Guidelines for the presentation of contact allergy case reports

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Summary

Case reports constitute a classic publication format that is being increasingly appreciated, for example because of its educational value. In the field of contact dermatitis research, case reports often serve as sentinel publications concerning new allergens, or new exposures to known allergens, or regarding other conditions leading to contact dermatitis. The CARE guideline published in 2013 addresses standardized and complete reporting of case reports in all fields of medicine. The present article takes up the CARE suggestions, and further specifies these in terms of application to case reports in the field of contact dermatitis. The objective of this structured guidance is to provide junior or inexperienced doctors and researchers with an annotated list, against which the fulfilment of essential or optional items of a complete, high-quality case report to be submitted to *Contact Dermatitis* or other journals can be checked.

Key words: case report as topic; contact allergy; dermatitis; guideline.

Case reports constitute an important format in the medical literature, for several reasons: (i) They have the role of a sentinel, often being the first hint of an upcoming problem, be it the human immunodeficiency virus infection epidemic, or an epidemic of contact allergy, for example to methylisothiazolinone (1). (ii) Furthermore, even if it turns out that no epidemic is actually following the first report of a new allergen or the like, the ever-growing collection of such evidence expands our medical and scientific knowledge, to the benefit of patient care and counselling, and supports risk assessment in the public health domain. (iii) The educational value of case reports should not be underestimated: the carefully presented history, symptoms and findings, diagnostic procedures, and, eventually, diagnosis, therapy and outcome of an unusual or 'difficult' patient constitute a valuable supplement to textbook knowledge on more common and well-known diseases. Indeed, specialized journals have even been set up to cater for the need to publish case reports.

On this background of (growing) appreciation of case reports, the Case Reports (CARE) guidelines (http://www.care-statement.org/; last accessed 8 August 2016) have recently been elaborated (2). They intend to provide guidance for a style and completeness of reporting that should offer the maximum benefit for the scientific community and are generic, in the sense that their scope is not restricted to certain medical specialties. However, as recently pointed out, editorial policies (or simple non-awareness of the CARE guidelines) have led to a situation whereby 'guidelines for authors' of major

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dermatological journals, including *Contact Dermatitis*, are in conflict with, and thus discourage the use of, the CARE guidelines (3).

The following guidance is intended to provide a detailed extension and specification of requirements suggested by the CARE consortium that are relevant for case reports in the field of contact allergy. Moreover, a past editorial on transparent and complete reporting of methodology in *Contact Dermatitis* (4) can be regarded as a motivation for the present educational publication. Some CARE suggestions are either not compatible with, or meaningful for, submission of Contact Points to *Contact Dermatitis*, but may be pertinent to other journals accepting case reports in this field. These aspects are specifically noted. Moreover, formal aspects are adjusted to *Contact Dermatitis*, but may need to be adapted to the style of a different journal.

Objective and Methods

This guideline is mainly intended for (junior) researchers and dermatologists (in training) planning to write a case report in the field of contact dermatitis. The annotated checklist presented may, however, already be of help during diagnostic work-up. Indeed, taking into account all the aspects from the checklist might even be of direct benefit to the patient who is being cared for, and whose history will later be reported. The guideline is supplemental to other pertinent guidelines, most notably the European Society of Contact Dermatitis (ESCD) patch test guideline (5). Hence, strictly technical aspects are covered only briefly here.

A group of experts (see author list) collaborated in compiling those aspects that are considered to be important for the reporting of cases of contact allergy. In that sense, the present guideline is based on expert consensus; no formal process has been employed. However, in the development (i) the target group mentioned above was involved in giving critical feedback regarding the usefulness and readability of the guideline, which was included in the revisions, and (ii) all members of the European Environmental and Contact Dermatitis Research Group beyond the actual authors have had an opportunity to discuss the present recommendations.

Title

According to the CARE guideline, the words 'case report' or 'case study' should appear in the title, together with information describing important aspects of the case. A PubMed query for 'case report' identified 229 191 hits (http://www.ncbi.nlm.nih.gov/pubmed/?term=''case+report''; 3 November 2015). Among these, 29 of the first 100 entries, all from 2015, taken as a sample, did not include the term 'case report' in the title, but, did include it in, for example, the abstract and/or keywords. In *Contact Dermatitis*, most, but not all, Contact Points are case reports. Nevertheless, it appears redundant to always mention this characteristic in the title. However, to aid in indexing, it is helpful to add 'case report' as an additional keyword, where appropriate, in particular because 'Case Reports' is a term of the National Library of Medicine 'Medical Subjects Headings', a controlled terminology (MeSH; http://www.ncbi.nlm.nih.gov/mesh/68002363; last accessed 8 August 2016) under 'Publication Type Category'/'Study Characteristics'.

Keywords

Three or more keywords should describe the contents. Chemical Abstract Service (CAS) numbers can serve as a largely unambiguous identifier for a substance, or a few substances, independently from issues of nomenclature and synonyms of chemicals. Concerning nomenclature, the International Nomenclature for Cosmetic Ingredients (INCI) (see CosIng database; http://ec.europa.eu/growth/tools-databases/cosing/; last accessed 8 August 2016) is the preferred nomenclature whenever ingredients of cosmetics are concerned, and International Nonproprietary Names (INNs) by the World Health Organization are preferred for drugs (http://www.who.int/medicines/services/inn/en/; last accessed 8 August 2016). As mentioned above, the list of keywords should include the term 'case report'.

Abstract

In view of the limited length of Contact Points, an abstract may be unnecessary. However, the existence of an abstract, as recommended by the CARE guidelines, has the evident advantage of offering much more extensive metadata to a publication, for example for bibliographic databases such as MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed, last accessed 8 August 2016). This increases the chance that a publication will actually be identified by literature searches pertinent to the topic.

Introduction

A few sentences should briefly introduce the problem presented in the case report. One reference, or just a few references, to relevant medical literature may be included, and these can later be expanded in the discussion of the case.

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Patient Information

Information on the patient should normally include the items listed below. Duplicate information should be avoided. The order should 'tell a story', following the flow of a medical examination, but possibly with information added in hindsight that had proven important for the understanding of the case.

Demographic information	Age and sex are mandatory. If relevant, ethnicity, occupation, including previous occupations and leisure activities should be reported
Patient's history and symptoms	The onset/duration of skin lesions with associated exposures (if known), primary anatomical site affected, spread (if any), morphology (if this can be described clearly or has perhaps been photographed by the patient), course, e.g. chronic or relapsing, related to work or other activities, current symptoms (itching; burning) and previous topical or systemic treatments and their effects on the skin disease
Medical or other relevant history	Only insofar as relevant, e.g. concerning atopic (skin or respiratory) diseases, medications and underlying conditions [in cases of cutaneous adverse drug reactions (CADRs)], past patch or prick tests and their results, and other information as relevant for the case. Written in retrospect, the case report can focus on those aspects that have been proven to be relevant. However, as discussed later, diagnostic errors, detours etc. can possibly contribute to an educational message, and should be briefly reported in this case

Clinical Findings

Findings made on clinical examination should be described, namely anatomical site(s) affected and morphology, with the use of standard dermatological terminology. The degree of detail should be sufficiently precise; for example, in cases of 'periorbital dermatitis' it should be mentioned whether the upper or lower lid, or both, are affected. If the patient presents without current skin lesions, this should be mentioned; in this case, the history, perhaps supplemented with a photograph taken by the patient, if of sufficient quality, is particularly important. Generally, a photograph of clinical lesions is often an excellent addition to the publication in all but the most 'classic' skin lesions.

When a photograph is taken, illumination and focus should be adequate; the colour balance can later be amended, if necessary. The frame should be such that the extents of lesions can clearly be seen, but not overly large. It is not, for instance, necessary to take a photograph of the entire arm to document contact dermatitis limited to the hands or fingers. Additional close-ups showing the morphology are sometimes instructive.

Timeline

The CARE guidelines suggest the inclusion of important dates and times of the case in a table or figure. This is not usually necessary for Contact Points submitted to *Contact Dermatitis*, as a verbal summary of the patient's history will suffice (see above). However, in selected cases, such as when presenting the sequence of multiple CADRs, with their dates, medications, and related skin lesions, a strictly chronological, tabular presentation may indeed help to add clarity and increase the readability of the case presentation.

Diagnostic Assessment

Diagnostic assessment is certainly one of the cornerstones of case reports in the field of contact dermatitis. Hence, it is normally not acceptable if a case report on presumptive allergic contact dermatitis is presented without the results of an adequate patch test, or a case of contact urticaria/protein contact dermatitis without sufficient allergological work-up. In contrast, clearly toxic/caustic reactions or reactions to, for example, physical agents do not require patch testing, whereas, in cases of irritant contact dermatitis, patch testing is certainly very often indicated to rule out additional contact allergy. Possibly, other diagnostic approaches are appropriate that cannot be addressed here. Instead, this section will focus on patch testing for delayed-type hypersensitivity and some important aspects of the diagnosis of immediate-type hypersensitivity. The ESCD guideline on patch testing should be consulted concerning further details (5).

Patch test allergens used	The manufacturer/provider of patch test allergens should be mentioned (6), even if adherence to good manufacturing and pharmaceutical-grade standards should provide a sufficiently reliable and uniform level of quality (7). It should be stated whether the baseline series has been tested (or why not), and which additional test series have been applied. Also include the vehicle(s) and concentration(s) used to test the allergens relevant for the case and the publication
Allergen names	For cosmetic ingredients, INCI nomenclature must be used, and for drugs, INNs; see above under 'Keywords'. Particularly in the case of substances that are not available as commercial allergens, the CAS no. should be given in the text or a table, as appropriate

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Patch test system used	If an investigator-loaded system is used, the chambers and adhesive should be mentioned. If the TRUE Test® is used, this should be mentioned, and also whether additional allergens have been used, for example, to supplement the TRUE Test® to achieve full coverage of the baseline series, for example the European baseline series (8) or baseline series from other areas of the world
Patch test with the patient's own material	If products brought in by the patient, such as cosmetics or work materials, are patch tested, the vehicle and concentration must be mentioned, if they are not tested 'as is', which should also be mentioned In case break-down tests are (subsequently) performed, name of product ingredient, concentration and vehicle need to be stated; see text below Moreover, extracts of products or materials handled by the patient may be useful to use for patch testing; their preparation for plants [e.g. (9)] or other materials (10) should be described at least briefly, and a pertinent reference should be cited
Modifications of the standard procedure	Any modification of the patch test procedure (pretreatment; early readings before termination of exposure) must be indicated
Timing and scoring of the patch test (readings)	Exposure time (usually 2 days) and reading times must be indicated. The ICDRG/ESCD reading scale must be used, and it needs to be indicated at which reading time the reaction was observed
Other (validation) tests	If a repeated open application test (ROAT) (11) or provocative use test (PUT) is performed, the method should be described briefly, and the result in terms of (i) the concentration (or preferably dose/area) leading to a positive reaction, and (ii) the number of days until the occurrence of a positive result
Control tests	For cases in which the patient reacted positively to a new allergen, see text below
Clinical relevance	The assessment of clinical relevance is outlined in the ESCD guideline (5). The link between contact allergy to a certain substance as diagnosed by the patch test or otherwise, and current or (also) previous allergic contact dermatitis, as appropriate, is indeed a core element of a convincing case report in this field

Product break-down testing

Patch testing with all single ingredients of a product that is suspected to have caused or aggravated allergic contact dermatitis is usually performed after a positive patch test result with the product itself. Details can be found in (5). Experience indicates that some manufacturers provide all ingredients as stock solutions, clearly labelled with the substance name, concentration, and vehicle, whereas other manufacturers just send coded ingredients. The latter is normally not acceptable, as the dermatologist needs to know the substances that are to be applied to the patient. In products falling under the Cosmetics Regulation, ingredient labelling should not be a problem, as this is required on the package anyway, whereas, in cases of industrial products, ingredients are often (i) not labelled, or (ii) not provided even upon request, or (iii) possibly not even known by the downstream supplier. Another problem is the fact that substances are sometimes supplied in the concentration as used in the product. However, this concentration may be, or, in the case of cosmetic ingredients usually is, too low for patch testing (but can be used for use tests such as the ROAT or PUT). When the results are reported, the methods need to be clearly described, to enable readers to appreciate the findings. The associated challenges faced, and how they have been solved, may be an important educational message of the case report.

Control tests

When chemically defined substances or (usually less well-defined) natural mixtures have been tested and yielded test reactions interpreted as positive (allergic), and insufficient or no evidence at all exists concerning adequate test concentrations and/or vehicles, it is advisable to perform control tests. These can be performed on healthy volunteers or other patients patch tested to rule out a false-positive patch test reaction – evidently after obtaining informed consent according to national and institutional standards. There is no minimum number of required control tests; certainly, 'the more, the better'; 10 or 20 are commonly used, and these numbers are quite acceptable. The statistical comparison between 1 patient who is putatively sensitized and has a positive reaction in the patch test versus 20 presumably non-sensitized/non-exposed controls who have negative results in the patch test will yield a significant result ($p < 0.05$, Fisher's exact test), and is thus preferred, if feasible. Negative results of such control tests corroborate the diagnosis of contact allergy for the patient, and thus support individual counselling, and they also increase the validity of findings reported to the scientific community.

If applicable, the following details should be addressed when a patient with contact urticaria (syndrome) possibly with additional respiratory symptoms (exclusive respiratory disease is out of the scope of *Contact Dermatitis*) or protein contact dermatitis is reported:

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Prick test allergens used	Report the manufacturer of extracts, and the preparation of native materials for prick-to-prick tests; vegetables, fruit, meat, fish and other foodstuffs are usually tested 'as is' [see reviews and guidelines, e.g. (12, 13)]
Allergen names	In cases of plant and animal materials, provide the Latin botanical and zoological names, if they are not from an everyday species
Scoring system used	Indicate the scoring with regard to reading times and scoring of erythema/wheal: diameters, areas, and classification against positive and negative control
Other immediate-type tests	Describe the method and scoring of tests other than prick tests, citing pertinent reference literature, if available
Laboratory methods	Beyond the determination of specific IgE with routine methods (which need to be described by referring to the brand and manufacturer of the enzyme-linked immunosorbent assay kit), a detailed description of laboratory methods is mandatory

Therapeutic Intervention and Secondary Prevention

Therapy given to the patient after the final diagnosis has been established can be briefly mentioned, if at all. The recommended measures for secondary prevention are of greater interest, if they include more than general advice on 'allergen avoidance', that is, specific measures. This may include considerations of adequate protective gloves [adequate in the sense of durable for the required work and impermeable – for a useful period – to the offending allergen(s)], the identification of substitute products, and the like. Measures that may be of interest beyond the individual case should be described in sufficient detail to be valuable for other clinicians and on a more general level.

Follow-up and Outcomes

Ideally, information on the further course of contact dermatitis, after diagnosis, therapy and counselling, should be briefly included. This information will enable readers to appreciate the effectiveness of the specific advice given. Such follow-up information may include the patient's and the doctor's global view, adherence to advice given, the tolerability or practicability of measures, and any adverse events resulting from the recommendations.

Discussion

The four aspects of the discussion of a case report proposed by the CARE guidelines (2) are fully supported and should be considered on a case-by-case basis:

'a) The strengths and limitations of the management of this case'	Authors will usually be motivated to submit their case report by the perceived strengths – i.e. novelty, relevance, and general benefit for potential readers – and thus will not find it difficult to point out the strengths of their case (report), usually in the covering letter. However, difficulties and shortcomings encountered, either resolved or unresolved, often have an important educational message. Hence, they should be discussed, as appropriate
'b) The relevant medical literature'	This is a self-evident aspect of discussion, which nevertheless is sometimes not appropriately addressed; see text below
'c) The rationale for conclusions (…)'	A core point of any discussion, as of any medical letter, albeit more refined than in a letter, is as follows: why has contact allergy (or any other condition) been diagnosed, why has a certain exposure been considered to be important, and why has a positive reaction been deemed to be clinically relevant, possibly supported by evidence provided by related publications?
'd) The main "take-away" lessons of this case'	A very important, final aspect of the discussion is: what is the conclusion from the case, and what can a clinician learn from the presented case? This should be outlined in one or a few sentences at the end of the discussion

Relevant medical literature

In the format of case reports, criteria for the relevance of medical literature are applied that are different from those in a systematic review, or original articles addressing a certain topic in more depth. In *Contact Dermatitis*, the number of references included in a case report is not formally restricted, but should normally not exceed 10. Preference should be given to references that are (1) pertinent, (2) recent, and (3) internationally available:

1. The aspect of pertinence is probably the most difficult one, and there are no firm rules. Usually, previous publications are pertinent if they address a similar, or the same, cause of disease as the present

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case, or special methods are applied in the present case and are described in the paper cited. Almost by definition, the patch test guidelines of the ESCD (5) are pertinent to case reports involving patch testing.

2. Authors should check for current articles relevant for the topic by appropriate searches in bibliographic databases (e.g. MEDLINE, Web of Science™, and Google Scholar).
3. International availability usually implies articles written in English; however, if justified by the other two aspects, other international languages such as French or Spanish, or even, exceptionally, other languages may be acceptable.

In some cases, non-medical scientific literature, for example from the natural or technical sciences, may add an important aspect to the discussion and should thus be cited. However, in view of the readership of *Contact Dermatitis*, the implications of such evidence for the given case should be explained sufficiently. In yet other cases, information is cited not from the scientific literature, but from resources on the Internet, which may be either freely available, or availble after subscription. Both are acceptable, but, given similar validity, free sources should be preferred. The date of last access must be indicated. Although short, possibly general, URLs can be inserted in the text, long URLs need to be put into a separate reference, as they hamper easy reading of the text. There may be different requirements for different journals.

Patient Perspective and Informed Consent

The CARE guideline states that 'the patient should share his or her perspective or experience whenever possible'. For the purpose of Contact Points, this perspective is best included in the aspect 'follow-up and outcomes'.

Informed consent is mandatory if photographs are reproduced that identify the patient (meaning mostly facial views). However, case reports provide a profile of the patient that may render the patients recognizable, in principle, by matching the published characteristics, such as age, sex, area of residence, or occupational or other activities with publicly available information, potentially leading to the identification of one or a few eligible persons. It is hard to imagine why professionals reading medical journals should have an interest in this. However, the wide electronic availability of both scientific journal contents and personal information from various sources, including from sources provided by the individuals themselves, makes misuse at least easier than it was in the historical times of paper issues in medical libraries and no Internet.

As a consequence, potentially identifying information should be selected with caution – usually including age, sex, and relevant (non-)occupational activity (see above), but usually excluding the place or region of residence or specific workplace. In case of doubt, it is recommended to obtain and archive the portrayed patient's written informed consent to the publication of the case report, even if no photograph of the patient is shown; this procedure should follow national and institutional standards.

Disclaimer

Adherence to these guidelines is a prerequisite for acceptability of submissions as Contact Points to *Contact Dermatitis*, but does not guarantee eventual acceptance, which is based on additional criteria of originality and educational or other interest. Concerning publications in other journals, it is not expected that adherence to the guidance presented here will conflict with their respective author guidelines, but this needs to be verified case-by-case.

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