Title Page

CARE 2013 Explanations and Elaborations: Reporting Guidelines for Case Reports

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Abstract
Well-written and transparent case reports (1) reveal early signals of potential benefits, harms, and information on the use of resources; (2) provide information for clinical research and feedback on clinical practice guidelines (CPGs), and (3) inform medical education. High-quality case reports are more likely when authors follow reporting guidelines.

During 2011-2012 a group of clinicians, researchers, and journal editors developed recommendations for the accurate reporting of information in case reports that resulted in the CARE (CAse REport) Statement and Checklist. They were presented at the 2013 International Congress on Peer Review and Biomedical Publication, have been endorsed by multiple medical journals, and translated into nine languages.

This explanation and elaboration document has the objective to increase the use and dissemination of the CARE Checklist in writing and publishing case reports. Each item from the CARE Checklist is explained and accompanied by published examples. The explanations and examples in this document are designed to support the writing of high-quality case reports by authors and their critical appraisal by editors, peer reviewers, and readers. This article and the 2013 CARE Statement and Checklist, available from the CARE website [www.care-statement.org] and the EQUATOR Network, [www.equator-network.org] are resources for improving the completeness and transparency of case reports.

Keywords
Case report, [delete "case study"], EQUATOR Network, health research reporting guidelines, CARE guidelines

Introduction
Case reports describe a patient's medical problems and clinical management for scientific or educational purposes. Historically, case reports have been important in (1) recognizing new or rare diseases, (2) evaluating the beneficial and harmful effects of an intervention, and (3) medical education. [Vandenbroucke 2001, Aronson 2003] They comprise a significant proportion of the articles in many indexed medical journals—case report volume, indexed on EMBASE and MEDLINE, increased by 45% from 49,918 in 2000 to 72,388 in 2010. [Sun 2013] New medical journals focusing on case reports have emerged in the past 10 years, some from publishers who have been labelled "predatory publishers". [Akers 2016] Most are open access, others are "supplements" or "companions" to established medical journals, such as *Neurology Clinical Practice*, a companion journal to *Neurology* from the American Academy of Neurology. The table below is a partial list of peer-reviewed journals that explicitly accept case reports.

JOURNAL TITLE*	INDEXED	PUBLISHER
1. ACG Case Reports journal	PMC	American College of Gastroenterology
2. Acta Radiologica Open	PMC	SAGE
3. Advances in Integrative Medicine [1]	Scopus	Elsevier
4. AHRQ WebM&M	psnet.ahrq.gov/webmm	AHRQ
5. Alternative Therapies in Health and Medicine [1]	IF, MEDLINE, Scopus	Innovision Health Media
6. American Journal of Case Reports	MEDLINE, PMC, Scopus	International Scientific Information
7. American Journal of Ophthalmology Case Reports	Scopus	Elsevier
8. American Journal of Perinatology (AJP) Reports	PMC	Thieme
9. Anais Brasileiros de Dermatologia [1]	PMC	Sociedade Brasileira de Dermatologia
10. APSP Journal of Case Reports	PMC	EL-MED Publishers Pakistan
11. BMJ Case Reports [1]	MEDLINE, Scopus	BMJ Publishing Group
12. Case Reports in Anesthesiology	PMC	Hindawi
13. Case Reports in Cardiology	PMC	Hindawi
14. Case Reports in Critical Care	PMC	Hindawi
15. Case Reports in Dermatological Medicine	PMC	Hindawi
16. Case Reports in Dermatology	PMC	Karger
17. Case Reports in Emergency Medicine	PMC	Hindawi
18. Case Reports in Endocrinology	PMC	Hindawi
19. Case Reports in Gastroenterology	PMC	Karger
20. Case Reports in Gastrointestinal Medicine	PMC	Hindawi
21. Case Reports in Genetics	PMC	Hindawi
22. Case Reports in Hematology	PMC	Hindawi
23. Case Reports in Hepatology	PMC	Hindawi
24. Case Reports in Immunology	PMC	Hindawi
25. Case Reports in Infectious Diseases	PMC	Hindawi
26. Case Reports in Medicine	PMC	Hindawi
27. Case Reports in Nephrology	PMC	Hindawi
28. Case Reports in Nephrology and Dialysis	PMC	Karger
29. Case Reports in Neurological Medicine	PMC	Hindawi
30. Case Reports in Neurology	PMC	Karger
31. Case Reports in Obstetrics and Gynecology	PMC	Hindawi
32. Case Reports in Oncological Medicine	PMC	Hindawi
33. Case Reports in Oncology	PMC	Karger
34. Case Reports in Ophthalmological Medicine	PMC	Hindawi
35. Case Reports in Ophthalmology	PMC	Karger
36. Case Reports in Orthopedics	PMC	Hindawi
37. Case Reports in Otolaryngology	PMC	Hindawi
38. Case Reports in Pathology	PMC	Hindawi
39. Case Reports in Pediatrics	PMC	Hindawi
40. Case Reports in Psychiatry	PMC	Hindawi
41. Case Reports in Pulmonology	PMC	Hindawi
42. Case Reports in Radiology	PMC	Hindawi
43. Case Reports in Rheumatology	PMC	Hindawi
44. Case Reports in Surgery	PMC	Hindawi
45. Case Reports in Transplantation	PMC	Hindawi
46. Case Reports in Urology	PMC	Hindawi
47. Case Reports in Vascular Medicine	PMC	Hindawi
48. Case Reports in Women's Health	Scopus	Elsevier
49. CEN (Clinical and Experimental Nephrology) Case Reports	PMC	Springer
50. Cephalgia [1]	IF, Scopus	SAGE
51. Clinical Case Reports	PMC	Wiley
52. Clinical Cases in Mineral and Bone Metabolism	PMC	CIC Edizioni Internazionali
53. Columbian Journal of Anesthesiology [1]	Hinari	Elsevier
54. Case Reports in Plastic surgery and Hand surgery	PMC	Taylor and Francis
55. Deutsche Ärzteblatt [1]	MEDLINE, Scopus	German Medical Association

56. Endocrinology, Diabetes and Metabolism Case Reports	PMC	Bioscientifica Ltd.
57. Epilepsy and Behavior Case Reports	PMC, Scopus	Elsevier
58. European Journal of Case Reports in Internal Medicine	MEDLINE, Scopus	SMC media Sri
59. European Journal of Pediatric Surgery Reports	PMC	Thieme
60. Explore—The Journal of Science and Healing [1]	IF, MEDLINE, Scopus	Elsevier
61. Global Advances in Health and Medicine [1]	PMC, Hinari	SAGE
62. Gynecologic Oncology Case Reports	PMC, Scopus	Elsevier
63. Headache [1]	IF, MEDLINE, Scopus	Wiley
64. HeartRhythm Case Reports	Scopus	Elsevier
65. Human Pathology: Case Reports	Scopus	Elsevier
66. Integrative Medicine: A Clinician's Journal [1]	PMC	Innovision Health Media
67. International Journal of Surgery Case Reports	PMC, Scopus	Elsevier
68. International Medical Case Reports Journal	PMC	Dove Medical Press
69. JAAD Case Reports (Dermatology)	Scopus	Elsevier
70. Journal of Clinical Epidemiology [1]	IF, MEDLINE, Scopus	Elsevier
71. Journal of Dermatological Case Reports	PMC	Poland - Spejaliści Dermatolodzy
72. Journal of Dietary Supplements [1]	MEDLINE, Scopus	Taylor and Francis
73. Journal of Endourology Case Reports	PMC	Mary Ann Liebert
74. Journal of Investigative Med. High Impact Case Reports	PMC	SAGE
75. Journal of Medical Case Reports [1]	MEDLINE, PMC, Scopus	Biomed Central
76. Journal of Neurological Surgery Reports	PMC	Thieme
77. Journal of Orthopedic Case Reports	PMC	Indian Orthopedic Research Group
78. Journal of Pediatric Surgery Case Reports	Scopus	Elsevier
79. Journal of Radiology Case Reports	PMC	EduRad Publishing
80. Journal of Surgical Case Reports	PMC	Oxford
81. Medical Mycology Case Reports	PMC, Scopus	Elsevier
82. Neurocase	IF, MEDLINE, Scopus	Taylor and Francis
83. Neurology: Clinical Practice	PMC, Scopus	American Academy of Neurology
84. Oxford Medical Case Reports	PMC	Oxford
85. Radiology Case Reports	Scopus	Elsevier
86. Rare Tumors	PMC	Page Press
87. Respiratory Medicine Case Reports	PMC, Scopus	Elsevier
88. Retinal Cases and Brief Reports	MEDLINE, Scopus	Wolters Kluwer Health
89. SAGE Open Medical Case Reports	PMC	SAGE
90. The Permanente Journal [1, **]	MEDLINE, PMC, Scopus	The Permanente Press
91. Thoracic and Cardiovascular Surgeon Reports	PMC	Thieme

* — Other medical journals may publish case reports within articles; 1 — Endorsed Care Guidelines; ** — open access, no article processing charge (APC)

Abbreviations: AHRQ – Agency for Healthcare Research and Quality; CRs - Case Reports; IF – Impact Factor (Journal Citation Reports); Med. – Medicine; PMC – PubMed Central

Table 1 — Partial List of Medical Journals that Accept Case Reports

Seminal examples published in the past 60 years illustrate how cases reported in the peer-reviewed medical literature have broadened our knowledge of emerging or existing conditions and their management. In 1961, *The Lancet* published a letter to the editor describing an increased incidence of congenital abnormalities in babies delivered of women who were given thalidomide during pregnancy as an anti-emetic or sedative. [McBride 1961] The *Morbidity and Mortality Weekly Report* (*MMWR*) published five case reports of *Pneumocystis carinii* pneumonia (PCP) in 1981 that turned out to be early signals of AIDS. [CDC 1981] The *Journal of Medical Case Reports* in 2013 reported that women who suffer a stroke may have May-Thurner syndrome (MTS), a condition affecting nearly 1 in 2,000 women. [Rison 2013] And in 2016, the *New England*

Journal of Medicine published a report on Zika virus infection that included a case report of a patient with prolonged maternal viremia and fetal brain abnormalities—serologic evidence of infection. [Driggers 2016]

Improving the Quality of Case Reports

The usefulness of case reports has been limited by inconsistent and incomplete reporting. When written without reporting guidelines they are often insufficiently rigorous [Kaszkin-Bettag 2012] and fail to provide information related to clinical management that would increase transparency and the likelihood of replication. [Richason 2009]

In 2011, a group of clinicians, researchers, and journal editors developed reporting guidelines for case reports following guideline development recommendations. [Moher 2010] This process consisted of (1) a literature review, interviews, using a modified Delphi process to generate items for a case report checklist, (2) a consensus meeting to draft reporting guidelines for case reports, and (3) a post-meeting evaluation, finalization, and publication of the reporting guidelines for case reports. [Gagnier 2013] The 2013 CARE Statement and Checklist were presented at the 2013 International Congress on Peer Review and Biomedical Publication, published in and endorsed by multiple medical journals, and translated into nine languages. The objective of this document is to support the publication of accurate, complete, and transparent case reports.

Using this Document

Each CARE Checklist item and subsection are explained and accompanied by one or more [delete "illustrative"] examples to guide authors writing case reports, and editors, peer reviewers, and readers critically appraising case reports. [delete "familiarity with"] Reporting guidelines form part of the foundation of editorial competency and their use in the critical appraisal of manuscripts by medical journal editors and peer reviewers is important. [Galipeau 2016]

This document and the CARE statement (available at www.care-statement.org) are resources to improve the quality of case reports. With the CARE Checklist as a framework, the writing of case reports continues to be an art, allowing author choices in focusing the case, sharing objective information and a patient's story in a way that appeals to readers and provides information for scientific and educational purposes.

The CARE Checklist

The 2013 CARE Checklist (see Figure 1) provides a framework for writing case reports that can be adapted to include specialty-specific information as outlined in the TIDieR guidelines [Hoffmann 2014].

The Narrative: A case report tells a story in a narrative format that includes the presenting concerns, clinical findings, diagnoses, interventions, outcomes (including adverse events), and follow-up. The narrative should include a discussion of the rationale for any conclusions and any takeaway messages.		
Section	**Item**	**Item Description**
Title	1	The words "case report" (or "case study") should be in the title along with phenomenon of greatest interest (eg, symptom, diagnosis, test, intervention)
Keywords	2	The key elements of this case in 2 – 5 words.
Abstract	3	a) Introduction – What does this case add? b) Case Presentation: – The main symptoms of the patient – The main clinical findings – The main diagnoses and interventions – The main outcomes c) Conclusion - What were the main "take-away" lessons from this case?
Introduction	4	Brief background summary of the case referencing the relevant medical literature.
Patient Information	5	a) Demographic information of the patient (age, gender, ethnicity, occupation) b) Main symptoms of the patient (his or her chief complaints) c) Medical, family, and psychosocial history —including diet, lifestyle and genetic information whenever possible, and details about relevant co-morbidities and past interventions and their outcomes
Clinical Findings	6	Describe the relevant physical examination (PE) findings
Timeline	7	Depict important dates and times in the case (table or figure)
Diagnostic Assessment	8	a) Diagnostic methods (eg, PE, laboratory testing, imaging, questionnaires) b) Diagnostic challenges (eg, financial, language/cultural) c) Diagnostic reasoning including other diagnoses considered d) Prognostic characteristics (eg, staging) where applicable
Therapeutic Interventions	9	a) Types of intervention (eg, pharmacologic, surgical, preventive, self-care) b) Administration (eg, dosage, strength, duration) c) Changes in intervention (with rationale)
Follow-up and Outcomes	10	a) Clinician and patient-assessed outcomes b) Important follow-up test results (positive or negative) c) Intervention adherence and tolerability (and how this was assessed) d) Adverse and unanticipated events
Discussion	11	a) Strengths and limitations of the management of this case b) Relevant medical literature c) Rationale for conclusions (including assessments of cause and effect) d) Main "take-away" lessons of this case report
Patient Perspective	12	The patient should share their perspective or experience whenever possible.
Informed Consent	13	Did the patient give informed consent? Please provide if requested.

Figure 1 – The 2013 CARE checklist

The CARE Checklist – Explanation and Elaboration

In this section, each of the CARE Checklist items and sub-items are explained, accompanied by examples from peer reviewed, general and specialty medical journals.

Item 1. Title Section

CARE Checklist description: The words "case report" (or "case study") should appear in the title along with phenomenon of greatest interest (eg symptoms, diagnoses, tests, interventions)

Explanation

The title should be succinct and help readers clearly identify the focus of the case report (eg, medical condition, intervention, outcome, population). It is useful if the article is identified as a case report. [Jenicek - 2001] This facilitates indexing in databases and may improve search results. "Case reports" are in MeSH (Medical Subject Headings - available at www.pubmed.com), a National Library of Medicine controlled vocabulary thesaurus used for indexing articles included in MEDLINE®.

Example

"Successful Heart Transplantation After 13 Hours of Donor Heart Ischemia with the Use of HTK Solution: A Case Report" [Wei 2005]

Item 2. Keywords Section

CARE Checklist description: The key elements of this case in 2 – 5 words.

Explanation

Medical journals sometimes require authors to choose key words for case reports. Key words that identify the focus of the case report can be selected using MeSH terminology (available at www.pubmed.com) or Google Scholar. Include the word "case report" as one of the key words to identify the type of publication and aid database searches.

Example

- Impending aortic aneurysm rupture - a case report and review of the warning signs. [Gish 2006]

Key words: "abdominal aortic aneurysm; aorta; case report; hyperattenuating crescent; imaging; mural thrombus; review; rupture"

Item 3. Abstract Section

CARE Checklist description:

3a Introduction—What does this case add?

3b Case Presentation:

- ***The main symptoms of the patient(s).***
- ***The main clinical findings.***
- ***The main diagnoses and interventions.***
- ***The main outcomes.***

3c Conclusion—What are the main "take-away" lessons from this case?

Explanation

The abstract is often the first section a reader encounters, providing a summary to help them determine their interest in the case report. [Cooper 2015, Jha 2014] Abstracts provide a balanced and succinct summary of the full report and customarily range from 100 to 250 words, depending on the journal [Cohen 2006]. The abstract also aids indexing and identification of case reports in electronic databases. [Hopewell 2008].

The case report abstract first briefly summarizes the background information in a sentence or two to orient the reader to the relationship between existing knowledge and the case. Second, the case report identifies the focus of the case report and summarizes this episode of care. Finally, the abstract concludes with one to two

sentences that highlight the "take-away" lesson from the case report, with an emphasis on a single priority message. [Davidson 2012, Vandenbroucke 1999]

When written last, the abstract can often more accurately reflect the completed case report. Medical journals vary in their requirements for an unstructured versus a structured abstract. A structured abstract for a case report typically includes three sections: the introduction, case presentation, and conclusion. [Cooper 2015, Cohen 2006]

Two Examples

Unstructured

- Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome (AIDS). [Barré-Sinoussi 1983]

"A retrovirus belonging to the family of recently discovered human T-cell leukemia viruses (HTLV), but clearly distinct from each previous isolate, has been isolated from a Caucasian patient with signs and symptoms that often precede the acquired immune deficiency syndrome (AIDS). This virus is a typical type-C RNA tumor virus, buds from the cell membrane, prefers magnesium for reverse transcriptase activity, and has an internal antigen (p25) similar to HTLV p24. Antibodies from serum of this patient react with proteins from viruses of the HTLV-I subgroup, but type-specific antisera to HTLV-I do not precipitate proteins of the new isolate. The virus from this patient has been transmitted into cord blood lymphocytes, and the virus produced by these cells is similar to the original isolate. From these studies, it is concluded that this virus as well as the previous HTLV isolates belong to a general family of T-lymphotropic retroviruses that are horizontally transmitted in humans and may be involved in several pathological syndromes, including AIDS."

Structured

- Association between isotretinoin use and central retinal vein occlusion in an adolescent with minor predisposition for thrombotic incidents: a case report. [Labiris 2009]

"Introduction: We report an adolescent boy with minimal pre-existing risk for thromboses who suffered central retinal vein occlusion associated with isotretinoin use for acne. To the best of our knowledge, this is the first well documented case of this association.

Case presentation: An otherwise healthy 17-year-old white man who was treated with systemic isotretinoin for recalcitrant acne was referred with central retinal vein occlusion in one eye. Although a detailed investigation was negative, DNA testing revealed that the patient was a heterozygous carrier of the G20210A mutation of the prothrombin gene. Despite the fact that this particular mutation is thought to represent only a minor risk factor for thromboses, it is probable that isotretinoin treatment greatly increased the risk of a vaso-occlusive incident in this patient.

Conclusion: Isotretinoin use may be associated with sight- and life-threatening thrombotic adverse effects even in young patients with otherwise minimal thrombophilic risk. Physicians should be aware of such potential dangers."

Item 4. Introduction Section

CARE Checklist description: Brief background summary of the case referencing the relevant medical literature.

Explanation

The introduction provides context for the case report related to the patient's episode of care and may elaborate a demonstration of need. The most important studies may be cited to introduce readers to the topic; however, a detailed discussion of relevant studies—such as a comprehensive literature review accompanying the case report is best left to the discussion section. [Green 2006, Jha 2014, Rison 2013] We recommend that case reports following the CARE Guidelines should include the following statement: "This case report was prepared

following the CARE Guidelines" and include a citation of the CARE Statement publication. Referencing the guidelines informs the reader of the standards for reporting and facilitates the evaluation of the adherence to the guidelines. [Turner 2012] The introduction generally ends with a 1-3 sentence synopsis of the case that identifies a question and/or gap in knowledge, the importance of this patient case, and a single priority message. [Cohen - 2006]

Examples

- Extensive deep vein thrombosis following prolonged gaming ('gamer's thrombosis'): a case report. [Chang 2013]

"A period of prolonged seated immobility is recognized as one of the major risk factors for developing venous thrombosis. Long-distance air travel and prolonged sitting in relation to work or recreation have been shown to increase the risk of venous thrombosis [1,2]. A recent survey has found that the average time spent playing video games is increasing and that gamers in the United States spend an average of 13 hours each week playing computer games [3]. Prolonged immobility associated with gaming may therefore be an important risk factor for venous thromboembolism (VTE). We report a case of a 31-year-old man who developed extensive deep vein thrombosis (DVT) associated with prolonged playing of PlayStation® games."

- Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men; evidence of a new acquired cellular immunodeficiency. [Gottlieb 1981]

"Acquired T-cell defects are well known to occur in adults with untreated Hodgkin's disease, sarcoidosis, and viral infections.[1,2] These noniatrogenic T-cell deficiencies are marked by cutaneous anergy and diminished proliferative responses to mitogens and antigens in vitro. Opportunistic infections rarely occur in the absence of immunosuppressive therapy. We recently treated several young, previously healthy, homosexual men for multiple episodes of *Pneumocystis carinii* pneumonia, extensive mucosal candidiasis, and severe viral infections.[3] The clinical manifestations and studies of cellular immune function in these patients indicated a similar severe acquired T-cell defect. Several lines of evidence suggested that cytomegalovirus infection was a major factor in the pathogenesis of the immunocompromised state. This syndrome represents a potentially transmissible immune deficiency."

Item 5. Patient Information Section

CARE Checklist description:

5a – Demographic information of the patient (age, gender, ethnicity, occupation)

5b – Main symptoms of the patient (chief complaint)

5c – Medical, family, and psychosocial history - including lifestyle and genetic information whenever possible, details about relevant co-morbidities, and past interventions and their outcomes

Explanation

We suggest including relevant demographic information about the patient while maintaining anonymity. Characteristics to identify the patient should ideally include age, sex and gender, race, and ethnicity—these characteristics may become important if many cases are subsequently reported. See the table below, from the US Department of Health and Human Services, of some personal identifiers that should not be used in a case report because they might reveal the patient's identity.

Patient identifiers to be excluded in the United States
http://www.hhs.gov/sites/default/files/hipaa-simplification-201303.pdf
• Names • Geographic regions • Elements of dates including birth date, date of death, and admission/discharge date • Listing ages over 89 require additional consent unless providing a single category of age > 90 • Telephone numbers, fax numbers, and e-mail addresses • Personal identifying numbers (eg, social security numbers, medical record numbers) • Web Universal Resource Locators (URLs) and Internet Protocol (IP) addresses • Biometric identifiers, photos and images (without specific additional permission [Lang 2014]), • Other unique, identifying characteristics or codes

Table 2 – US Patient Identifiers

When appropriate, include the patient's own words about their chief complaint or symptoms that led to their initial visit. Specify how long symptoms have been present and if relevant, the frequency, intensity, location, and aggravating or alleviating factors. Distinguish comorbidities, when they began, whether they are recurring, past and current interventions and their outcomes. When discussing a history of allergies, include allergens, dates of reactions, and the type of allergic manifestation. [Cohen 2006]

Other historical factors may be relevant, such as:

- Perinatal history, such as type of birth, length of pregnancy, if breast-fed and for how long
- Psychosocial history (eg, occupation, social support, education level)
- Type of health insurance
- Environmental exposures (living and working environment, potential toxic exposures)
- Lifestyle (sleep, stress management, exercise, recreational drug use, smoking, alcohol consumption, and nutrition/diet)
- Family medical history (eg, if family members have similar conditions as the patient)
- Genetic information (relevant to the case)

Examples

5a, 5b, and 5c – Patient Information

- Familial thrombophilia due to a previously unrecognized mechanism characterized by poor anticoagulant response to activated protein C: Prediction of a cofactor to activated protein C. [Dählback 1993]

"Case Report. The proband is a male born in 1942. At the age of 19 years, he had his first episode of deep venous thrombosis in one leg. After this, he was healthy and free of thrombosis for almost 20 years. Between 1980 and 1987 he had multiple episodes of deep venous thrombosis, at least once a year. The thrombotic events were treated with vitamin K antagonists for periods of up to 3 months. The presence of a thrombus was verified with phlebography on at least two occasions. The proband has developed a postthrombotic syndrome in his legs but has no other disorders. Several members of the proband's family have similar histories of multiple episodes of deep venous thrombosis (Fig. 1). His older brother by 10 years (III-2) has had deep venous thrombosis (in the legs) on several occasions, most of them occurring between the ages of 45 and 50. Also his uncle (11-7) and aunt (II-5) have both had multiple episodes of thrombosis.

A younger relative (IV-2) had clinically suspected deep venous thrombosis during her third pregnancy, but phlebography failed technically. The proband's father, who had no history of thrombosis, is deceased. Nineteen of the family members (all living members of generations II-IV) were available for testing. Two additional,

unrelated cases with thrombophilia and inherited poor response to APC were identified; their medical histories are briefly described in the legend to Fig. 6.

- Quinacrine-induced Cholestatic Hepatitis in Undifferentiated Connective Tissue Disease. [Namas 2015]

"A 45-year-old African American woman presented to the rheumatology clinic with a history of undifferentiated connective tissue disease (UCTD), manifesting as biopsy-proven urticarial dermatitis, inflammatory arthritis, fatigue, and weight loss in the setting of positive immunofluorescence antinuclear antibodies (1:160, speckled pattern), anti-RNP, anti-Sm/RNP, and antichromatin antibodies."

Item 6. Clinical Findings Section

CARE Checklist description: Describe the relevant physical examination (PE) findings.

Explanation

Report relevant data from the physical examination (PE) and other significant clinical findings identified at the onset of care in the clinical findings section, along with an explanation of the examination methods, if necessary. These can be listed in the text and may include de-identified photos. In some subspecialties, the notation used to describe the physical examination (eg, ophthalmology) is unique, and the description of the examination may require additional explanation. If the physical findings are extensive they may be organized as a summary table or figure. Record relevant findings that occurred during the course of care, with dates, in the "Follow-Up and Outcomes" section.

Example

- Mycobacterium tuberculosis monoarthritis in a child. [Rajakumar 2008]

"At age 2 years 10 months this previously healthy North American Indian girl presented with a 3-week history of left knee swelling and morning stiffness without associated symptoms. There were no infectious contacts reported at first presentation. On initial physical examination, the left knee was moderately swollen and warm with signs of both intra-articular fluid and synovial hypertrophy. Flexion and extension were limited by 10 degrees. The child was afebrile and appeared otherwise healthy. There were no abnormal pulmonary signs and no peripheral lymphadenopathy. The remainder of the examination was normal."

Item 7. Timeline Section

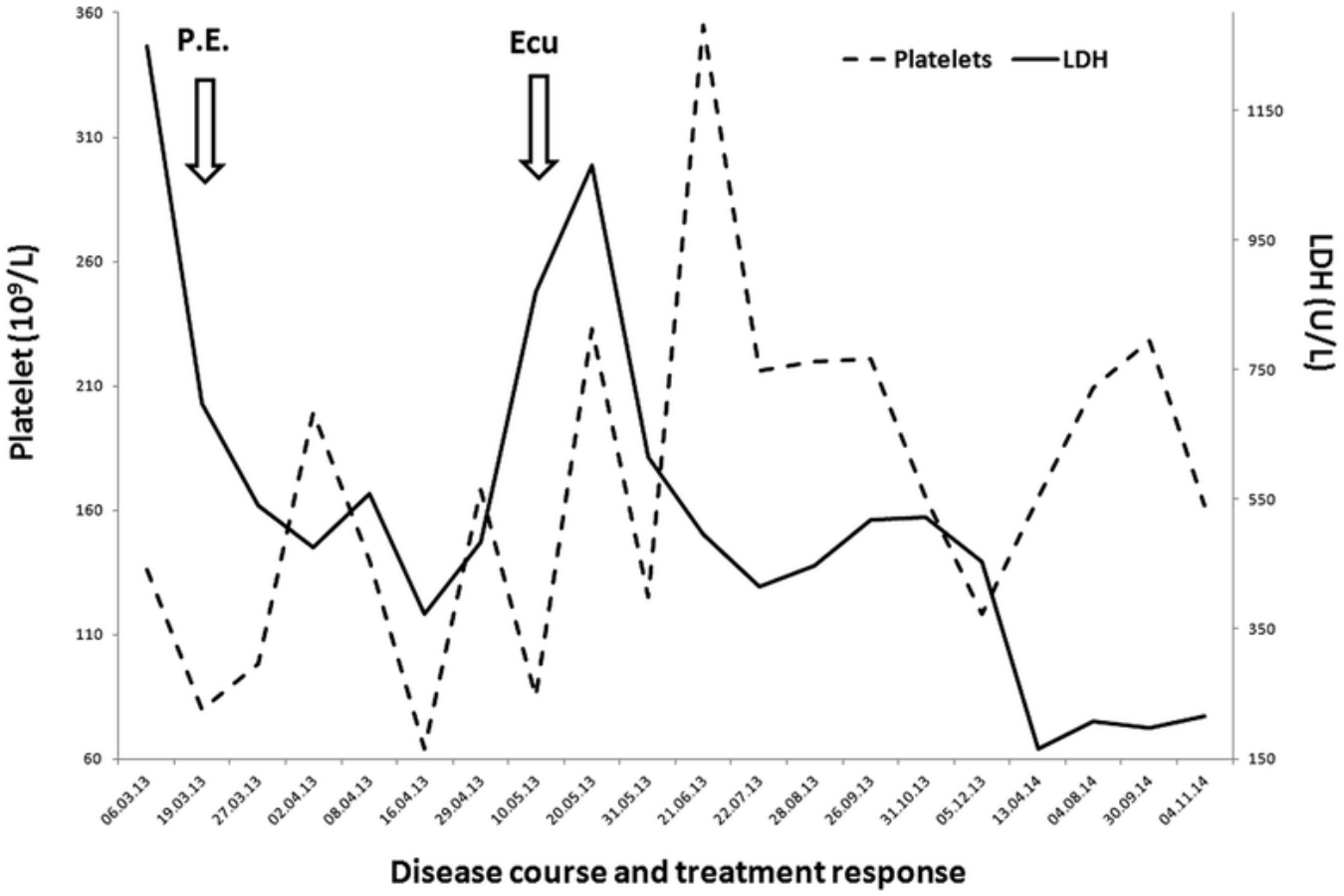
CARE Checklist description: Depict important date and times in this case (table or figure)

Explanation

A timeline presents relevant events in the patient's history in chronological order in a figure or table and offers a succinct summary of one or more key events in the case, enabling the reader to readily view core elements of the case report. These core elements might include: a brief patient and family medical history; chief complaints; factors related to susceptibility; diagnostic evaluations; therapeutic interventions; care received from other clinicians; follow-up and outcomes. In some cases, pictures may be incorporated into the timeline.

Examples

- Plasma resistant atypical hemolytic uremic syndrome associated with a CFH mutation treated with eculizumab: a case report. [Sevinc 2015]


P.E.
Ecu
Platelets
LDH
Platelet (10⁹/L)
LDH (U/L)
360
310
260
210
160
110
60
1150
950
750
550
350
150
06.03.13
19.03.13
27.03.13
02.04.13
08.04.13
16.04.13
29.04.13
10.05.13
20.05.13
31.05.13
21.06.13
22.07.13
28.08.13
26.09.13
31.10.13
05.12.13
13.04.14
04.08.14
30.09.14
04.11.14
Disease course and treatment response

Timeline 1

- Patient-centered Diabetes Care in Children: An Integrated, Individualized, Systems-oriented, and Multidisciplinary Approach. [Kienle 2013]

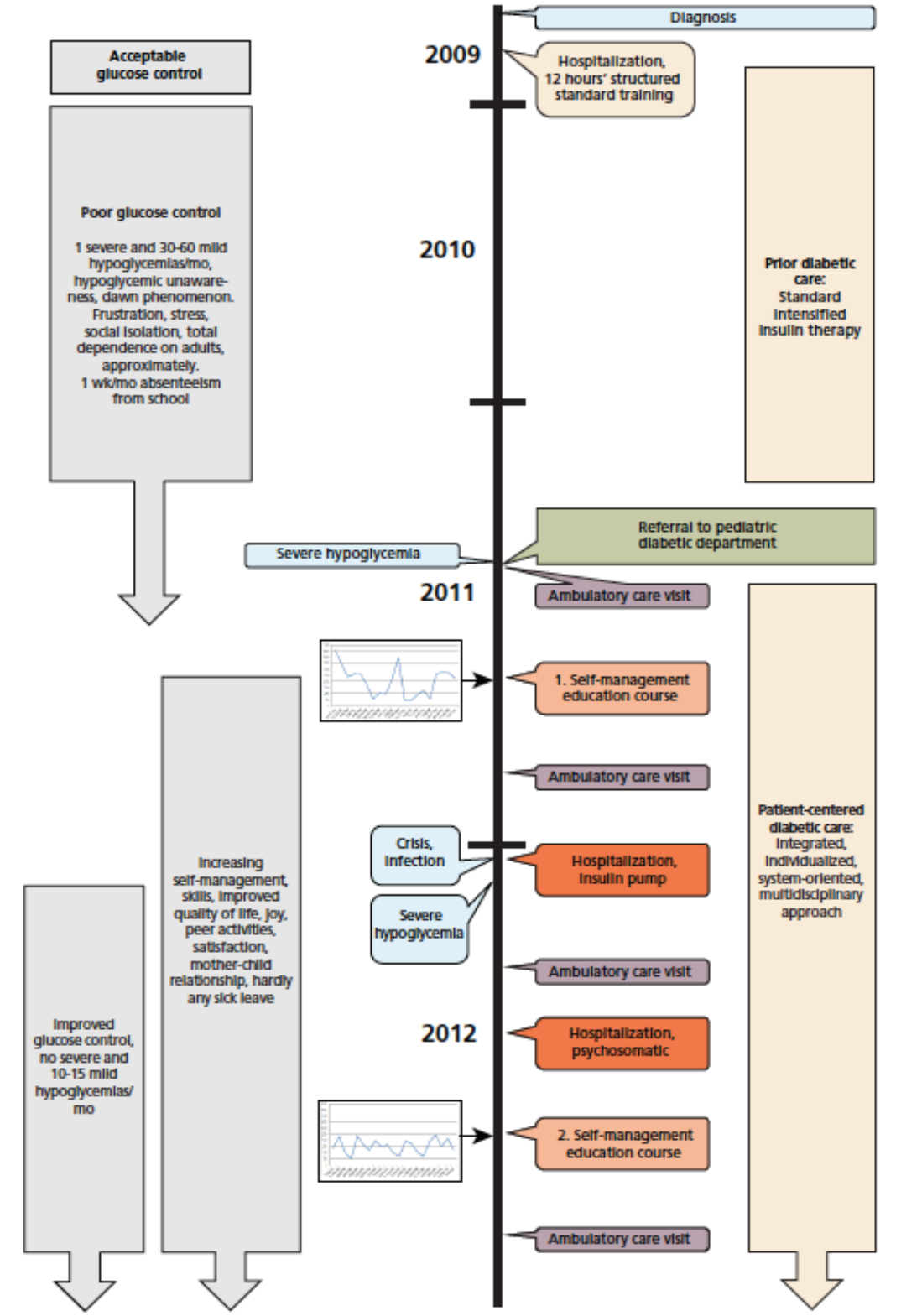


Figure 1 Timeline of interventions and outcomes.

Timeline 2

Item 8. Diagnostic Assessment and Diagnosis Section

CARE Checklist description:

8a – Diagnostic methods (eg, physical examination, laboratory testing, imaging, questionnaires)

8b – Diagnostic challenges (eg, financial, language, or cultural)

8c – Diagnostic reasoning including other diagnoses considered

8d – Prognostic characteristics (eg, staging) where applicable

Explanation

Most case reports describe patients whose presentation is either a rare manifestation of an established disease or the first clue to a previously unknown disease. In either case, an accurate diagnosis is *the* essential element of a case report, and the author must provide a complete description of the diagnostic process. Whether a patient whose presentation is a rare manifestation of an established disease or the first clue to a previously unknown disease, the diagnostic assessments are essential. We recommend reporting relevant de-identified results of diagnostic evaluations with the dates they were performed. These could include laboratory results, radiographic and cardiographic images, and patient reported outcome measurement surveys. [Cella 2015] Include a brief explanation of the relevant results with reference ranges if necessary. [Cohen 2006]. When trying to establish a cause and effect relationship between an exposure and a clinical event, document time course and dose of exposure to the onset of the clinical syndrome [Hill 1965] Important follow-up diagnostic assessments should be reported in the "Follow-up and Outcomes" section.

A case report should, if possible, cite literature references that support or challenge the main diagnostic hypotheses. Other diagnostic challenges such as obstacles to completing the evaluation may be important to mention. Likewise, discuss the evidence for the prognosis which may be affected by factors such as histological and genetic abnormalities, concomitant diagnoses, and therapeutic interventions used. These can be further elaborated in the discussion section.

Examples

8a – Diagnostic methods (eg, PE, laboratory testing, imaging, questionnaires)

- Branch facial nerve trauma after superficial temporal artery biopsy: a case report. [Rison 2011]

"Investigations were significant for a magnetic resonance imaging study with and without contrast that revealed cerebral ischemic gliosis compatible with the patient's age without acute intracranial pathology. There were no abnormalities noted along the course of either cranial seventh nerve. Her left STAB incision did not show evidence of thrombus, inflammation or giant cells and hence was without evidence of temporal arteritis."

8b – Diagnostic challenges (eg, financial, language, or cultural)

- Chiari malformation type I with cervicothoracic syringomyelia masquerading as bibrachial amyotrophy: a case report. [Mora 2015]

"Delay of diagnosis resulted in a severe gradual deterioration in our patient. His initial clinical diagnosis of muscular dystrophy was further confirmed with diagnostic studies, according to the family, although we acknowledge that another muscle biopsy may be needed to exclude a diagnosis of muscular dystrophy (though we doubt that this was the actual diagnosis). As a result of the original diagnosis, however, our patient did not seek further evaluation for several years because he understood that there was no treatment for his condition. Decades later, further work-up with simple imaging techniques easily confirmed the etiology of his symptoms. Unfortunately, this delay in diagnosis resulted in the development of irreversible severe chronic muscle wasting. With such advanced atrophy and severe weakness, surgery will likely not provide significant functional benefit.

The differential diagnosis of bibrachial atrophy and syringomyelia is important. While we cannot definitively exclude that both the cervicothoracic syringomyelia and the bibrachial amyotrophy occurred as two separate entities, we doubt this…. We do not know why our patient' s symptoms were stable for over 20 years. Although there was no history of any preceding head or neck trauma, perhaps the syrinx rapidly enlarged in the process of the disease. Without prior imaging, this is impossible to say with any certainty."

8c – Diagnostic reasoning including other diagnoses considered

- Severe liver involvement in two patients with long-term history of fever: remember familial Mediterranean fever. [Gatselis 2016]

"DIFFERENTIAL DIAGNOSIS
Taking carefully into account the previous in-depth history of both patients, a molecular analysis of the MEFV gene was decided. A rapid screening test of the entire coding sequence of MEFV gene, combined with targeted sequencing, revealed that both patients suffered from FMF as no other aetiology had been identified thus far, whereas there was an appropriate exclusion of infectious, malignant, autoimmune, rheumatic, and liver and biliary diseases at their last submission. Actually, the mutational analysis revealed that the male patient carried the R202Q/R202Q homozygous alteration in exon 2 of the MEFV gene, while the female young patient was heterozygous for the M694V/0 conservative mutation in exon 10 and homozygous for the R202Q/R202Q mutation in exon 2."

8d – Prognostic characteristics (eg, staging) where applicable

- Procalcitonin as a diagnostic and prognostic marker for sepsis caused by intestinal infection: a case report. [Lui 2013]

"Procalcitonin is a useful tool in the early diagnosis of sepsis, differentiating from other inflammatory syndrome. The high PCT level (10 ng/ml) in this case could suggest serious bacterial infection and sepsis, and also predicts mortality and worse outcome."

Item 9. Therapeutic Interventions Section

CARE Checklist description:

9a – Types of intervention (eg, pharmacologic, surgical, preventive, self-care)

9b - Administration (eg, dosage, strength, duration)

9c - Changes in intervention (with rationale)

Explanation

Therapeutic interventions are often the focus of case reports or they may provide key diagnostic information. In either case, we recommend reporting them in enough detail to facilitate replication. Complex or poorly defined interventions may benefit from use of the TIDieR guideline (a CONSORT extension) to enhance the accuracy, transparency, and reproducibility of an intervention. [Hoffmann 2014]

A brief explanation of why the patient received a particular intervention *(*such as the target condition, the pre-exposure clinical course, etc.) should be provided in this section; however, we suggest reserving a more detailed rationale for the discussion section. The general format for reporting interventions is outlined below (see Table). Case reports focusing on harms should include the manufacturer and brand of the products in question. Explain changes made to an intervention and describe care received from other providers.

All Interventions
• Specify type of intervention, indicated condition, and intervention [Hoffman 2014]
Pharmaceuticals (over-the-counter and prescription drugs)
• International non-proprietary name (INN), dosing regimen, and length of intervention • For formulations that are administered as volumes of a fluid (e.g. intravenous infusions or oral liquid formulations) state the concentration of the formulation • Provide manufacturer and brand names if relevant
Dietary Supplements and Botanical Medicines
• Ingredients and dosing regimen (e.g., EPA (eicosapentaenoic acid) 750 mg plus DHA (docosahexaenoic acid) 250 mg, 1 capsule orally once daily for 6 months) • If medicinal plants are used, indicate plant species using the Latin binomial name, the quantity of herbal substance or constituents, and the parts of the plant • Provide manufacturer and brand names if relevant
Lifestyle Recommendations (e.g., physical activity or exercise)
• Frequency, intensity, timing, and type

Table 3 – Intervention Description

Examples

9a – Types of intervention (eg, pharmacologic, surgical, preventive, self-care)

- Eight years of follow-up after laminectomy of calcium pyrophosphate crystal deposition in the cervical yellow ligament of patient with Coffin–Lowry syndrome: a case report. [Morino 2016]

"***Surgery***

Under general anesthesia in the prone position, the C1 to C7 laminae were exposed. Twenty millimeters of the width of the C2 to C7 laminae were removed using a high-speed drill. Adhesions between the calcification and dura mater were gently stripped off, and the laminae were resected *en block* with the calcification. Fifteen millimeters of the width of the C1 posterior arch was removed using a high-speed drill. Pulsating dura mater was observed after laminectomy, but the pulse was weak. The dura mater appeared hypertrophic; however, we did not incise the dura mater."

9b - Administration (eg, dosage, strength, duration)

- Maintenance eculizumab dose adjustment in the treatment of atypical hemolytic uremic syndrome: a case report and review of the literature. [Thomson 2016]

"The patient was started on induction eculizumab at 900 mg IV weekly for 4 weeks and responded well with improvement in platelet count and renal function. He was transitioned to every-other-week maintenance eculizumab and hemodialysis was discontinued."

- Polysubstance-induced relapse of schizoaffective disorder refractory to high-dose antipsychotic medications: a case report. [Tucker 2016]

"Rapid sedation was commenced with ziprasidone, lorazepam, droperidol, and zuclopenthixol acetate (Table 1). Benztropine was administered for prophylaxis against extrapyramidal side effects of the antipsychotic medications. The level of sedation attained was unsatisfactory as he remained severely agitated and combative interspersed with only brief periods of drowsiness. He could not follow direction or adhere to boundaries established by staff. All attempts at de-escalation and distraction were met with aggression.

Time	Medication name, dose, and route	Behavioral observations
1720	Approximate time of presentation to our emergency department	Extremely aggressive, threatening, and offensive behavior and language
1726	Ziprasidone 20 mg IM, lorazepam 2 mg IM	
1730	Lorazepam 2 mg IM	
1740	Zuclopenthixol acetate 150 mg IM, benztropine 2 mg IM	
1805	Lorazepam 2 mg IV	Vital signs and IV access obtained, blood sampled
1830	Droperidol 10 mg IM	Verbally abusive, threatening, aggressive
2230	Ziprasidone 20 mg IM	
2300	Lorazepam 2 mg IV	
0100		Sedated and quiet
0400	Droperidol 10 mg IM, Lorazepam 2 mg IV	Yelling, abusive, shaking bed, threatening staff
0600		Sedated but intermittent abuse and threats
1120	Ziprasidone 20 mg IM	
1300	Droperidol 25 mg IM	Acute arousal, combative during transport to psychiatric ward"

9c – Changes in intervention (with rationale)

- Severe refractory autoimmune hemolytic anemia with both warm and cold autoantibodies that responded completely to a single cycle of rituximab: a case report. [Gupta 2011]

"Partial resolution of the hemolytic process was observed while the patient was treated with daily plasmapheresis with 5% albumin, at a volume of 3L to 4L. A total of seven daily plasmapheresis treatments were performed, which resulted in a gradual decrease of the patient's LDH and bilirubin and a rise in his level of haptoglobin. However, the patient still required almost daily blood transfusions. On the basis of earlier reports indicating an anecdotal benefit of rituximab treatment for immune cytopenias, plasmapheresis was discontinued and our patient was placed on rituximab therapy at a dose of 375 mg/m^2 every week. A total of four doses were administered over a period of four weeks. Although an initial increase in LDH level after the initiation of rituximab treatment was noted, there was no evidence of worsening hemolysis. After the first two courses of rituximab therapy, the patient showed a marked clinical improvement. His hemoglobin level stabilized… and he no longer required blood transfusions."

Item 10. Follow-up and Outcomes Section

CARE Checklist description:

10a - Clinician and patient-assessed outcomes

10b - Important follow-up test results (positive and negative)

10c - Intervention adherence and tolerability (and how this was assessed)

10d - Adverse and unanticipated events

Explanation

We recommend reporting objective and subjective findings throughout the course of care, to track changes in the outcomes of interest. Clinician-assessed outcomes could include objective outcome measures, such as

laboratory biomarkers, physical findings, and imaging. Longitudinal clinical findings may help to create a convincing case and support the discussion of temporal or other relationships between outcomes and treatment, a topic to be explored further in the discussion section. [Cohen 2006, Rison 2013]

Reporting results from longitudinal data including patient-assessed and clinician-assessed outcomes may strengthen the case for a causal link. We suggest reporting other clinical management received by the patient, along with its potential impact on outcomes. Consulting with other providers and including their perspective may be helpful.

If the intervention is a focus of the case report, include patient adherence to that intervention and how this information was obtained (eg, diary/ log, telephone call, electronic methods). If available, describe harms attributed to an intervention and make note of the patient's words; reporting what the adverse outcomes were, how often they occurred, and with what intensity. [Davidson 2012] All case reports should explicitly mention the presence or absence of adverse events.

Examples

10a - Clinician and patient-assessed outcomes

- Self-directed Mindfulness Training and Improvement in Blood Pressure, Migraine Frequency, and Quality of Life. [Oberg 2013]

"The results of 8 weeks of self-directed mindfulness training plus 3 additional weeks of customized mindfulness practice resulted in both personally and clinically meaningful outcomes.

From the patient's perspective, perceived stress was dramatically reduced. Not only was MR calmer about her previously overwhelming workload but her workload actually decreased because of increases in her efficiency and focus. For example, her email inbox, a source of perpetual stress, came under control… Using MBSR focusing techniques, she turned email into tasks that were immediately accomplished and the email inbox was successfully reduced to very few items and is now emptied several times a day.

Clinically important objective measures of disease risk also improved during her mindfulness meditation experience. MR measured and recorded her blood pressure using an automated blood pressure monitor (Omron model HEM-609, Lake Forest, Illinois) immediately before and after her meditation sessions (Table). In the first 8 weeks of mindfulness training, baseline blood pressure was typically elevated and classifiable as Stage I hypertension. Following 45 minutes of meditation, blood pressure was reduced into the prehypertensive range and into the normal range after 10 weeks of practice. The maximal mean reduction in both systolic and diastolic blood pressure occurred after approximately 4 weeks (-18.5 mm Hg systolic and -25.8 mm Hg diastolic). By week 7, both systolic and diastolic blood pressure had come within the prehypertensive range and continued to decline to optimal levels (Figure 1). At the end of the 8-week program and an additional 3 weeks of continued self-directed practice and data recording, premeditation mean systolic and diastolic blood pressures were significantly reduced. When all daily blood pressure observations were combined, the mean reductions were highly significant: $P < .0001$ for systolic and $P < .0004$ for diastolic blood pressure reductions over the 11-week period (Figure 2). Notably, as blood pressure came within the normal range, the difference before and after meditation also decreased, suggesting MR was maintaining a lower sympathetic tone.

The additional symptoms and behaviors she tracked, such as migraines and exercise, also were reviewed. Migraine frequency was decreased, and through MR's mindful attention to her inner experience, it was determined that migraines were now occurring only in conjunction with the phase of her menstrual cycle.

Knowledge of this enabled her to plan accordingly and use her migraine abortive medications appropriately. Body weight, which has been a long-term struggle, has not changed in the 11 weeks of mindfulness meditation. MR has taken the "attitudes and commitment" portion of her 8-week MBSR training very seriously."

10b – Important follow-up test results (positive and negative)

- Acute cerebellitis successful managed with temporary cerebrospinal fluid diversion using a long tunnel external ventricular drain [EVD]: a long-term radiological follow-up of two cases. [Waqas 2016]

"OUTCOME AND FOLLOW-UP [Case 1]
The child was extubated on day 3 but the EVD was retained and kept at 10 cm H2O. It was removed after challenge on day 9. A repeat MRI showed markedly decreased cerebellar oedema. The child regained a Glasgow Coma Scale score of 15/15 and was discharged on the 11th day of admission, with no neurological deficits. He remained asymptomatic at 2-year follow-up, at which time an MRI was also found to be normal."

"OUTCOME AND FOLLOW-UP [Case 2]
The infant's condition gradually improved and he started tolerating breast feed. The EVD was removed after 10 days and a repeat MRI with and without contrast, and MR venogram, showed no venous involvement and resolution of all pathological findings, including the cerebellar swelling, tonsillar herniation and hydrocephalus. The patient was discharged on oral dexamethasone tapered over several weeks. At 1-year follow-up, the patient showed no neurological deficits, and displayed normal growth and development."

10c - Intervention adherence and tolerability (and how this was assessed)

- Quetiapine-induced sleep-related eating disorder like behavior: a case series. [Tamanna 2012]

"Our patients had a few important predisposing factors for parasomnia including increased work-related stress, depression and severe sleep apnea with high arousal index. If a patient with parasomnia has any other concomitant primary sleep disorder, the treatment is initially directed towards that aspect which often resolves the parasomnia. Our first patient had severe sleep apnea that was treated adequately, but he continued to have sleepwalking and SRED despite good compliance with treatment probably because his SWS had increased after using BiPAP. Our second patient was not able to be compliant with the CPAP initially until she stopped taking quetiapine."

10d – Adverse and unanticipated events

- Altered distribution of digoxin in renal failure—a cause of digoxin toxicity? [Aronson 1976]

"A 56-year-old man weighing 77 kg was admitted with an acute anterior myocardial infarct having had a previous myocardial infarct 2 years before. He had pulmonary oedema due to left ventricular failure which partly responded to treatment with frusemide and diamorphine and he had occasional ventricular extra systoles which were controlled with small doses of lignocaine. On admission he was in mild renal failure and over the next 36 h this deteriorated to the point where his plasma urea was 125 mg% and creatinine 2.03 mg%. At that time, he was given a total of 1 mg of digoxin orally (13 μg/kg) in three divided doses and shortly after the third developed the various arrhythmias which are shown in Figure 2; just before a further dose of 0.25 mg intramuscularly, however, he had reverted to sinus rhythm and following that dose he once more developed various arrhythmias. Treatment at different times with intravenous procainamide and intravenous and oral practolol did not affect his arrhythmias and he had already reverted to sinus rhythm when only one dose of diphenylhydantoin (50 mg) had been given orally. Other drugs which he received were heparin, warfarin, ampicillin, potassium chloride and diazepam. His plasma digoxin levels following the fourth dose of digoxin are shown in Figure 2. Only when the plasma digoxin level fell below 1.7 ng/ml was he free from arrhythmias. His $T_{½\beta}$ was 37.9 h and his V_d 264 litres (32.4 litres/kg). At a later date, when his renal function

had improved slightly (urea 47 mg%, creatinine 1.37 mg%, creatinine clearance 41 ml/min) his steady-state plasma level on a reintroduced daily maintenance dose of 0.125 mg orally was 0.5 ng/ml indicating a V_d of 349 litres (4.5 litres/kg)."

11. Discussion (including conclusion) Section

CARE Checklist: Discussion (including conclusion):

11a - Strengths and limitations of the management of this case

11b - Relevant medical literature

11c - Rationale for conclusions (including assessment of cause and effect)

11d - Main "take-away" lessons of this case report

Explanation

Case reports may offer new perspectives on new or rare diseases, unusual disease presentations, therapeutic interventions, or harms. [Hauben 2007] Succinctly discuss the key features of the case and what was learned. Basic mechanisms or principles (eg, pathophysiological, immunological, social) and diagnostic challenges may be important, particularly if they help explain observations. Compare the results in the case with results from clinical trials and case reports. [Cooper 2015, Davidson 2012] Support recommendations for additional research with published references. It is important to transparently discuss limitations, including mentioning that the results from a single case may not be applicable to patients in general. [Cooper 2015]

The conclusion section is often brief and focuses on the primary lessons learned from the case report.

Examples

11a - Strengths and limitations of the management of this case

- Altered distribution of digoxin in renal failure—a case of digoxin toxicity? [Aronson 1976]

"The data which we have presented here have been limited by the restrictions of clinical practice and in the appendix we have outlined the major shortcomings of the pharmacokinetic calculations we have made. However, despite the difficulties in deriving accurate estimates of the true apparent volumes of distribution involved, the changes we have observed are too large merely to be accounted for by pharmacokinetic inaccuracies; indeed, any over-estimation of the true volumes strengthens the argument. We believe that the changes we have observed are real and have contributed to the digoxin toxicity which occurred in these patients. Further characterization of the cause of the abnormal distribution of digoxin in renal failure by more precise prospective clinical studies is required."

11b - Relevant medical literature

- Successful Heart Transplantation After 13 Hours of Donor Heart Ischemia with the Use of HTK Solution: A Case Report. [Wei 2005]

"Dr Barnard successfully used a hypothermic perfusion system to protect a donor heart for more than 16 hours in heterotopic HTx.[1] However, surgeons are more conservative while performing orthotopic HTx. Few series are using donor hearts with IT longer than 6 hours. Long-term follow-up of HTx recipients at Columbia University in New York and Alfred Hospital in Australia have demonstrated that prolonged IT (average 5 hours) did not adversely affect immediate or long-term survival or the incidence of transplant coronary artery disease.[2, 3] The University of Western Ontario in Canada and The University of Alabama at Birmingham have also demonstrated that long-term survival of HTx was not affected by prolonged IT (longest times 457 minutes and 479 minutes, respectively).[4, 5]"

[References from the above example]

1. Wicomb WN, Cooper DKC, Novitzky D, et al: Cardiac transplantation following storage of the donor

heart by a portable hypothermic perfusion system. Ann Thorac Surg 37:243, 1984
2. Morgan JA, John R, Weinberg AD, et al: Prolonged donor ischemic time does not adversely affect long-term survival in adult patients undergoing cardiac transplantation. J Thorac Cardiovasc Surg 126:1624, 2003
3. Briganti EM, Bergin PJ, Rosenfeldt FL, et al: Successful long-term outcome with prolonged ischemic time cardiac allografts. J Heart Lung Transplant 14:840, 1995
4. Del Rizzo DF, Menkis AH, Pflugfelder PW, et al: The role of donor age and ischemic time on survival following orthotopic heart transplantation. J Heart Lung Transplant 18:310, 1999
5. Canter C, Naftel D, Caldwell R, et al: Survival and risk factors for death after cardiac transplantation in infants: a multi-institutional study. Circulation J 96:227, 1997

11c - Rationale for conclusions (including assessment of cause and effect)

- Statin-associated weakness in myasthenia gravis: a case report. [Keogh 2010]

"The actual incidence of statin-exacerbated myasthenia is unknown, and only a handful of reports of statin associated myasthenia gravis have ever been described. Out of 6 published case reports, only 5 patients were noted to have some degree of recovery and only one patient had a complete recovery upon termination of statin therapy.

How statins could appear to exacerbate MG is unclear. It is possible that the mechanism actually reflects a "double hit" phenomenon of defective neuromuscular transmission secondary to antibody-mediated post-synaptic acetylcholine receptor dysfunction in combination with a statin-induced myopathy.

The clear development of a statin myopathy with simvastatin treatment prior to the onset of myasthenia in our patient is consistent with the possibility of a second (atorvastatin- induced) myopathy coalescing with the onset of myasthenia gravis. The symptomatic improvement that followed his withdrawal from atorvastatin treatment resulted from the resolution of this statin myopathy.

We also considered other potential causes of deterioration such as sepsis, steroid-induced worsening of MG, steroid myopathy, and cholinergic crisis, but we considered their development less likely based on clinical grounds.

We cannot rule out completely the possibility that the worsening of our patient' s MG simply reflected a progression of his MG. However, the clinical course of his condition, as well as the statin-induced proximal limb pain and weakness (without bulbar features) he experienced prior to his presentation, raises at the very least the possibility that a component of his initial deterioration was statin-related.

Similarly, we note that his improvement could have reflected the immunosuppressive effects of therapy for his MG rather than the withdrawal of his atorvastatin treatment. It seems probable, however, that both factors played a significant role in the improvement of his clinical state.

The development of other autoimmune disorders such as dermatomyositis, polymyalgia rheumatica, vasculitis, and Lupus-like syndrome upon initiation of statin therapy raises the possibility that in predisposed individuals, statins may precipitate an immunological trigger that is analogous to penicillamine induced MG although clearly different in temporal respect. However, given the paucity of reports and the widespread use of statins, the possibility of chance association cannot be excluded still."

11d - Main "take-away" lessons of this case report

- Prolonged unassisted survival in an infant with anencephaly. [Dickman 2016]

"This infant met the diagnostic criteria of the Medical Task Force on Anencephaly. Therefore, she was the longest surviving anencephalic infant who did not require any life-sustaining treatments such as intubation or feeding tubes. Knowing this rare possibility, the physician and family should make goal-oriented decisions on how to care for the infant. The provider should offer immunisations and well-childcare to each family if the infant survives the immediate newborn period. This case should affect the practice of physicians who interact with expectant mothers of a child affected by anencephaly."

Item 12. Patient Perspective Section

CARE Checklist description: When appropriate patients should share their perspectives on the treatments they received.

Explanation

Whenever possible and relevant, provide patients with an opportunity to briefly share their perspectives on the episode of care. They may describe their motivations for seeking care, changes they associate with an intervention, or the impact of care on their quality of life. The report of a truly novel treatment may rely heavily on a patient's perspective. Patients can be co-authors, which may require additional consent, owing to the loss of anonymity. A proxy, such as the parent of a minor, can provide a perspective when appropriate. In some cases the line is blurred and the author—usually a clinician—is also the patient. [Lundberg 2016]

Example

- Chronic Rhinosinusitis and Irritable Bowel Syndrome: A Case Report. [Kogan 2016]

"I am a very active person and enjoy playing tennis and gardening. My symptoms prior to coming to George Washington (GW) Center for Integrative Medicine prevented me from participating in the leisure activities that I enjoy. The quality of my sleep and my overall quality of life were not good. After coming to the GW Center for Integrative Medicine all of my symptoms improved and I experienced a drastic improvement in my quality of life.

I did not follow an "Elimination Diet" per se, but rather was instructed to follow a diet with foods to avoid based on my testing. I experienced a relapse of my sinus symptoms when I deviated too much from the diet, but am now able to control the symptoms by adjusting my diet accordingly."

Item 13. Informed Consent Section

CARE Checklist description: Did the patient give informed consent? Please provide if requested

Explanation

Informed consent is customarily required by medical journals. Whenever possible, obtain signed consent to write and publish the case report from the patient. Some cases may require additional consent (eg, when potentially identifiable information is unavoidable, when the patient is older than 90 years of age in the United States there is a photograph or image, or has a rare disease).

In exceptional circumstances or if the patient is unable to provide consent, consent may be obtained from a close relative. For children who are too young to consent themselves, obtain consent from a guardian.

Case reports often include a statement that signed consent was obtained from the patient or if it is impossible to receive consent, that all possible attempts were made.

Examples (journal informed consent guidelines)

- BMJ Case Reports - http://casereports.bmj.com/site/about/guidelines.xhtml#patientconsent (Accessed October 22, 2016)

"Patient consent

Publication of any personal information about an identifiable living patient requires the explicit consent of the patient or guardian. This is a requirement under the UK's Data Protection legislation. We expect authors to use the BMJ consent form which is available in several languages. You must have signed informed consent from patients (or relatives/guardians) before submitting to BMJ Case Reports. Please anonymize the patient's details as much as possible, eg, specific ages, ethnicity, occupations. **For living patients this is a legal requirement and we will not send your document for review without explicit consent from the patient or guardian.** If the patient is dead the Data Protection Act does not apply, but the authors must seek permission from a relative (ideally the next of kin). If you don't have signed consent from a deceased patient, guardian or family, the head of your medical team/hospital or legal team must take responsibility that exhaustive attempts have been made to contact the family and that the paper has been sufficiently anonymised not to cause harm to the patient or their family. **You will need to upload a signed document to this effect."**

Discussion

Case reports document the opportunities and challenges associated with the care of individual patients and empower clinicians to document care through scholarly contributions in peer-reviewed medical journals. [Akers 2016] Evidence-based medicine (EBM) also focuses on individual patient care through the integration of "clinical expertise with the best available external clinical evidence from systematic research." [Sackett 1996] Experienced clinicians combine clinical expertise (the judgement and skill acquired through patient care) and external evidence as part of the recipe for providing better care to their patients. We believe that using the CARE reporting guidelines in case reports can facilitate and document the integration of evidence with expertise to inform clinical research, clinical practice guidelines, and medical education. [Califf 2016]

Clinical research is driven by hypotheses. The evidence that hypotheses are not false is associated with the prior probability of an association between variables—for example, a diagnostic single nucleotide polymorphism (SNP) test and a disease. [Wacholder 2004, Ioannidis 2016] We believe that high-quality case reports offer supporting evidence regarding prior probability which may reduce the number of false positive or false negative findings. Case reports, and the systematic review of case reports, [Buonfrate 2013] also provide information that informs clinical practice guidelines. [IOM 2011]

Medical education uses problem-based teaching to cultivate clinical reasoning skills, first with evidence-based case simulations [Barrows 1986] and continuing with teaching rounds. [Irby 1994] We believe that high-quality case reports provide real-world examples that can enhance critical thinking, improve documentation of patient care, and create life-long learning skills.

Limitations of case reports

While case reports have the potential to detect signals of causal relations, [Kiene 2013, Hauben 2007] they usually cannot exclude the possibility of a chance association. The selection of patients whose care makes up most case reports is subject to selection bias and may represent outliers in clinical practice, necessitating caution regarding the generalizability of results. [Hay 1988] A causal relationship may be identified by N-of-1

Case Reports following the CARE guidelines

- Retrospective, practice-based
- No protocols or controls
- Systematic data collection
- Consent required before publication.

N-of-1 trials

- Prospective, research- or practice-based
- Protocols and controls
- *A priori* consent required
- Optional patient input into design

studies [Shamseer 2016], case reports focusing on patterns (delete: "physical, biological, or psychological phenomena") integrated as a functional unit, or case reports that include re-challenge with a potential causal agent [Badalov 2007].

Accurate and transparent case reports are challenging to write and publish. Medical records are often incomplete, inaccurate, or difficult to access, relevant interventions from other practitioners may be unavailable, and follow-ups are often not adequately documented. Published case reports are not cited as often as meta-analyses or randomized controlled trials and have a limited impact on academic advancement [Patsopoulos 2005]—these factors may limit the number of case reports written and therefore published.

Conclusion

This explanation and elaboration document was developed to annotate the CARE Checklist, provide examples of good reporting, and address some of the limitations often associated with case reports. Systematic data collection from the point of care is now feasible; case reports following reporting guidelines can help offer the correct intervention to the right patient at the right time. We believe that case reports have the potential to offer evidence from the point of care that can be useful for clinical research, inform clinical practice guidelines and improve medical education.

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Author's contribution

DSR, MSB, JJG, GSK, DM and LS developed the format for this article with input from other co-authors. The co-authors participated in the development of the CARE guidelines, offered insightful suggestions, and reviewed this manuscript. DSR organized the writing of this manuscript and the publication process with input from MSB, JJG, GSK, and other co-authors.

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Items 1 and 2 – Title and Keyword

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