Fwd: JBCPP.2020.0464 - DecisionRevise with Major Modifications

From: niswahnilam (niswahnilam@gmail.com)

To: hanikhidayati@yahoo.com

Date: Wednesday, January 13, 2021 at 06:59 PM GMT+7

Dikirim dari Redmi 4 saya
---------- Pesan terusan----------
Dari: niswahnilam <niswahnilam@gmail.com>
Tanggal: 5 Jan 2021 3.38 AM
Subjek: Fwd: JBCPP.2020.0464 - DecisionRevise with Major Modifications
Kepada: oktafiananurhidayati <oktafiananurhidayati@gmail.com>
Cc:

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Dari: Journal of Basic and Clinical Physiology and Pharmacology <onbehalfof@manuscriptcentral.com>
Tanggal: 3 Jan 2021 11.00 AM
Subjek: JBCPP.2020.0464 - DecisionRevise with Major Modifications
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Cc: scientificicph@ff.unair.ac.id

02-Jan-2021

Dear Mrs. Qonita:

Thank you again for submitting your manuscript ID JBCPP.2020.0464 entitled "A Case Report: Effect of Hydrocortisone on Hypocorticolism
Caused by Pituitary Adenoma" to Journal of Basic and Clinical Physiology and Pharmacology (JBCPP). Your manuscript has been reviewed and requires major modifications prior to acceptance. The comments of the reviewer(s) are included at the bottom of this letter.

I invite you to respond to the reviewer(s)' comments and revise your manuscript.

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Once again, thank you for submitting your manuscript to JBCPP. I look forward to receiving your revision.

Kind regards
Dr. Suciati Suciati
Guest Editor, Journal of Basic and Clinical Physiology and Pharmacology

Reviewer(s)' Comments to Author:

Reviewer: 1

Comments to the Author
The manuscript describes the case of Hypocortisolism that was treated with Hydrocortisone. The background of the case needs to be focused on why this case needs to be reported. The case report is relatively clear. The discussion could be improved by focusing on the phenomena during treatment and the reasoning behind the drug of choice.
Major concern:
1. The author needs to consult professional proofreading services due to many ineffective sentences, typological errors, and uncommon medical diction.
2. It is still unclear why the case report is needed in this case.
3. Conclusion: Hydrocortisone is a therapy used for hypocortisolism in pituitary adenomas. This should not be the conclusion of the case study. The case study conclusion should focus on the clinical phenomena that occurred under the therapy. The decision of effectiveness may only be a possibility because no RCT method is done during this study.
4. The hydrocortisone given is a high dose of hydrocortisone, so to stop the therapy, tapering off is done to avoid side effects. This conclusion is elusive. There is no information focused on the tapering down of the medicine in the case.

Minor notes:
Please prevent to use “will” or “can” to illustrate a theoretical statement.
It is uncommon to use the following phrase in the medical reports; “In the history..”, “laboratory exam and support..”, “with oxygen mask of ...”, “ex. ...”
No need to attach the informed consent. The crucial issue inside the consent is more important to be reported.

Reviewer: 2

Comments to the Author
As attached in files.

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JBCPP.2020.0464_Proof_hi- review_NHMH_01012021.pdf
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DE GRUYTER **Journal of Basic and Clinical Physiology and Pharmacology**

A Case Report: Effect of Hydrocortisone on Hypocorticolism Caused by Pituitary Adenoma

Journal:	*Journal of Basic and Clinical Physiology and Pharmacology*
Manuscript ID	JBCPP.2020.0464
Manuscript Type:	Case Report
Date Submitted by the Author:	29-Nov-2020
Complete List of Authors:	Qonita, Niswah; Airlangga University, Master of Clinical Pharmacy Progam Hidayati, Hanik B; Dr Soetomo General Hospital, Department of Neurology
Section/Category:	• Behavior and Neuroprotection
Keywords:	Hydrocortisone, hypocorticolism, pituitary adenoma
Abstract:	Background: Pituitary adenoma is a tumor that can cause hormone secretion disorders, one of which is hypocorticolism. Hypocorticolism has a negative impact, namely an increase in proinflammatory cyctokines and immune system activation. The therapy given for hypocorticolism is high doses of hydrocortisone. This case report is presented hypocorticolism therapy with hydrocortisone in a patient with pituitary adeoma. Case Presentation: A 17 year old boy presented with loss of right eye vision, headache, and difficulty swallowing. During hospitalization the patient experienced mild depression. Magnetic resonance imaging (MRI) examination of the brain with contrast revealed an intracellar supratentrial axial lesion extending to the suprasellar. Based on the results of the history, physical examination, laboratory examination and support, the patient was diagnosed with hophysis macroadenoma. On laboratory examination, there was a hypocorticolism <0.5 μg / dL (reference value 4,30-22,40 μg/dL). Patients receive hydrocortisone therapy 200 mg / day, then tappering off to 100 mg / day, tappering off is done to avoid the side effects of giving high doses of hydrocortisone. In addition, patients received endoscopic endonasal transshenoidal hypophysectomy (EETH). There was an increase in pre-treatment cortisol <0.5 μg / dL and 5.3 μg / dL post-treatment and there was no side effect while the patient was hospitalized. Conclusion: Hydrocortisone is a therapy used for hypokoricolism in pituitary adenomas. The hydrocortisone given is a high dose of hydrocortisone, so to stop the therapy, tappering off is done to avoid side effects.

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Niswah N. Qonita, Hanik B. Hidayati*

A case report: effect of hydrocortisone on hypocorticolism caused by pituitary adenoma

DOI: https://doi.org/xxxxx/xxxxxxxxxx

Received: Month Day, Year; **Accepted:** Month Day, Year

Abstract

Objectives: Pituitary adenoma is a tumor that can cause hormone secretion disorders, one of which is hypocorticolism. Hypocorticolism has a negative impact, namely an increase in proinflammatory cyctokines and immune system activation. The therapy given for hypocorticolism is high doses of hydrocortisone. This case report is presented hypocorticolism therapy with hydrocortisone in a patient with pituitary adeoma.

Case Presentation: A 17 year old boy presented with loss of right eye vision, headache, and difficulty swallowing. During hospitalization the patient experienced mild depression. Magnetic resonance imaging (MRI) examination of the brain with contrast revealed an intracellar supratentrial axial lesion extending to the suprasellar. Based on the results of the history, physical examination, laboratory examination and support, the patient was diagnosed with hophysis macroadenoma. On laboratory examination, there was a hypocorticolism <0.5 µg / dL (reference value 4,30-22,40 µg/dL). Patients receive hydrocortisone therapy 200 mg / day, then tappering off to 100 mg / day, tappering off is done to avoid the side effects of giving high doses of hydrocortisone. In addition, patients received endoscopic endonasal transshenoidal hypophysectomy (EETH). There was an increase in pre-treatment cortisol <0.5 µg / dL and 5.3 µg / dL post-treatment and there was no side effect while the patient was hospitalized.

Conclusions: Hydrocortisone is a therapy used for hypokoricolism in pituitary adenomas. The hydrocortisone given is a high dose of hydrocortisone, so to stop the therapy, tappering off is done to avoid side effects.

Keywords: hydrocortisone; hypocorticolism; pituitary adenoma

Introduction

Pituitary adenoma is a tumor of the pituitary gland which usually appears in the anterior pituitary[1]. Pituitary adenoma is an intracranial tumor that often occurs in adolescents to middle age, with the same incidence of women and men. Based on the size of the pituitary adenoma, it is classified into three types, micro adenoma (<10mm), macro adenoma (> 10mm), and giant adenoma (> 40mm) [2].Pituitary adenoma is also divided based on the presence or absence of clinical

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4 syndromes due to hormonal hypersecretion, namely the functioning of the pituitary adenoma and non-functioning pituitary
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6 adenoma[3].

The prevalence of pituitary adenoma is estimated at 0.2% with incidence of 2 cases out of 100,000 population[4]. About 30% of pituitary adenoma tumors are non-functioning pituitary adenomas. The exact prevalence of a non-functioning pituitary adenoma is difficult to determine because many patients are asymptomatic[3]. Meanwhile, the incidence of pituitary adenoma, both microadenoma and macroadenoma, is very rare in the population of children and adolescents, with a prevalence of 1: 1000.000[5].

The pathogenesis of most pituitary adenomas is still unknown with certainty. Therefore genetic evaluation does not guarantee cause of pituitary adenoma, unless the patient has a family history of [6]. Pituitary adenomas are not detected clinically or have no specific clinical manifestations, so it usually causes the diagnosis of pituitary adenoma to be delayed[7]. Clinical symptoms of pituitary adenoma develop due to hyperprolactinoma with or without hypopituitarism, as well as due to tumor mass effects. Hypopituitarism that often occurs is growth hormone deficiency and hypogonadism, while hypocorticolism is very rare[8].

The goals of pituitary adenoma therapy are to normalize serum prolactin, remove tumors or reduce tumor size, and improve hypopituitarism recovery[8]. Therapy in pituitary adenomas is pharmacological dopamine agonist therapy, surgery, and radiotherapy. Treatment of hypocortisolism is given glucocorticoid replecment.

Case Presentation

A 17 year old boy presents with headaches, difficulty swallowing, vomiting especially in the morning, and visual disturbances in the right eye. Vision problems experienced by the patient in the form of blurred eyes and double vision since 5 months before being admitted hospital. The patient experienced loss of vision in the right eye one week before admission hospital. The patient was diagnosed with pituitary macroadenoma in August 2019.

In the history, it was found that the patient had mild depression, blood pressure 110/80 mmHg, pulse 80 beats per minute, respiratory rate 20 times per minute, temperature 36.8 ° C, and oxygen saturation 98% with oxygen mask of 6 liters per minute. . Neurological examination on Glasgow E4V5M6 coma scale, negative meningeal sign, negative facial palsy, and negative lingual palsy. Based on the results of funduscopy and confrontation tests of the right and left eyes, it was found that atrophy and blindness in the right eye. Sensory examination within normal limits and motor skills suggest general weakness.

MRI examination of the brain with contrast revealed a supratentorial extra-axial lesion in intrasellar extending to the supracellar, a clear border of 1.3 x 2.1 x 2.31 cm irregular edge that pressed against the right optic nerve and optic chiasm and caused edema of the right optic nerve, which supports the appearance of pituitary macroadenoma (Figure 1).

In a preoperative laboratory examination on December 20, 2019, it was found that hypocortisol <0.5 μg / dL (reference value 4.30-22.40 μg / dL). On 23 December 2019, an Endoscopic Endonasal Transsphenoidal Approach (EETA) was performed. The results of the anatomical pathology examination showed pieces of tumor tissue arranged in sheets. The tumor consists of cells with a round nucleus, relatively monotonous, smooth chromatin, eosinophilic cytoplasm, no visible mitosis, no signs of malignancy. The results of the anatomical pathology examination are presented in Figure 2. Patients receive hydrocortisone therapy 200 mg / day, then tappering off to 100 mg / day. Patient consent was obtained by signing the informed consent form (attached).

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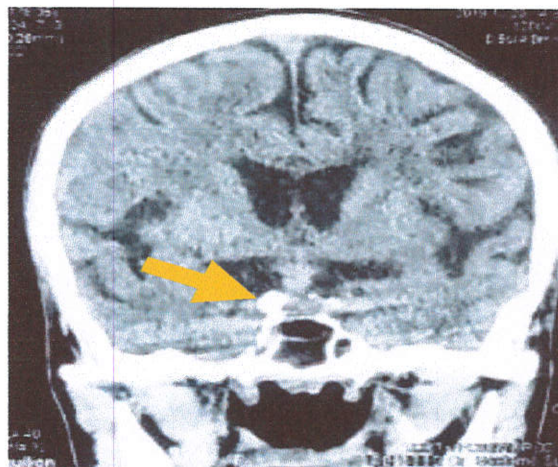

Figure 1. MRI results before the EETA procedure

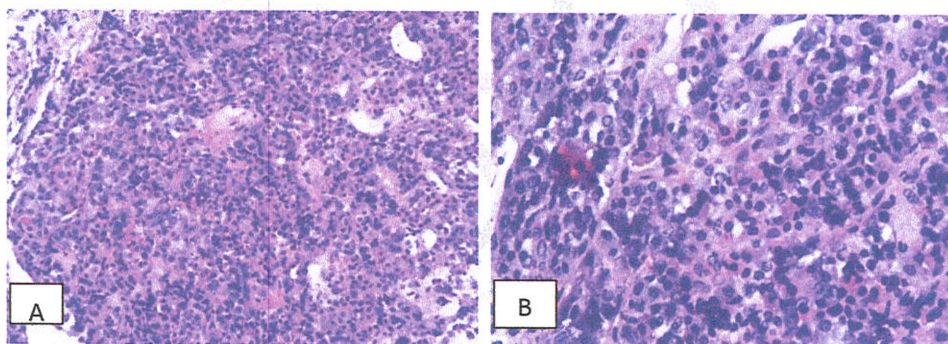

Figure 2. Tumor histopathological examination results

Discussion

Pituitary adenoma is one of intracranial tumor that often occurred in adult population but the prevalence in children and adolescents is small[3]. Prior studies reported pituitary adenoma only happened in 1 : 1000.000 of children population [5]. In our case patient was a 17 years old that diagnosed with macroadenoma hypophysis.

Pituitary adenoma are categorized as functioning adenoma (hormone secreting) and non-functioning adenoma (non-secreting). Functional adenomas are more common and tend to present earlier, in younger patients, with symtoms or signs of hormone excess (ex. Hyperprolactinaemia). In contrast, non-functioning adenomas are clinically silent until lesion has become large enough (usually >1 cm) to have mass effect [7]. Clinical symptoms of pituitary adenoma develop due to hyperprolactinoma with or without hypopituitarism, as well as due to tumor mass effects. Hypopituitarism that often occurs is growth hormone deficiency and hypogonadism, whereas hypocorticolism was less common [5].

Pasien presented an adrenal crisis, which characterized by hypotension, abdominal symptoms, nausea, vomiting, altered mental state, fatigue, fever, and laboratory abnormalities. Our patient presented with loss of right eye vision, headache, difficulty swallowing, and vomiting especially in the morning at admission. In addition, the patient also experienced hypocortisol <0.5 μg / dL (reference value 4.30-22.40 μg / dL).

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Hypocorticolism have wide spectrum of clinical symptoms and signs. Diagnosis of hypocorticolism recommend measuring serum cortisol level at 8-9 AM, and plasma corticotropin as the first line test for diagnosing. In addition, recommend measuring plasma aldosterone and renin activity. Corticol level < 3 μg / dL is indicative of hypocorticolism[9,10].

The daily physiological production of cortisol is about 5-6 mg/m² body surface area. Recommendation hormone replacement therapy for hypocorticolism is hydrocortisone 15-25 mg, usually given in two to three doses per day, with 50-66% given in the morning on awakening. If given two times a day, the second dose is usually given 6-8 h after the morning dose. If given three times per day, the second dose is given 4-6 h after the early morning dose and the third dose 4-6 h after this. Some clinicians recommend weight-adjusted dosing to reduce intervals of excess in cortisol concentrations during the day and decreases variability of cortisol profiles[11]. In acute illness possibly attributable to hypocorticolism, a different diagnostic strategy should be applied, because immediate therapeutic intervention is absolutely needed even before the diagnosis is formally confirmed[9].

In this patient who was diagnosed with pituitary macroadenoma apart from experiencing hypocorticolism, the patient also experienced hyperprolactinemia who would receive dopamine agonist therapy, namely bromocriptine and also EETA (Endoscopic Endonasal Transsphenoidal Approach). Hypocorticolism therapy modalities in patients undergoing pituitary surgery are recommended using stress doses of steroid before surgery and tapered doses after surgery before repeating testing. In these patients, hydrocortisone therapy before surgery. Patients received hydrocortisone 100 mg IV morning and night for four days from 21-24 December 2019, then tappering off to 100 mg / day. Tappering off is done to avoid the side effects of giving high doses of hydrocortisone. The EETA (Endoscopic Endonasal Transsphenoidal Approach) was carried out on 23 December 2019. There was an increase in pre-treatment cortisol <0.5 μg / dL and 5.3 μg / dL post-treatment and there was no side effect while the patient was hospitalized.

Hydrocortisone is short action glucocorticoid, with elimination half life 1-2 hours. Hydrocortisone is primarily bound to corticosteroid-binding globulin (transcortin). When transcortin binding sites are saturated, hydrocortisone binds to albumin. Only 5% to 10% is unbound and biologically active. Hydrocortisone is metabolized in the tissues and the liver to biologically inactive compounds, including glucuronides and sulfates. Hydrocortisone is excreted in renal, less than 1% of hydrocortisone is excreted unchanged in the urine [12].

Conclusions

Hydrocortisone is a therapy used for hypokoricolism in pituitary adenomas. The hydrocortisone given is a high dose of hydrocortisone, so to stop the therapy, tappering off is done to avoid side effects.

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This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you and/or any co-authors received, either directly or indirectly (via your institution), to enable the completion of the work. Checking „No" means that you and any co-authors did the work without receiving any financial support from any third party - that is, the work was supported by funds from the same institution that pays the salary and that institution did not receive third-party funds with which to pay you and/or any co-authors. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check „Yes".

3 RELEVANT FINANCIAL ACTIVITIES OUTSIDE THE SUBMITTED WORK

This section asks about any financial relationships you or any co-authors might have with entities in the scientific arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. Report all sources of revenue paid (or promised to be paid) directly to you, any co-authors or related institutions on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so. For grants you or any co-authors have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. This section also asks about intellectual property such as patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

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SECTION 1.

IDENTIFYING INFORMATION - SUBMISSION

1. Effective Date (Day-Month-Year) 29-11-2020
2. Manuscript Title A case report: effect of hydrocortisone on hypocorticolism caused by pituitary adenome
3. Manuscript Identifying Number (if you know it)

IDENTIFYING INFORMATION - SUBMITTING AUTHOR

1. Given Name (First Name) Niswah Nilam
2. Surname (Last Name) Qonita
3. Are you the corresponding author? Yes ☐ No ☑

Corresponding Author's Name Hanik Badriyah Hidayati

IDENTIFYING INFORMATION - CO-AUTHOR

Please add all co-authors of your manuscript. Please ensure that you collected all relevant information of your co-authors correctly, since the submitting author is responsible for the accuracy and completeness of the submitted information.

THE WORK UNDER CONSIDERATION FOR PUBLICATION		
Last name	First name	Initials
Qonita	Niswah N	NIL
Hidayati	Hanik B	HAN

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SECTION 2.

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Are there any relevant conflicts of interest? Yes [ ] No [x]

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	☐		☐	☐		
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Other	☐		☐	☐		
	☐		☐	☐		
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* This means money that your institution received for your efforts on this study.
** Use this section to provide any needed explanation.

SECTION 3.

RELEVANT FINANCIAL ACTIVITIES OUTSIDE THE SUBMITTED WORK

Place a check mark in the appropriate boxes in the table to indicate whether you or any co-author have financial relationships (regardless of the amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the „Add +". You should report relationships that were present during the 36 months prior to submission. Indicate the person involved by adding the initials in the respective row.

Are there any relevant conflicts of interest? Yes ☐ No ☑

If yes, please fill out the appropriate information below. Complete each row by checking "No" or providing the requested information.

If the relevant information exceeds the available rows, please fill in an additional form and upload this as separate file to the submission system.

RELEVANT FINANCIAL ACTIVITIES OUTSIDE THE SUBMITTED WORK						
Type of Relationship	No	Initials	Money paid to You	Money paid to Your Institution*	Name of Entity	Comments**
Board Membership	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Consultancy	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Employment	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Expert testimony	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		

Grants/grants pending	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Payment for lectures including service on speakers bureaus	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Payment for manuscript preparation	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Patents (planned, pending or issued)	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Royalties	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Payment for development of educational presentations	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Stock/stock options	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		

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Travel/accommodations/meeting expenses unrelated to activities listed	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
Other	☐		☐	☐		
	☐		☐	☐		
	☐		☐	☐		
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* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

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SECTION 4.

OTHER RELATIONSHIPS

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

- [x] No other relationships/conditions/circumstances that present a potential conflict of interest
- [ ] Yes, the following relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

SOURCES

This form is based on the ICMJE Form for Disclosure of Potential Conflicts of Interest form (to be found here: http://www.icmje.org/conflicts-of-interest/).

Strictlyadhere to the given format.
Statements on Informed consent and Ethical approval may be removed **if not applicable**.

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Author contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests

Authors state no conflict of interest.

Informed consent

Informed consent was obtained from all individuals included in this study.

Ethical approval

In Dr. Soetomo General Hospital do not need ethical approval for writing case report.