Author’s response to reviews

Title: Spinal epidural hematoma without significant trauma in children: Two case reports and review of the literature

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Dear editors

We would like to thank BMC Pediatrics for the review of our article entitled: “Spontaneous spinal epidural hematoma in children: Two case reports and systematic review of the literature”, which we submitted to BMC Pediatrics. We have read the comments of the 4 reviewers with
We were able to reply to most of the questions and comments. Reviewer 1 and Reviewer 4 also raised formal issues. As we only have a limited number of words, presentations and tables as well as references available in the current format (Case Report), we have decided to present a large part of the relevant information in tabular form in an appendix. We have also used the subtitles as indicated by your journal. We are of the opinion that the form of a case report with literature overview fits the topic well. However, if you would like us to submit the manuscript as a regular review article and adapt the manuscript accordingly, we would be happy to do so.

Thank you again for your kind review of the manuscript. If you have any additional questions, please feel free to contact us.

Yours sincerely

Sebastian Grunt for the whole research team

Response to Reviewers:

Reviewer reports:


This work described two case of acute pediatric spinal epidural hematoma with a pertinent review. The topic is interesting, but the study presents with some critical issues. From the title, the two cases are described and classified as "spontaneous". However, this definition has to be considered in appropriate, as reported in recent literature1: "We did not define any groups under the term "spontaneous" because, in the literature, this term is used to describe patients with idiopathic SEH as well as those with coagulopathy, female patients who were pregnant, patients undergoing treatment with antiplatelet drugs, those with vascular malformations, or patients with a combination of these conditions, leading to some confusion in terminology.". Indeed, the first of the cases is considered to be "idiopathic", without any known etiology, while the other one may be a consequence of an arteriovenous malformation.

We thank the reviewer for this important input. The term "spontaneous spinal epidural hematoma" which is often used in literature is indeed not always accurate. We have therefore decided to omit the term "spontaneous spinal epidural hematoma" and replace it with “spinal epidural hematoma without significant trauma”. In the revised article we specifically mentioned this as follows:

“In literature, the term "spontaneous spinal epidural hematoma" was used to describe SEH without clear traumatic etiology. Since this term, however, covers cases of idiopathic SEH,
bleeding due to coagulopathy or vascular malformations and hemorrhages after minor trauma, it was recommended to avoid the terminology. In the present article we therefore use the term “SEH without significant trauma”. (Page 4, lines 1-6)

We additionally referred to the mentioned reference (now reference 1). The corresponding text passages in the manuscript and abstract have also been adapted accordingly. The title has now been changed to "Spinal epidural hematoma without significant trauma in children: Two case reports and systematic review of the literature".

The introduction is replaced by a "Background" reporting some improper conclusions (Pag. 4). Line 6: "It is mostly observed in adults during the fourth and fifth decades," whereas it has been recently1 reported that "The age distribution curve in decades was bimodal with peak prevalence in the 2nd and 6th decades.". This finding allows to distinguish the etiology in young and adult patients separately, and should be discussed in this work.

We thank the reviewer for this helpful explanation. In the introduction we have now noted the following:

“The condition mostly observed in adults with a bimodal distribution with peak prevalence in the 2nd and 6th decades with an estimated incidence of 0.1 per 100,000 patients per year.” (Page 4, line 6-8)

Line 25: "Early surgical decompression likely leads to good outcomes" whereas it has been stated in literature that "Coagulopathy, greater size (length) of SSEH, and preoperative complete spinal dysfunction were found to contribute to poor postoperative functional recovery (p &lt; 0.05).". Regardless of etiology, pre-operative status and size of hematoma, early surgical intervention is not the only factor able to influence the outcome.

We thank the reviewer for this important input. We have now adapted the text accordingly and noted the following:

Although surgery seems to be preferred to conservative treatment in adults, some factor are determining in the choice of treatment: preoperative neurological status, coagulopathy and the length of SEH contribute to poor postoperative functional recovery. (Page 4, lines 16-19)

Paragraphs on Materials and Methods and Results are lacking. Section about Discussion and Conclusions include all previous issues.

The layout of the text and the subtitles of the article followed the guidelines of the journal. Other case reports with systematic literature reviews were also presented in the same manner in BMC Pediatrics. We would like to leave it to the editors whether the layout and/or the subtitles of the article should be adapted according to these comments of the reviewers or not.

Pag. 6 e 7 of Discussion and Conclusions, comprising the cited tables, describe results of the review in relation to "Appendix 1", which is not cited in the work.
Since the references concerning the literature search exceeded the number of references allowed, we have decided to mention all references (130 in number) in an appendix, which also summarizes the cases described. We leave it up to the editors whether these references should be mentioned in the manuscript itself or whether the currently selected presentation with the appendix is sufficient.

Despite the literature reported, conclusions do not suggest new insights about etiology and treatment of pediatric epidural hematomas. In conclusion, even though the topic is undoubtedly interesting, the way through which the work has been built is poor, it does not perform an accurate review of the literature and does not distinguish pediatric features of this pathology from those of the general population. In such a presentation, publication is not advised, even if it might occur with a huge review of the work.

We thank the reviewer for his critical words. In fact, it was difficult to summarize all aspects of a review in the form of a case report. Like previous articles with case presentations and literature reviews in the same journal, we have followed the journal's guidelines and tried to cover the paediatric aspects as best as possible. If the editors wish us to use a different form of presentation, we will be happy to adapt this. We are however of the opinion that, despite the limitation of the given presentation, we have nevertheless succeeded in pointing out important aspects of this rare but threatening disease in childhood.

References

1) - Domenicucci M et al.: Spinal epidural hematomas: personal experience and literature review of more than 1000 cases. J Neurosurg Spine; 27(2):198-208, 2017

Domenicucci Maurizio MD

Jonathan Roth (Reviewer 2): The paper relates to a rare by important pathology. Increase in awareness of these pathologies may reduce morbidity associated with spontaneous spine epidural hematomas. The paper is well written and gives a nice overview on this rare pathology. I recommend to accept as is.

We thank the reviewer for his positive evaluation

Hiroshi Yamaguchi (Reviewer 3): This paper reports two case reports of SSEH in children and there is also an extensive review of the pediatric literature for this entity. I think this an excellent review (with two case reports) of a fairly rare condition. The case report is well written, with a few minor changes.
General comments
- Authors mention that SSEH is defined as a spontaneous epidural hematoma without "traumatic etiology" and articles reporting cases of traumatic spinal epidural hematoma were excluded. However, authors describe that trivial spine trauma preceded SSEH in 20% and in 55% of the children with cervical SSEH, minor spinal trauma preceded the bleeding in discussion part. Please clarify this issue. Did authors exclude the articles which report SSEH after trivial trauma event?

We thank the reviewer for that question. In the literature search, cases with spinal epidural bleeding were included when a minor trauma (as in the case described) preceded bleeding, but only when the trauma was so minimal that it was not considered the primary etiology of the bleeding. Since the terminology for “spontaneous epidural haemorrhage” can be confusing (see also comments on Reviewer 1’s remarks), we have now chosen the term "spinal epidural hematoma without significant trauma" instead. We hope this will make it clearer what cases have been included.

Specific comments
Abstract
Background

- This case report and systematic review of the literature illustrates the clinical presentation, risk factors, and outcomes of spontaneous spinal epidural hematoma in children.

→"This case report and systematic review of the literature illustrates the clinical presentation, risk factors, evaluation, treatment and outcomes of spontaneous spinal epidural hematoma in children." may be better.

We have now adapted the manuscript accordingly (see page 3, lines 5-6).

Case presentation
It may be better to insert the location of epidural hematoma in both 2 cases in case presentation of the abstract.

This has been adjusted accordingly (see page 3, lines 10 and line 14)

Keywords
Authors do not need to include spontaneous spinal epidural hematoma because this is included in the title.

In the current version we have inserted the term "Spinal epidural hemorrhage" instead of "spontaneous spinal epidural hematoma " (page 3, line 25; see also comments to Reviewer 1)

Dimitrios Christos Nikas, MD (Reviewer 4): Although only two cases, there is little in the literature on the subject of management of spontaneous epidural hematoma (sEH) in children. The presentation, workup, and management of this pathology reflects well why children should not be managed as small adults.
The authors need to particularly be commented for the comprehensive literature review. They could make a stronger point in their conclusions if they included a more comprehensive list of the already published cases of sEH resolution without surgical management. A table including presentation, coagulation profile, management, time to resolution, residual deficits would serve the reader well.

We thank the reviewer for this important input. These points are recorded separately in Appendix 1. We have decided to present this detailed information on the individual cases described in the form of an appendix, as this table would probably be too long and too detailed for a regular placement within the article.

There have been several proposed mechanisms to explain the resolution of sEHs (associated fracture, pressure gradients, redistribution of hemorrhage, clot resorption due to proliferation of endothelial cells and dural supportive tissue). Based on presentation and serial imaging of the second case they describe, what do the authors advocate as the possible mechanism of spontaneous resolution in their case?

We thank the reviewer for this important comment. In this case, we cannot determine the exact mechanism. Since there is no fracture, all the factors listed by the reviewer are possible. We have therefore inserted the following passage in the text “The exact mechanism of blood clot dissolution in case 2 remains unclear. Various mechanisms - such as redistribution of bleeding, or absorption of the clot by proliferation of endothelial cells or dural supportive tissue - may be responsible.” (page 9, lines 19-22)

In the absence of trauma was non-accidental injury suspected or ruled out?

We thank the reviewer for this input. In both described cases there was no anamnestic evidence for a non accidental trauma. We have added this point in the manuscript (see page 5, lines 3-4 and page 5, line 21-22)

The authors of this manuscript provide further evidence that surgical intervention is not uniformly indicated when focal neurological findings are absent, and conservative management should always be considered for these patients, particularly in the pediatric population.

We thank the reviewer for that remark. In the current revision we have now noted:

“However, case 2 illustrates that not all cases with SEH without significant trauma in children require a surgical approach. In the literature review 36 of 151 patients did not undergo surgery, because of factor replacement for hemophilia (27 cases), rapid resolution of symptoms (4 cases), or no neurological deficit (5 cases). In cases (such as in our case 2) with long hematoma (less compressive) and in stable patients with minimal neurological deficit, or in cases with early resolution of the hematoma, conservative management may be considered.” (page 9, lines 14-19)