
UNIVERSITY OF THESSALY
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RESEARCH METHODOLOGY IN BIOMEDICINE,
BIOSTATISTICS AND CLINICAL BIOINFORMATICS

# Evaluating the Quality of Reporting of Case Reports in Spinal Cord Tumors (SCTs) using the CARE guidelines.

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by

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ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ
ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ
ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
Μεθοδολογια Βιοϊατρικης Ερευνας, Βιοστατιστικη και Κλινικη Βιοπληροφορικη

# Αξιολογώντας την ποιότητα αναφοράς περιγραφής περιπτώσεων στους Όγκους Νωτιαίου Μυελού χρησιμοποιώντας τις οδηγίες **CARE**

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

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# Contents

**Abstract**

**INTRODUCTION:** Spinal cord tumors are rare medical conditions, mainly described in the literature by observational studies (OS), the overwhelming majority of which are case reports (CRs)

**PURPOSE**: In this study, our goal is to analyze the reporting quality of these CRs using the CARE guidelines, alerting the medical community about the most common omissions. This will increase the total credibility of CRs.

**METHODS:** We searched the PubMed database for Systematic Reviews (SRs) of OS, from January 2020 to September 2020. Next, we analyzed the cited studies in these SRs using the CARE guidelines for the CRs. CARE(CAse REport) guidelines consist of 13 categories with 30 item descriptors. CARE evaluates the risk of bias, the transparency and credibility of CRs.

**RESULTS:** 2 SRs were eligible and included in our analysis, describing 42 different medical cases in 30 different articles. None of the CRs achieved a score higher than 90%;the median score was 61%. Additionally, seven descriptors were found to be statistically different between the two SRs. None of the CRs included patients' perspectives or patient-assessed outcomes, 2% included the term "case report" in its key-words and 7% a timeline. All of the cases described patients' primary concerns, symptoms and de-identified information satisfactorily, while maintaining enough scientific rationale for any conclusions. Articles publicated after 2013 (CARE introduction) achieved higher reported items' rates in timeline and changes in therapeutic intervention. In between SRs case report analysis, showed significant differences of reporting of seven items. Finally, IF analysis resulted in mixed results.

**CONCLUSIONS:** None of the CRs on Spinal Cord Tumors completely followed the CARE guidelines. Items and item descriptors scored between between 30-86%. Most reports consisted of a lengthy diagnostic approach and a summary of the bibliography about the topic. They did not include the limitations of the reports, neither provided a section for the patient's shared perspective, nor about their informed consent. Greater quality CRs, and observational studies overall, would be useful in the diagnostic approach, informing for rare diseases and improving clinical practice.

**Key words:** *Case Report*; *CARE Guidelines*; *Spinal Cord Tumors*; *Epidemiology*; *Observational Studies*

*List of Abbreviations*

*CARE:* CAse REport
*CR:* case report
*IF:* Impact Factor
*ISCM:* Intramedullary Spinal Cord Metastasis
*ICSCT:* Intramedullary cervical spinal cord teratoma
*OS:* Observational Study
*RCC:* Renal Cell Carcinoma
SCARE: Surgical CAse REports

**Περίληψη**

**ΕΙΣΑΓΩΓΗ**: Οι όγκοι του νωτιαίου μυελού είναι σπάνιες ιατρικές οντότητες, που περιγράφονται στη βιβλιογραφία κυρίως από μελέτες παρατήρησης (Observational Studies - OS), η συντριπτική πλειονότητα των οποίων είναι αναφορές περιπτώσεων (Case Ceports - CR).

**ΣΚΟΠΟΣ**: Στην μελέτη αυτήν, στόχος μας είναι να αναλύσουμε την ποιότητα αναφοράς αυτών των CR χρησιμοποιώντας τις οδηγίες CARE , προειδοποιώντας την ιατρική κοινότητα για τις πιο κοινές παραλείψεις. Αυτό θα αυξήσει τη συνολική αξιοπιστία των CR.

**ΜΕΘΟΔΟΙ**:Ψάξαμε τη βάση δεδομένων PubMed για Συστηματικές Ανασκοπήσεις (SRs)μελετών παρατήρησης, από τον Ιανουάριο του 2020 έως τον Σεπτέμβριο του 2020. Στη συνέχεια, αναλύσαμε τις αναφερόμενες μελέτες σε αυτά τα SR χρησιμοποιώντας τις οδηγίες CARE για τις CR . Οι οδηγίες CARE (CAse REport) αποτελούνται από 13 στοιχεία και συνολικά από 30 παραμέτρους περιγραφής. Το CARE αξιολογεί τον κίνδυνο μεροληψίας, τη διαφάνεια και την αξιοπιστία των CR.

**ΑΠΟΤΕΛΕΣΜΑΤΑ**: 2 SR (Συστηματικές Ανασκοπήσεις) ήταν κατάλληλα προς ανάλυση και συμπεριλήφθηκαν στην εργασία μας, περιγράφοντας 42 διαφορετικές ιατρικές περιπτώσεις. Καμία CR δεν πέτυχε βαθμολογία άνω του 90%. Η διάμεση τιμή ήταν 61%. Επιπλέον, επτά παράμετροι βρέθηκαν να είναι στατιστικά σημαντικά διαφορετικές μεταξύ των δύο SR . Καμία από τις CR δεν περιλάμβανε τις εκτιμήσεις των ασθενών για το κλινικό αποτέλεσμα, το 2% περιλάμβανε τον όρο ≪case report≫ στις λέξεις-κλειδιά και το 7% περιείχε χρονοδιάγραμμα. Σε όλες τις περιπτώσεις περιγράφηκαν σε ικανοποιητικό βαθμό οι πρωταρχικές ανησυχίες των ασθενών, τα συμπτώματα και οι αποπροσωποποιημένες τους πληροφορίες, τηρώντας παράλληλα επιστημονικό συλλογισμό για οποιαδήποτε συμπεράσματα. Άρθρα που δημοσιεύτηκαν μετά το 2013 ( Εισαγωγή του CARE), πέτυχαν ψηλότερα επίπεδα αναφοράς στα αντικείμενα του χρονοδιαγράμματος και στην αναφορά τυχόν θεραπευτικών αλλαγών . Στην ανάλυση αναφερόμενων περιστατικών μεταξύ των 2 SR , βρέθηκαν 7 αντικείμενα να διαφέρουν. Η ανάλυση των IF έδειξε μεικτά αποτελέσματα.

**ΣΥΜΠΕΡΑΣΜΑΤΑ**:Καμία από τις CR για όγκους του νωτιαίου μυελού δεν ακολούθησε πλήρως τις οδηγίες CARE . Η συνολική βαθμολογία των στοιχείων και των παραμέτρων τους κυμάνθηκε μεταξύ 30-86% . Οι περισσότερες αναφορές αποτελούνταν από μια μακρά διαγνωστική προσέγγιση και μια περίληψη της βιβλιογραφίας για το θέμα. Δεν περιλάμβαναν τους περιορισμούς των αναφορών, ούτε παρείχαν μια ενότητα για την κοινή προοπτική του ασθενούς, ούτε τη συγκατάθεσή του μετά από ενημέρωση. Ποιοτικά καλύτερες CR , και μελέτες παρατήρησης συνολικά, θα ήταν χρήσιμες στη διαγνωστική προσέγγιση, την ενημέρωση για σπάνιες ασθένειες και τη βελτίωση της κλινικής πρακτικής.

**Λέξεις ευρετηρίου**: Αναφορά περιστατικού, Οδηγίες CARE , Όγκοι Νωτιαίου Μυελού, Επιδημιολογία, Μελέτες Παρατήρησης

# 1 INTRODUCTION

## 1.1 Spinal Cord Tumors and Case Reports

Medical research studies are categorized in primary and secondary studies, depending on the type of the performed research. Secondary studies -consisting of meta-analysis, reviews and systematic reviews- provide a summary of other studies, the so-called primary studies, which contain the actual primary research [14] . Primary studies, are subdivided further to: basic medical research, clinical research and epidemiological research.

Observational studies include: cohort, cross-sectional and case control studies, that fall into the epidemiological research category, and finally case reports that fall into the clinical research category. In epidemiology, observational studies(non-interventional) contain weaker evidence than interventional studies [3] [7] [22] . Non-interventional studies can be described as studies, in the context of which, the extracted data from the applied therapies to patients is evaluated epidemiologically. All diagnosis, therapies, and medical evaluations do not follow any predefined study protocol and are subjects of medical practice. [26]

Traditionally, case reports have been useful for (1) describing new or rare medical conditions such as SCTs' variations (2) analyzing variant pharmacological, surgical and radiation treatments (3), estimating adverse effects and/or costs of interventions, and (4) meliorating the medical diagnostic approach and education.[35] [15] They play a critical role estimating the effectiveness and efficacy, describing real-world medical situations in contrast with clinical trials and other interventional studies that describe medical events in a controlled environment. Both interventional and non- interventional studies benefit the medical research and science.

Case report publications have seen an increase the last years in peer-reviewed journals suggesting their importance in epidemiology.[33] They consisted crucial medical resources for the initial exploring and detection of AIDS, Zika virus and diethylstilboestrol adverse effects.[10] CARE guidelines aim to augment the credibility, transparency and validity of such studies, providing a quantitative estimate of their overall quality.[13]

Nowadays, the use and establishment of such evaluating tools is more important than ever.[2] Many different tools have been constructed for this purpose, each of which evaluates an alternative or the same study type with a slightly different way. [25] [9] [21]

In this study, we used the CARE guidelines to evaluate the quality of reporting of case control studies, which are consisting a remarkable proportion of all SCT studies. CARE guidelines (for CAse REports) were introduced in 2013 aiming to strengthen the quality of case reports such as their efficacy, transparency and accuracy. Given the growing number of CR publications, an objective tool assessing the quality of this type of clinical research studies is necessary. CRs in accordance with the CARE guidelines can easily be utilized for useful data extraction including (1) clinician- and patient-assessed outcomes, (2) effectiveness of Clinical Practice Guidelines (CPGs), and (3) the return on investment (ROI). Equator Network officially supports the use of these guidelines.[6]

## 1.2 Spinal Cord tumors

Spinal Cord tumors (SCTs) are rare medical entities .[30] Due to their nature, they are mainly described by CRs across the international bibliography.[16] Their histologic types and commonly responded locations are critical for their diagnosis and therapy.

They are grouped in 3 categories:[31]

*Intradural-extramedullary:* The tumor expands into the dura, but out of the actual spinal cord. This is the most frequently reported type of SCT and it coreresponds to 4 out of 10 cases. It includes meningiomas, schwannomas, neurofibromas and filum terminale ependymomas. Meningiomas are the most common primary intramedullary tumors, they are mostly benign and sometimes recur after excision[12] . Schwannomas and neurofibromas tend to be benign, although neurofibromas could potentially undergo malignant turnover. Filum terminale ependymomas tend to occupy more space and its not easy to be removed.

*Intramedullary:* These are intra(*=into) spinal* cord tumors. They further divide into gliomas, ependymomas and astrocytomas( mostly seen in children.[34] They comprise 5% of the cases. Cervical and thoracic regions are the most commonly seen locations for astrocytomas. Filum terminale ependymomas consist the most frequent type of ependymomas. They tend to follow a benign course and they are surgically difficult to be excised. Intramedullary lipomas arise congenitally and and in rare occasions, and are primarily found in the cervical and thoracic regions.

*Extradural:* They grow out of the dura. They are less frequent and usually arise from metastatic cancer cells or less frequently they derive from the cells covering the nerve roots. Schwannomas can also infiltrate the dura and expand extramedullary. Expansion of an extramedullary tumors could cause serious complications due to compression of vertebral canal.[4]

# 2 METHODS

## 2.1 Database search strategy

We searched in the PubMed database, one of the largest databases of human medicine resources , [5] for papers from 2020 January to 2020 September. Our search terms included: " Spinal Cord Tumors"," metastasis", " cancer", " intramedullary tumors", "extramedullary tumors", " primary tumors", " ependymoma", meningioma"," astrocytoma","ganglioma"," spinal glioblastoma multiforme" as single terms or combined terms. The conclusive advanced search that produced all the possibly eligible SRs collectively ,was: *"spinal cord tumors"*[*All Fields*] *OR "spinal cord neoplasms"*[*MeSH Terms*] *OR ("spinal"*[*All Fields*] *AND "cord"*[*All Fields*] *AND "neoplasms"*[*All Fields*]*) OR "spinal cord neoplasms"*[*All Fields*] *OR ("spinal"*[*All Fields*] *AND "cord"*[*All Fields*] *AND "tumors"*[*All Fields*]*) OR "spinal cord tumors"*[*All Fields*]

The search was limited to the title and the abstract. Our PubMed selection tool included *English* as main language, *human* as species and *SR* as study type. All meta-analysis excluded as they investigate clinical trials , which are intervention studies. [39] [27]

## 2.2 Selection Phase

The first sorting phase comprised the evaluation of these studies. SRs with irrelevant topics were excluded.

After, the cited articles in each SR were extracted, retrieved and analyzed as full text articles. Further quality control was performed for each one of these articles to evaluate its eligibility for our methodological analysis. There was no limitation for publication dates of CRs.

A full list of the 30 articles analyzed in this study, are shown in Table 1. A diagram of the studies selection phase is shown in Flowchart 1.

## 2.3 Study Quality Evaluation

CARE guidelines contain the following 13 categories of items: *title, keywords, abstract, introduction, patient information, clinical findings, timeline, diagnostic assessment , therapeutic interventions, follow-up and outcomes, discussion, patient perspective* and *informed consent*. Some of the items contain sub-items. A summary of the 13 items and 30 item descriptors are shown in the Table 1.

The articles to be studied were analyzed with the use of CARE tool. We reported the rate of compliance to the CARE's checklist items, scoring with 1 when in compliance and 0 in non-compliance.

Exceptions were made in the evaluation of reporting of item descriptors in instances which they were not relevant to the case reports.. This occurred, in the following cases:

a. if surgery was a monotherapy, then items 9b and 9c was irrelevant.

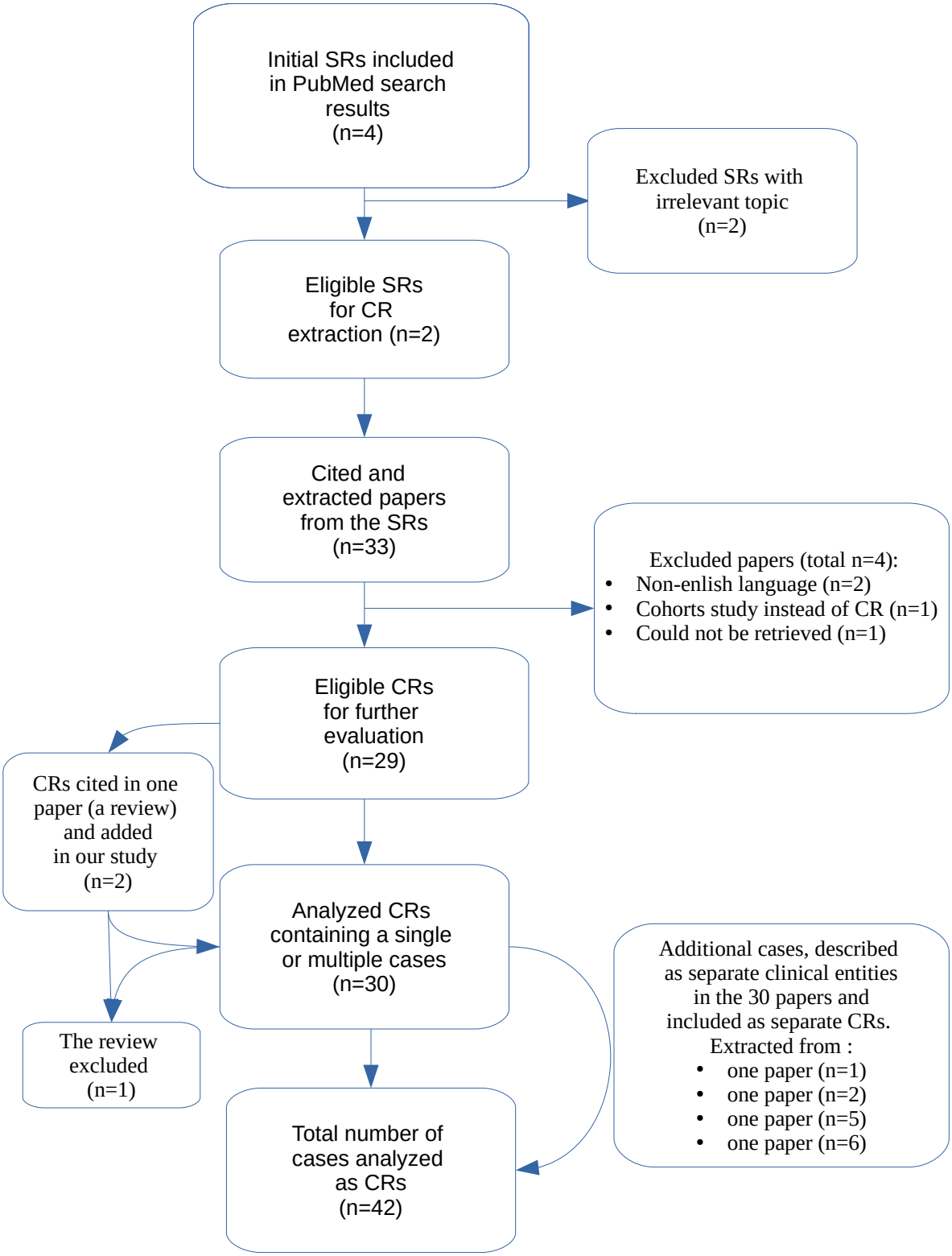
b. in studies containing multiple cases, if differential diagnosis was not stated clearly in the "Discussion Section", then item 8c was excluded.

In any other unclear situation, value of 0 reported.

## 2.4 Statistical Analysis

Pearson's chi square used for the analysis of categorical variables. Chi-squared test used to determine whether there is a statistically significant difference between the expected frequencies and the observed frequencies in high (>3) and low ( $< 3$) IF journals, new CRs (2013 and after) and older CRs (before 2013), and finally CRs cited in different SRs.

"2013" considered as the Cut-off point for publication date, as this was the introductory year for the CARE guidelines. The cut-off point "3"for the IF journal classification was made taking into account that the top 20% of the journals are ranked above IF $> 3$. [8]




**Flowchart 1.** Methodological screening steps selecting Systematic Reviews and Case Reports.

**Table 1.** Relative frequencies % of reporting of the items following CARE guidelines overall, and for the 2 systematic reviews.

| | | | Reporting Rate % | | | |
|---|---|---|---|---|---|---|
| | | | CRs (n=42) | ISCT RCC(n=32) | ICSCT (n=10) | p value |
| *TITLE* | 1 | The diagnosis or intervention of primary focus followed by the words “case report” | 52 | 10 | 66 | **0.002** |
| *KEYWORDS* | 2 | 2 to 5 key words that identify diagnoses or interventions in this case report, including "case report" | 2 | 10 | 0 | 0.07 |
| *ABSTRACT* | 3a | Introduction: What is unique about this case and what does it add to the scientific literature? | 95 | 90 | 97 | 0.373 |
| | 3b | Main symptoms and/or important clinical findings | 74 | 80 | 74 | 0.61 |
| | 3c | The main diagnoses, therapeutic interventions, and outcomes | 79 | 70 | 81 | 0.449 |
| | 3d | Conclusion—What is the main “take-away” lesson(s) from this case? | 74 | 40 | 87 | **0.005** |
| *INTRODUCTION* | 4 | One or two paragraphs summarizing why this case is unique (may include references) | 90 | 90 | 91 | 0.953 |
| *PATIENT INFORMATION* | 5a | De-identified patient specific information | 100 | 100 | 100 | 0.999 |
| | 5b | Primary concerns and symptoms of the patient | 100 | 100 | 100 | 0.999 |
| | 5c | Medical, family, and psycho-social history including relevant genetic information | 10 | 30 | 3 | **0.012** |
| | 5d | Relevant past interventions with outcomes | 76 | 40 | 88 | **0.002** |
| *CLINICAL FINDINGS* | 6 | Describe significant physical examination (PE) and important clinical findings | 10 | 100 | 100 | 0.999 |
| *TIMELINE* | 7 | Historical and current information from this episode of care organized as a timeline | 7 | 10 | 6 | 0.688 |
| *DIAGNOSTIC ASSESSMENT* | 8a | Diagnostic testing (such as PE, laboratory testing, imaging, surveys) | 86 | 100 | 81 | 0.139 |
| | 8b | Diagnostic challenges (such as access to testing, financial, or cultural) | 33 | 10 | 41 | 0.073 |
| | 8c | Diagnosis (including other diagnoses considered) | 60 | 100 | 47 | **0.003** |
| | 8d | Prognosis (such as staging in oncology) where applicable | 67 | 0 | 88 | **0.005** |
| *THERAPEUTIC INTERVENTIONS* | 9a | Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care) | 98 | 100 | 97 | 0.572 |
| | 9b | Administration of therapeutic intervention (such as dosage, strength, duration) | 23 | 20 | 24 | 0.9 |
| | 9c | Changes in therapeutic intervention (with rationale) | 53 | 20 | 64 | **0.045** |
| *FOLLOW-UP AND OUTCOMES* | 10a | Clinician and patient-assessed outcomes (if available) | 93 | 100 | 100 | 0.315 |
| | 10b | Important follow-up diagnostic and other test results | 80 | 100 | 74 | 0.058 |
| | 10c | Intervention adherence and tolerability (How was this assessed?) | 43 | 30 | 60 | 0.67 |
| | 10d | Adverse and unanticipated events | 55 | 40 | 61 | 0.283 |
| *DISCUSSION* | 11a | A scientific discussion of the strengths AND limitations associated with this case report | 10 | 10 | 12 | 0.953 |
| | 11b | Discussion of the relevant medical literature with references | 98 | 100 | 97 | 0.572 |
| | 11c | The scientific rationale for any conclusions (including assessment of possible causes) | 100 | 100 | 100 | 0.999 |
| | 11d | The primary “take-away” lessons of this case report (without references) in a one paragraph conclusion | 76 | 50 | 84 | **0.026** |
| *PATIENT PERSPECTIVE* | 12 | The patient should share their perspective in one to two paragraphs on the treatment(s) they received | 0 | 0 | 0 | 0.999 |
| *INFORMED CONSENT* | 13 | Did the patient give informed consent? | 19 | 0 | 25 | 0.079 |
| | | *OVERALL* | 62 | 64 | 55 | 0.16 |

**Table 2.** Reporting of item Rate %, in 24 studies, using CARE guidelines, by IF score.

| | | Reporting Rate % | | |
|---|---|---|---|---|
| | | Low Rank IF≤3(n=19) | High Rank IF>3(n=6) | p value |
| 1 | The diagnosis or intervention of primary focus followed by the words “case report” | 47 | 67 | 0.41 |
| 2 | 2 to 5 key words that identify diagnoses or interventions in this case report, including "case report" | 0 | 0 | 0.99 |
| 3a | Introduction: What is unique about this case and what does it add to the scientific literature? | 89 | 100 | 0.41 |
| 3b | Main symptoms and/or important clinical findings | 58 | 100 | **0.05** |
| 3c | The main diagnoses, therapeutic interventions, and outcomes | 63 | 100 | 0.1 |
| 3d | Conclusion—What is the main “take-away” lesson(s) from this case? | 58 | 100 | **0.05** |
| 4 | One or two paragraphs summarizing why this case is unique (may include references) | 89 | 100 | 0.41 |
| 5a | De-identified patient specific information | 100 | 100 | 0.99 |
| 5b | Primary concerns and symptoms of the patient | 100 | 100 | 0.99 |
| 5c | Medical, family, and psycho-social history including relevant genetic information | 16 | 0 | 0.3 |
| 5d | Relevant past interventions with outcomes | 89 | 33 | **0.01** |
| 6 | Describe significant physical examination (PE) and important clinical findings | 100 | 100 | 0.99 |
| 7 | Historical and current information from this episode of care organized as a timeline | 11 | 17 | 0.69 |
| 8a | Diagnostic testing (such as PE, laboratory testing, imaging, surveys) | 100 | 83 | 0.07 |
| 8b | Diagnostic challenges (such as access to testing, financial, or cultural) | 42 | 17 | 0.26 |
| 8c | Diagnosis (including other diagnoses considered) | 74 | 67 | 0.74 |
| 8d | Prognosis (such as staging in oncology) where applicable | 74 | 50 | 0.28 |
| 9a | Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care) | 100 | 100 | 0.99 |
| 9b | Administration of therapeutic intervention (such as dosage, strength, duration) | 31 | 33 | 0.74 |
| 9c | Changes in therapeutic intervention (with rationale) | 56 | 40 | 0.55 |
| 10a | Clinician and patient-assessed outcomes (if available) | 89 | 100 | 0.41 |
| 10b | Important follow-up diagnostic and other test results | 79 | 83 | 0.82 |
| 10c | Intervention adherence and tolerability (How was this assessed?) | 47 | 20 | 0.26 |
| 10d | Adverse and unanticipated events | 53 | 67 | 0.55 |
| 11a | A scientific discussion of the strengths AND limitations associated with this case report | 16 | 0 | 0.3 |
| 11b | Discussion of the relevant medical literature with references | 100 | 100 | 0.99 |
| 11c | The scientific rationale for any conclusions (including assessment of possible causes) | 100 | 100 | 0.99 |
| 11d | The primary “take-away” lessons of this case report (without references) in a one paragraph conclusion | 79 | 83 | 0.82 |
| 12 | The patient should share their perspective in one to two paragraphs on the treatment(s) they received | 0 | 0 | 0.99 |
| 13 | Did the patient give informed consent? | 32 | 0 | 0.114 |
| | *OVERALL* | 63 | 62 | 0.91 |

# 3 RESULTS

## 3.1 Screening of Studies

*SR screening*: PubMed search resulted in 4 SRs. 2 SRs were eligible for our primary CR analysis. One study referring to Intramedullary Spinal Cord Metastasis from Renal Cell Carcinoma (ISCM from RCC) [38] and one to Intramedullary cervical spinal cord teratoma (ICSCT)[36] . Two studies were excluded due to irrelevant reviewed topics to SCT . [40] [29]

*CR screening:* 33 different papers included in the 2 SRs. 2 of them were excluded due to non-English language [18] [23] , 1 as a cohort study[32] and we were unable to retrieve one [37] . From the remaining 29 studies we were able to retrieve 42 different medical cases, and we analyzed them as independent case reports. 2 cases were retrieved from one review study, which shortly after excluded. In a paper there were distinct cases, in another one there were 3, in a third one 5 and in a fourth one 6. Lastly, a single case was retrieved and analyzed directly from one of the 2 SRs, . Flowchart 1 describes the screening methodology in Appendix Section.

## 3.2 Statistics and classification

From the 32 different papers, 5 were published in High ranked Impact Factor journals (IF>3), 19 in Low rank (IF >3) and 8 didn't have an IF score due to old journals or publications. Table 2, shows the differences % among high and low IF CRs. Among 32 studies, there was one cohort study (3%) and 31 case reports (97%). 7 out 32 CRs (22%) were published after the CARE guidelines introduction. An other classification made according to publication date. 7 Studies were published after 2013 and 35 published before. Table 3, describes the main differences between the two publication groups.

## 3.3 Main Analysis

Analyzing the 42 eligible CRs, we found that 52% of them included the term "case report" in their title, and only 10% included the same term in their key-words. Almost all of the reports described the uniqueness and rarity of the medical case, both in the abstract and in the introduction. Additionally, they managed, in total, to delineate patients' de-identified information, as well as their primary concerns and symptoms, type of therapy given, clinician's assessed outcomes, while also reviewing the literature, in the end, and concluding with a scientific rationale. The abstract effectively contained main symptoms, diagnoses and conclusions in 3/4 of the cases. Diagnostic testing, relevant past interventions, important follow-up and primary take-away lessons were presented in more than 3/4 cases. None of the CRs included patient-assessed outcomes or their shared perspective. Finally, only 19% of the cases mentioned patient's informed consent. More detailed information is presented in Table 1 and Figure 1.

Cumulatively, 28 cases (67%) matched a score between 50-70%. 40/42 (95%) matched a score between 30-80%. No study was found to be perfect (>90%) or completely inaccurate (<30%). Graphical representation is shown in Figure 1.

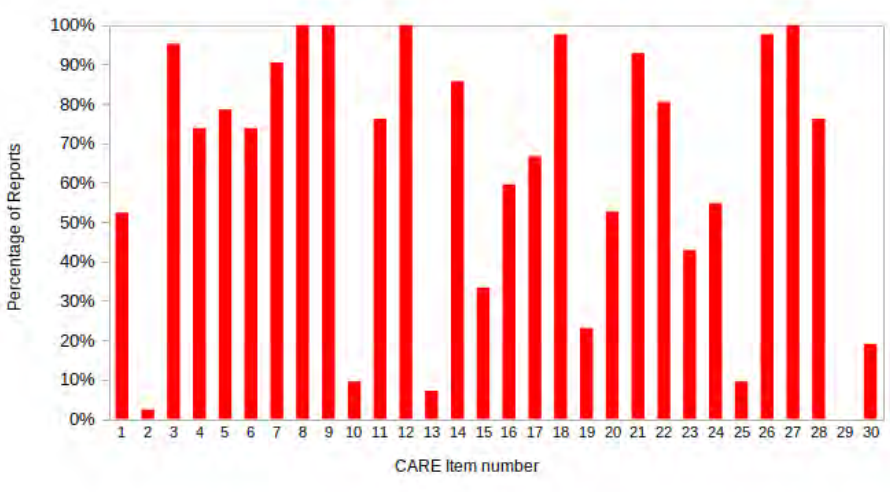



Figure 1: Rate % of Reporting of the 30 CARE item descriptors

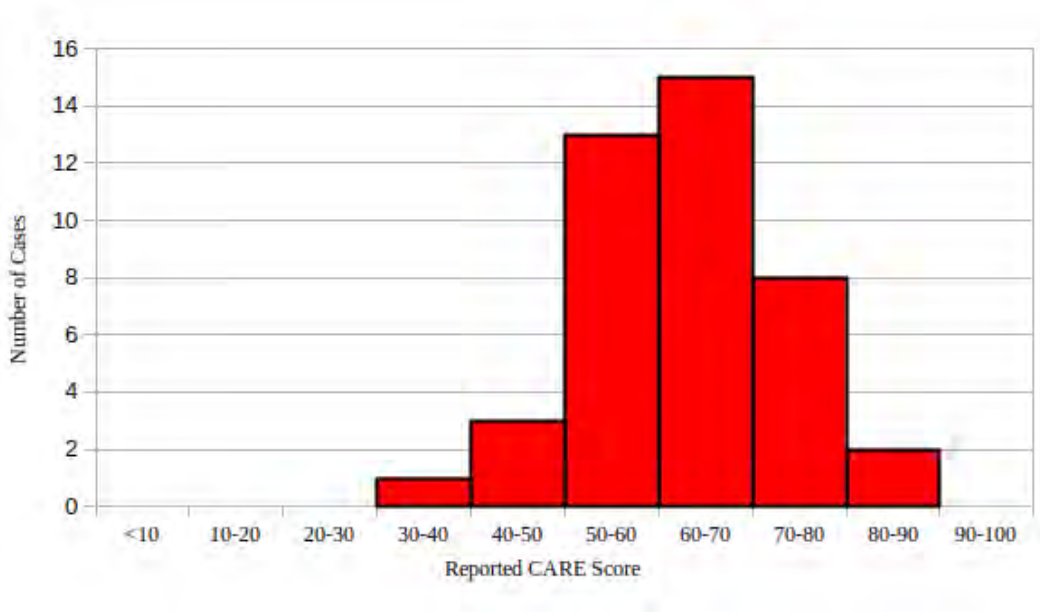



Figure 2: Absolute frequences of cases (vertical axis) and their respective Reported % score for CARE items(horizontal axis)

### 3.4 In Between SR differences

In Table 2 we present the percentage of harmonization with the CARE guidelines of a total of 42 studies, which were found to have a mean of 62%. We also calculated the percentages for the 2 SRs separately. CRs cited in the ISCM due to RCC review were found to have 76% harmonization with CARE guidelines and 55% in ICSCT and ICSCT 55%. Overall differences were not signifficant (p=0.16). See Table 1

### 3.5 IF correlation

P values (a=0.05) and chi-square tests were used to examine statistically significant differences. Higher Impact Factor (IF) journals were found to marginally outclass the lower IF ones only in Main Symptoms and/or Important Clinical Finding, for Relevant Past Interventions with outcomes the lower IF ones outclass the higher ones. All other item descriptors were not significant among different IF categories. Overall differences were not significant (p=0.91). See Table 2

### 3.6 Date of Publication as a factor for differences

Analyzing the 2 pubication groups indepentantly, we found 2 statistically differences in item 7(p=0.016), *Historical and current information from this episode of care 7 organized as a timeline* and item 9d(p=0.017), *Changes in therapeutic intervention (with rationale)*. The rest of items found not to differ significantly. Table 3, presents analytically the effect of publication date, calculating the p value of chi test (a=0.05). No overall statistical difference was found between the 2 groups (p=0.16). See Table 3

**Table 3.** Reporting of item Rate %, in 42 cases, using CARE guidelines, by publication date; before and after 2013.

| | | Reported Item rate % | | | |
|---|---|---|---|---|---|
| | | All the CRs (n=42) | Older CRs Before 2013 (n=35) | New CRs After 2013 (n=7) | p value |
| 1 | The diagnosis or intervention of primary focus followed by the words “case report” | 52 | 54 | 43 | 0.58 |
| 2 | 2 to 5 key words that identify diagnoses or interventions in this case report, including "case report" | 2 | 3 | 0 | 0.65 |
| 3a | Introduction: What is unique about this case and what does it add to the scientific literature? | 95 | 97 | 86 | 0.20 |
| 3b | Main symptoms and/or important clinical findings | 74 | 76 | 71 | 0.88 |
| 3c | The main diagnoses, therapeutic interventions, and outcomes | 79 | 8 | 71 | 0.85 |
| 3d | Conclusion—What is the main “take-away” lesson(s) from this case? | 74 | 74 | 71 | 0.88 |
| 4 | One or two paragraphs summarizing why this case is unique (may include references) | 90 | 91 | 86 | 0.64 |
| 5a | De-identified patient specific information | 100 | 100 | 100 | 0.99 |
| 5b | Primary concerns and symptoms of the patient | 100 | 100 | 100 | 0.99 |
| 5c | Medical, family, and psycho-social history including relevant genetic information | 10 | 11 | 0 | 0.35 |
| 5d | Relevant past interventions with outcomes | 76 | 74 | 86 | 0.52 |
| 6 | Describe significant physical examination (PE) and important clinical findings | 10 | 100 | 100 | 0.99 |
| 7 | Historical and current information from this episode of care organized as a timeline | 7 | 3 | 29 | **0.02** |
| 8a | Diagnostic testing (such as PE, laboratory testing, imaging, surveys) | 86 | 83 | 100 | 0.24 |
| 8b | Diagnostic challenges (such as access to testing, financial, or cultural) | 33 | 31 | 43 | 0.56 |
| 8c | Diagnosis (including other diagnoses considered) | 60 | 57 | 71 | 0.48 |
| 8d | Prognosis (such as staging in oncology) where applicable | 67 | 66 | 71 | 0.77 |
| 9a | Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care) | 98 | 97 | 100 | 0.65 |
| 9b | Administration of therapeutic intervention (such as dosage, strength, duration) | 23 | 22 | 29 | 0.70 |
| 9c | Changes in therapeutic intervention (with rationale) | 53 | 45 | 100 | **0.02** |
| 10a | Clinician and patient-assessed outcomes (if available) | 93 | 94 | 86 | 0.42 |
| 10b | Important follow-up diagnostic and other test results | 80 | 82 | 71 | 0.51 |
| 10c | Intervention adherence and tolerability (How was this assessed?) | 43 | 45 | 33 | 0.61 |
| 10d | Adverse and unanticipated events | 55 | 60 | 29 | 0.13 |
| 11a | A scientific discussion of the strengths AND limitations associated with this case report | 10 | 9 | 14 | 0.64 |
| 11b | Discussion of the relevant medical literature with references | 98 | 97 | 100 | 0.65 |
| 11c | The scientific rationale for any conclusions (including assessment of possible causes) | 100 | 100 | 100 | 0.99 |
| 11d | The primary “take-away” lessons of this case report (without references) in a one paragraph conclusion | 76 | 74 | 86 | 0.52 |
| 12 | The patient should share their perspective in one to two paragraphs on the treatment(s) they received | 0 | 0 | 0 | 0.99 |
| 13 | Did the patient give informed consent? | 19 | 14 | 43 | 0.08 |
| | *OVERALL* | 62 | 64 | 55 | 0.16 |

# 4 CONCLUSIONS

Concluding, none of the analyzed studies marked a perfect score. Best performing categories were the abstract and introduction. Authors overall failed to describe the diagnostic approach efficiently. Family, genetic and psycho-social history was rarely mentioned. Data describing patient's interaction such as his opinion, perspectives, assessed-outcomes even his consent was systematically missing. The explicit referral of "case report" in key-words or the title was absent.

Newer publications found to be superior only in *History and Timeline* and in *Changes in therapeutic intervention.* IF played an ambiguous role, where high ranked journals scored better in describing in *Abstract main symptoms* and *Take-away lessons* but worse in *Relevant past interventions with outcomes.* Finally, the two SRs were statistically different in 7 different item descriptors. This was alerting for possible selection bias.

In a previous SR analyzing splenic metastasis, [11] respective evidence supports our results. More specifically, no CR followed CARE guidelines completely; the median score was 63% (vs 61%) and 80% was the best score (vs 85.7%). Most case included the *type of intervention* (96.4% vs 100%). Deviations observed in the *administration of treatment* (96.4% vs 25%). None of these SRs included patient-assessed outcomes or the patient's perspective either. In another study[19] best reporting rate found to be 78% (vs 85.7), worst 44% (vs 43.3%) and median of 66.7% (vs 61%). It concludes that diagnosis, history, psycho-sociological profile and conclusions were not described satisfactorily.

This study has various limitations. First of all, the small number of CRs analyzed (n=42), increases the possibility of statistical errors.[24] The topic selected may be quite specific thus limiting the number of available studies. Additionally, only two SRs evaluated, further restricting the topic to cervical teratomas and renal cell metastasis. Generalization of the results in other topics may also be affected due above limitations .

Our search was limited to PubMed results. Additional databases such as Cochrane or Scopus should also be considered. The study design comprised two screening phases, one selecting the SRs and one sorting the CRs. This design is developed for a more efficient search strategy especially when the data analysis includes many SRs. In our case, this could have played a role in selection bias.[28]

From 30 studies ,42 different medical cases were retrieved, and analyzed as independent CRs. 12 of these cases found sharing common papers. Deviations were observed to the reporting of 19 statements. This heterogeneity, in conjunction with the uniqueness of each of these rare cases, alongside the extended chronological ranges between cases included in the same paper, and differentiation in the way cases were described and analyzed, are factors upon which this methodological study analysis is based, and the reason for considering these medical cases as independent case reports. However, this method of analysis could have caused bias in our study. In fact, we observed that cases in the same paper, were tending to share identical reporting values for the following statements: 1, 2, 3a, 3b, 3c, 3d, 4, 11a, 11b, 11c, 11d (n=11).

Given the therapeutic importance of surgery in SCTs, SCARE guidelines also were considered as evaluating tool for our study.[1] However, various treatments were found frequently to be selected in recent or past bibliography (ig radiotherapy or corticosteroids) would be excluded from analysis. [17] [20]

There are no many studies analyzing the quality of reporting of CRs and OSs in internationally. More evidence evaluating the quality of reporting of CRs, using tools such as CARE or SCARE guidelines, could increase the epidemiological interest in CRs. Scientific rationale about the detection and management of rare diseases could meliorate significantly.

# 5 Appendix

**Table 4.** Describing SR group, year of publication scores and CARE and IF scores for papers cited in the 2 eligible SRs.

| No | Article Name | SR† | Publication Date | IF | CARE SCORE* |
|---|---|---|---|---|---|
| 1 | Han et al. | 1 | 2015 | 38.1 | 20 /30 |
| 2 | Moon et al. | 1 | 2010 | 1.98 | 17 /30 |
| 3 | Ghostine et al. | 1 | 2009 | 3.27 | 17 /30 |
| 4 | Arvin et al. | 1 | 2009 | 2.97 | 16 /30 |
| 5 | Makary et al | 1 | 2007 | 2.04 | 17 /30 |
| 6 | Ak et al | 1 | 2006 | 1.5 | 13 /30 |
| 7 | Paterakis et al. | 1 | 2006 | 1.6 | 18 /30 |
| 8 | Nonomura et al. | 1 | 2002 | 30.4 | 16 /30 |
| 9 | Cybulski et al. | 1 | 1984 | *** | 15 /30 |
| 10 | Padovani et al. | 1 | 1982 | *** | 16 /30 |
| 11 | Weng et al. | 2 | 2018 | 2.51 | 15 /30 |
| 12 | Altinoz et al. | 2 | 2005 | 1.8 | 22 /28 |
| 13 | Asadi et al. | 2 | 2009 | 1.53 | 25 /30 |
| 14 | Ateaque et al. | 2 | 2000 | 0.5 | 31 /30 |
| 15 | Donovan et al. | 2 | 2006 | 3.1 | 23 /30 |
| 16 | Fakih et al. | 2 | 2001 | 3.2 | ‡ |
| 17 | Gao et al.. | 2 | 2014 | 0.825 | 17 /30 |
| 18 | Gaylor et al. | 2 | 1938 | *** | 16 /30 |
| 19 | Kawakami et al. | 2 | 1973 | *** | 11 /28 |
| 20 | Kaya et al. | 2 | 2003 | 0.5 | ‡ |
| 21 | Malik et al. | 2 | 2018 | 0.5 | ‡ |
| 22 | Parikh et al. | 2 | 2009 | 1.5 | 23/30 |
| 23 | Park et al. | 2 | 2013 | 5.5 | 18/28 |
| 24 | Poggi et al. | 2 | 2001 | 0.42 | 14/30 |
| 25 | Schijns et al. | 2 | 2000 | 0.6 | 20/28 |
| 26 | Zakaria et al. | 2 | 2012 | 0.4 | 16 /28 |
| 27 | Soga et al. | 2 | 2016 | 2.71 | 21 /29 |
| 28 | Islam et al. | 2 | 2016 | 0.2 | 23 /30 |
| 29 | Komura et al. | 2 | 2011 | 0.1 | 20/30 |
| 30 | Isla et al. | ** | ** | ** | ** |
| 31 | Nomoto et al. | ** | ** | ** | ** |
| 32 | Weitzner et al. | ** | ** | ** | ** |
| 33 | Strickland et al. | ** | ** | ** | ** |

*Full names mentioned in Table 5*

*Based on CARE Guidelines.

** Excluded studies

*** Items exluded due to older publication dates. Eligible if greater than 1997

† 1 means ICSCT study, 2 means RCC due to ISCM study

‡ partial scores: Fakih et al.: 19 /30,17 /30,14 /30,19 /30,20 /30,21 /30
Kaya et al. : 20 /24, 29 /28
Malik et al. : 18 /30,19 /29, 18 /29, 19/30,
18 /30, 20 /30, 17 /30, 18 /30

**Table 5.** Retrieved and analyzed papers(CRs and SRs)

| | |
|---|---|
| 1 | Han, Z., Du, Y., Qi, H., Zheng, S., & Yin, W. (2015). Cervical intramedullary immature teratoma with metastatic recurrence in an adult. Spinal Cord Series and Cases, 1(1), 1-4. |
| 2 | Moon, H. J., Shin, B. K., Kim, J. H., Kim, J. H., Kwon, T. H., Chung, H. S., & Park, Y. K. (2010). Adult cervical intramedullary teratoma: first reported immature case: Case report. Journal of Neurosurgery: Spine, 13(2), 283-287. |
| 3 | Ghostine, S., Perry, E., Vaynman, S., Raghavan, R., Tong, K. A., Samudrala, S., ... & Colohan, A. (2009). The rare case of an intramedullary cervical spinal cord teratoma in an elderly adult: case report and literature review. Spine, 34(26), E973-E978. |
| 4 | Arvin, B., Pohl, U., & David, K. (2009). Intramedullary cervical teratoma in an adult. The Spine Journal, 9(5), e14-e18. |
| 5 | Makary, R., Wolfson, D., Dasilva, V., Mohammadi, A., & Shuja, S. (2007). Intramedullary mature teratoma of the cervical spinal cord at C12 associated with occult spinal dysraphism in an adult: case report and review of the literature. Journal of Neurosurgery: Spine, 6(6), 579-584. |
| 6 | Ak, H., Ulu, M. O., Sar, M., Albayram, S., Aydın, S., & Uzan, M. (2006). Adult intramedullary mature teratoma of the spinal cord: review of the literature illustrated with an unusual example. Acta neurochirurgica, 148(6), 663-669. |
| 7 | Paterakis, K. N., Karantanas, A. H., Barbanis, S., Hadjigeorgiou, G. M., & Karavelis, A. (2006). Cervical spinal cord intramedullary teratoma. Clinical neurology and neurosurgery, 108(5), 514-517. |
| 8 | Nonomura, Y., Miyamoto, K., Wada, E., Hosoe, H., Nishimoto, H., Ogura, H., & Shimizu, K. (2002). Intramedullary teratoma of the spine: report of two adult cases. Spinal Cord, 40(1), 40-43. |
| 9 | Cybulski, G. R., Von Roenn, K. A., & Bailey, O. T. (1984). Intramedullary cystic teratoid tumor of the cervical spinal cord in association with a teratoma of the ovary. Surgical neurology, 22(3), 267-272. |
| 10 | Padovani, R., Tognetti, F., Sanpaolo, P., Pozzati, E., Gaist, G., & Kuba, I. (1982). Intramedullary cystic teratoma. Acta neurochirurgica, 62(1-2), 101-108. |
| 11 | Weng, Y., Zhan, R., Shen, J., Pan, J., Jiang, H., Huang, K., ... & Huang, H. (2018). Intramedullary spinal cord metastasis from renal cell carcinoma: a systematic review of the literature. BioMed Research International, 2018. |
| 12 | Altinoz, M. A., Santaguida, C., Guiot, M. C., & Del Maestro, R. F. (2005). Spinal hemangioblastoma containing metastatic renal cell carcinoma in von HippelLindau disease: Case report and review of the literature. Journal of Neurosurgery: Spine, 3(6), 495-500. |
| 13 | Asadi, M., Rokni-Yazdi, H., Salehinia, F., & Allameh, F. S. (2009). Metastatic renal cell carcinoma initially presented with an intramedullary spinal cord lesion: a case report. Cases Journal, 2(1), 1-4. |
| 14 | Ateaque, JL Martin, C. O 'Brien, A. (2000). Intramedullary spinal cord metastases from a hypernephroma 11 years following the diagnosis and treatment of the primary lesion. British journal of neurosurgery, 14(5), 474-476. |
| 15 | Donovan, D. J., & Freeman, J. H. (2006). Solitary intramedullary spinal cord tumor presenting as the initial manifestation of metastatic renal cell carcinoma: case report. Spine, 31(14), E460-E463. |
| 16 | Fakih, M., Schiff, D., Erlich, R., & Logan, T. F. (2001). Intramedullary spinal cord metastasis (ISCM) in renal cell carcinoma: a series of six cases. Annals of oncology, 12(8), 1173-1177. |
| 17 | Metastazı, O. (2014). Intramedullary spinal cord metastasis of renal cell carcinoma 6 years following the nephrectomy. Turkish neurosurgery, 24(2), 294-296. |
| 18 | Gaylor, J. B., & Howie, J. W. (1938). Brown-Séquard syndrome: A case of unusual aetiology. Journal of neurology and psychiatry, 1(4), 301. |
| 19 | Kawakami, Y., & Mair, W. G. P. (1973). Haematomyelia associated with anticoagulant therapy, an intramedullary ependymoma and Schwann cells. Acta neuropathologica, 26(3), 253-258. |
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| 22 | Parikh, S., & Heron, D. E. (2009). Fractionated radiosurgical management of intramedullary spinal cord metastasis: a case report and review of the literature. Clinical neurology and neurosurgery, 111(10), 858-861. |
| 23 | Park, J., Chung, S. W., Kim, K. T., Cho, D. C., Hwang, J. H., Sung, J. K., & Lee, D. (2013). Intramedullary spinal cord metastasis in renal cell carcinoma: a case report of the surgical experience. Journal of Korean medical science, 28(8), 1253-1256. |
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| 26 | Zakaria, Z., Fenton, E., Jansen, M., & O'Brien, D. (2012). The occult nature of intramedullary spinal cord metastases from renal cell carcinoma. Case Reports, 2012, bcr2012007476. |
| 27 | Soga, H., & Imanishi, O. (2016). Case of intramedullary spinal cord metastasis of renal cell carcinoma. World Journal of Clinical Urology, 5(1), 72-74. |
| 28 | Islam, M. R., Rahman, T., Habib, R., Rahman, A., Bhowmik, N. B., & Haque, M. A. (2016). Renal Cell Carcinoma presented with An Intramedullary Spinal Cord Metastasis: A Case Report. Bangladesh Critical Care Journal, 4(1), 51-53. |
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| 30 | Isla, A., Pérez-López, C., Budke, M., Gutiérrez, M., & Frutos, R. (2005). Intramedullary spinal cord metastasis as the first manifestation of a renal carcinoma. Neurocirugia (Asturias, Spain), 16(4), 359-364. |

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