [7,23-25].

Table 1. Scores of the children dermatology life quality index for children with Gianotti-Crosti syndrome, and for two control groups (children brought to consult us with atopic dermatitis and children brought to consult us for conditions unrelated to the skin)

Groups	Number of children	Total CDLQI [#] scores*	CDLQI for symptoms and feelings [†]	CDLQI for leisure [†]	CDLQI for school or holidays [†]	CDLQI for personal relationships [†]	CDLQI for sleep [†]	CDLQI for treatment [†]
Children with final diagnoses being Gianotti-Crosti syndrome	23	4.91 (16.4%)	2.39 (39.8%)	1.52 (16.9%)	0.26 (8.7%)	0.26 (4.3%)	0.26 (8.7%)	0.22 (7.3%)
Children brought to consult us for atopic dermatitis	23	13.39 (44.6%) [‡]	4.34 (72.3%) [‡]	2.04 (22.7%)	2.30 (76.7%) [‡]	1.65 (27.5%) [‡]	1.57 (52.0%) [‡]	1.48 (49.3%) [‡]
Children brought to consult us for conditions unrelated to the skin	23	0.52 (1.7%) [§]	0.26 (4.3%) [§]	0.09 (1.0%) [§]	0.04 (1.3%) [§]	0.13 (2.2%)	0.00 (0.0%)	0.00 (0.0%) [§]

[#] Children Dermatology Life Quality Index
^{*} CDLQI Total CDLQI % score = Total CDLQI score / 30 X 100%.
[†] As different parameters were assessed by different number of questions, the following adjustments were made in calculating the % scores:
 % score for symptoms and feelings and personal relationships = Score / 6 X 100%.
 % score for leisure = Score / 9 X 100%.
 % score for school or holidays, sleep, and treatment = Score / 3 X 100%.
[‡] Significantly higher than scores for Gianotti-Crosti syndrome, with two-tailed P-value lower than 0.05
[§] Significantly lower than scores for Gianotti-Crosti syndrome, with two-tailed P-value lower than 0.05

Table 2. Comparison of the scores of children dermatology life quality index for children with gianotti-crosti syndrome and children with pityriasis rosea [11]

Groups	Number of children	Total CDLQI scores	CDLQI for symptoms and feelings	CDLQI for leisure	CDLQI for school or holidays	CDLQI for personal relationships	CDLQI for sleep	CDLQI for treatment
Children with final diagnoses being Gianotti-Crosti syndrome*	23	4.91 (16.4%)	2.39 (39.8%)	1.52 (16.9%)	0.26 (8.7%)	0.26 (4.3%)	0.26 (8.7%)	0.22 (7.3%)
Children with final diagnoses being pityriasis rosea*	10	3.50 (11.7%)	1.40 (23.3%)	1.00 (11.1%)	0.00 (0.0%)	0.10 (1.7%)	0.50 (16.7%)	0.50 (16.7%)

* No significant difference was found for the total scores and scores for individual parameters for children of both groups

5. DISCUSSION

Having reported on the impact of skin diseases including AD [11,26], PR [11,27], and juvenile plantar dermatosis [13] on QOL of children, we have been asked whether chronic skin diseases like AD and subacute diseases like GCS and PR could be compared with the same tool. All 10 questions in CDLQI endorse the terms *over the last week*. For PR and juvenile plantar dermatosis, all children reported by us had acute phases of the skin disease lasting for at least two weeks.

To our best knowledge, the shortest duration of the active phase in children with GCS reported was five days [28]. This duration is exceptional. Most children with GCS have at least two weeks of acute phases [29]. The CDLQI was designed to assess the impacts over one week, and we have confirmed with the copyright holders of CDLQI (Finlay A, personal communication) that this index is appropriate to be applied to children with subacute dermatoses like PR and GCS.

Our findings indicate that GCS exerts little impact to the QOL of most children. We thus believe that symptomatic relief might be adequate for most children with GCS, and that antiviral agents might not be necessary or indeed indicated for this self-remitting dermatosis.

Another issue is clinician-rated and patient-rated outcome measures in clinical studies. For adults with PR, we have recommended that patient-oriented outcomes should be incorporated as primary outcomes for clinical trials [30]. We hope that patient-assessed outcomes could be incorporated as outcome measures in clinical trials for GCS in the future.

Lastly, and most importantly, the author would like to emphasise that the impacts of disease entities on the QOL of patients is not the most significant agenda in deciding whether a drug (such an antiviral agent) is to be prescribed to a patient (such as a child with GCS). There are many more significant parameters to consider relating to the disease, the patient, and the drug.

For the disease, extensiveness of the rash, severity of the clinical manifestations, and the probability of short-term or long-term complications would be significant factors. For the patient, symptoms of the rash, stigmatisation of having a skin disease, the threshold to consult medical practitioners, the educational levels of

the patients or their parents, and the culture for take medication for self-remitting rash can be of more significance than QOL. For the drug, the efficacy, adverse reactions, and the cost are significant considerations.

We recommend investigators performing clinical trials to incorporate patient-assessed parameters as one of the outcome measures. However, the impacts of the disease on the QOL of patients is only one of the methods to measure patient-assessed outcomes. Other factors related to the disease, the patient, and the drug could be of higher significance than scores on a QOL questionnaire.

6. CONCLUSION

GCS casts relatively low impacts on the QOL of children. These impacts were much lower than impacts exerted by AD.

CONSENT

The author declares that informed written consents were given by parents or legal guardians of the children.

ETHICAL APPROVAL

The author declares that the protocol and methodology of this study was in parallel to such as approved by the Ethics Committee, Faculty of Medicine, The University of Hong Kong (EC-1498-00).

COMPETING INTERESTS

Author has declared that no competing interests exist.

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