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Concurrent Isoniazid Toxicity and Eclampsia; Unveiling a Dual Pathology in Pregnancy; A Case Report

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ABSTRACT

Introduction: *This case study explores a unique medical presentation involving a 17-year-old primigravida female at 24 weeks gestation who arrived after experiencing witnessed convulsions at home. The following account details the patient's initial presentation, the management strategies, the outcomes, and the significant learning points around this case.*

Patient Presentation: *Initial examination showed a 17-year-old primigravida at 24 weeks gestation in a post-ictal state and elevated systolic blood pressure. Intervention commenced under the initial assumptive diagnosis of eclampsia. However, a collateral history obtained throughout the management revealed a possible secondary underlying pathology of Isoniazid toxicity with potential concomitant eclampsia.*

Management and Outcome: *Managing the patient necessitated addressing both the presumed eclampsia and Isoniazid toxicity simultaneously. Both the conditions were treated simultaneously rather than focusing on a single pathology. The case describes a positive outcome as both mother and infant survived.*

Conclusion and Contribution: *This case highlights the critical importance of considering and differentiating between multiple coexisting conditions, especially in an emergency setting where a single pathology will already explain the patient's signs and symptoms. It further highlights the risk stratification of different treatment modalities.*

Methodology

Study Design: *This report presents a single case study It was completed by the treating physicians at Kalafong Hospital Emergency unit. The patient presented in 2023.*

Participant Information, informed consent and ethical clearance: *The participant involved in this study was a single individual. Relevant informed consent was obtained (Annexure A). Ethical clearance was also obtained (Annexure B).*

Data Collection and Analysis: *Data pertaining to the patient was documented and reviewed following retrospective review of the patient records.*

Keywords

Eclampsia, Pre-eclampsia, Overdose, Isoniazid toxicity, Seizures.

Introduction

The case highlights complexity of diagnosing and treating pregnant patients who may have multiple concurrent pathologies. It shows the importance of a good collateral history, along with thorough clinical assessment, prompt diagnostic testing, and the administration of targeted therapies to address each pathology. In this instance, the patient's initial presentation pointed toward

Table 1: Series of blood gas results

	Immediately post 1st seizure in unit	Post Intubation	1 hour post intubation	2.5 hours post intubation and post pyridoxine administration
pH	6.588	6.762	7.014	7.219
pCO_2 (mmHg)	46.0	28.1	40.0	29.4
PO_2 (mmHg)	26.2	350	49.8	52.3
K (mmol/L)	4.9	3.3	3.6	3.3
Na (mmol/L)	154	140	139	140
Ca (mmol/L)	1.43	1.30	1.20	1.15
Cl (mmol/L)	113	107	109	111
Lactate (mmol/L)	28	21	13.1	8.4
Glucose (mmol/L)	12.3	12.8	10.0	6.9
Base Excess (mmol/L)	-28.7	-27.5	-20.5	-14.6
HCO_3 (mmol/L)	2.9	4.6	9.1	12.9
Anion Gap (mmol/L)	36.8	29.4	error	18.1

eclampsia, but concurrent concerns about Isoniazid toxicity complicated the diagnostic process.

Case Report

A 17-year-old primigravida female at 24 weeks gestation was brought into the emergency unit with a history of convulsions at home. The family suspected her of ingesting an unknown substance in a suicide attempt.

The patient was brought to the resuscitation area where on arrival she had a generalized tonic clonic seizure, which was aborted using Diazepam 5mg intravenously. After 2min the patient had a another seizure, again aborted with 5mg Diazepam intravenously.

Vital signs recorded: blood pressure 146/60 mmHg, pulse 137 bpm, axillary temperature 36.2°C, oxygen saturation 95% (on FiO2 of 80%) and a fingerpick blood glucose 12.3mmol/L.

During the initial examination the patient was noted to have an AVPU scale: Pain. The respiratory examination showed respiratory depression, prompting the decision to intubate the patient for both airway protection and respiratory support. As the nursing team prepared for a rapid sequence induction, an arterial blood gas was done (Table 1). An uneventful rapid sequence intubation was performed using Propofol 60mg and Rocuronium 100mg. Post intubation, a urinary catheter was inserted, and a urine dipstick test showed protein 2+.

The decision was taken to initiate treatment for eclampsia while obtaining a more thorough collateral history and performing appropriate further special investigations. Magnesium Sulphate 14g was administered according to the local protocol. The patient remained in the resuscitation area, being closely monitored and serial blood gasses were performed (Please see Table 1 at end of report). Post intubation the blood pressure was noted at 112/71mmHg, the trend thereafter was well below 140/90mmHg. At this point in time the only abnormality was a high anion gap metabolic acidosis on arterial blood gas. Approximately 20 minutes after intubation it was noted on the cardiac monitors and a 12 lead ECG that the patient had developed a sinus tachycardia ranging from 125 to 155beats per minute. This prompted a concern for the development of subclinical seizures. A family member presented two empty containers of Isoniazid tablets from home, shortly after intubation. The emergency team administered pyridoxine 5g (crushed) via nasogastric tube for presumed Isoniazid toxicity. The tachycardia promptly subsided after pyridoxine was given to a sinus rhythm and rate of 102bpm.

The gynaecology team was notified of the patient and opted to defer the removal of the fetus and placenta while the treatment for Isoniazid toxicity was commenced.

Considering the dual potential pathologies, the emergency team opted to treat both Isoniazid toxicity and suspected eclampsia concurrently by administering pyridoxine and magnesium sulfate. Notably, the patient's blood pressure, which initially exceeded the threshold for eclampsia, remained below the threshold for eclampsia after initiation of treatment, and for the entire period spent in the emergency unit.

The patient was then transferred to the ICU, where she was successfully extubated after 72 hours, made a full recovery, and was subsequently discharged home. The patient was not treated for eclampsia during her stay in ICU, as per gynaecology instructions. The patient celebrated her 18th. Birthday in ICU on the day informed consent was signed. Four weeks later an infant with a birth weight of 2140g was delivered via normal vaginal delivery (NVD) at 32 weeks of gestation, achieving Apgar scores of 9 and 10 at birth and 5min respectively.

Discussion and Literature Review

Isoniazid stands as an easily accessible medication across South Africa and the African continent. The burden of tuberculosis in South Africa is among the most formidable globally, with a prevalence (across all ages and forms) of 737 cases per 100,000 population in 2018 [1].

The clinical manifestations of Isoniazid toxicity vary from mild to severe. Mild neurological side effects include peripheral neuritis, dizziness, and insomnia, however severe toxicity can result in seizures, coma, and death [2,3]. Isoniazid toxicity should be considered in any patient with a triad of: seizures refractory

to anti-convulsant treatment, high anion gap metabolic acidosis (HAGMA) and coma.

Isoniazid interferes with γ-aminobutyric acid synthesis (GABA), a major inhibitory neurotransmitter of the central nervous system. Isoniazid directly inhibits glutamic acid decarboxylase by inhibiting a co-factor, namely pyridoxal 5-phosphate (the active form of pyridoxine/vitamin B6). A subsequent reduction in GABA levels, lowers the seizure threshold and can result in generalized tonic clonic seizures [4].

This depletion of vitamin B6 can thus be treated by the administration of a pyridoxine dose equivalent to that of isoniazid ingested. If the amount of isoniazid ingested is unknown, 5g pyridoxine should be administered intravenously or crushed via nasogastric tube. The dose can be repeated at 5-20 minutes intervals if the seizures recur, or the comatose state does not resolve [4].

Pre-eclampsia (the precursor of eclampsia) is defined as a new-onset systolic- and diastolic hypertension of 140/90mmHg, after 20 weeks of gestation with proteinuria and/or other signs of end-organ dysfunction. Eclampsia is defined as the new onset of generalized tonic-clonic seizures in a woman with preeclampsia [5].

The pathophysiology of pre-eclampsia, and subsequently eclampsia, is still unclear. Proposed theories include: placental ischemia, vasospasm, coagulopathy, vascular endothelial dysfunction, abnormal nitric oxide and lipid metabolism and leukocyte activation. The most recent evidence shows that abnormal angiogenesis, particularly an imbalance in soluble fms-like tyrosine kinase 1 (sFlt-1) : Placental growth factor (PLGF) ratio [6].

The management of eclampsia involves supportive management and magnesium sulphate. The regime of magnesium sulphate administration is dependent on local protocols.

Conclusion and Contribution

The presented case serves as a reminder of the challenges of managing pregnant patients with possible simultaneous medical conditions, especially in a primary care- or emergency care setting. It underscores the importance of considering multiple coexisting conditions and risk stratification of the individual treatment modalities.

Strengths and limitations Associated with this Report

Strength:

As with any case study a considerable amount of detail pertaining to the specific topic can be put up for peer review. The treating physicians themselves did the retrospective analysis.

Weaknesses:

This is a single case and almost no chance of replication. Physicians also did not have access to Isoniazid levels testing.

References

1. Van der Walt M, Moyo S. The first national TB prevalence survey: South Africa 2018. National Department of Health. 2021.
2. Gokhale YA, Vaidya MS, Mehta AD, et al. Isoniazid toxicity presenting as status epilepticus and severe metabolic acidosis. J Assoc Physicians India. 2009; 57: 70-71.
3. Tajender V, Saluja J. INH induced status epilepticus: response to pyridoxine. Indian J Chest Dis Allied Sci. 2006; 48: 205-206.
4. Okutur SK, Borlu F, ERSOY ÇY, et al. Acute Isoniazid Intoxication: Convulsion, rhabdomyolysis and metabolic acidosis. Turk J Med Sci. 2006; 36: 397-399.
5. Shivani A, Sharma K, Swarupa C, et al. Eclampsia and Its Treatment Modalities: A Review Article. Cureus. 2022; 14: e29080.
6. Levine RJ, Thadhani R, Qian C, et al. Urinary placental growth factor and risk of preeclampsia. JAMA. 2005; 293: 77-85.

Annexure A:

ICD 7

CONSENT TO USE HEALTH RECORDS AND INFORMATION FOR A CASE STUDY

Title: Simultaneous Presentation of Isoniazid Toxicity and Eclampsia in a Pregnant Female

Dear _____

I am _____Dr Rulé Human_____ from ___Kalafong hospital / University of Pretoria

I would like to ask your permission to use your medical information for a case study. A case study is where we use medical information to tell other healthcare workers about a rare or interesting case.

Since you are one of very few people in South Africa *with a complex presentation in pregnancy*,we think that other healthcare workers can learn a lot from your story. We would like to use your information for an article in a medical journal. We will never use your name or other personal details, so the healthcare workers will not know that we are talking about you.

If you agree to allow us to use your medical record for this study, we would need to access the following types of information: age, medical conditions and your clinical notes in your file at Kalafong hospital.

Your decision to allow your health information to be used for a case study is entirely voluntary. You are free to say no without any impact on your current or future treatment. Although you will not benefit directly from allowing your case to be presented, this information will help to advance our understanding *the complexities of diagnosing and treating multiple pathologies in pregnant patients*

Privacy and Confidentiality

Your privacy will be respected and all reasonable efforts will be made to protect your information. Only your doctor will have access to information identifying you. All of the data used for this study will be de-identified, which means that information such as your name and medical record number, will not be used.

Ethics approval

This Case study was submitted to the Faculty of Health Sciences Research Ethics Committee, University of Pretoria, telephone numbers 012 356 3084 / 012 356 3085 and written approval has been granted by that committee. The study has been structured in accordance with the Declaration

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of Helsinki (last update: October 2013), which deals with the recommendations guiding doctors in biomedical research involving human/subjects.

For More Information

You may see a copy of the final case study if you wish. If you have any questions, you may speak to me or any other person involved in your healthcare.

If you give permission for the use of your personal health information for this case study, I kindly ask that you sign the next page.

Consent Statement

- I have read (or someone has read to me) the information in this consent form.
- I understand the purpose and procedures and the possible risks and benefits of the study.
- I was given sufficient time to think about it.
- I had the opportunity to ask questions and have received satisfactory answers.
- I understand that I am free to withdraw from this study at any time for any reason and the decision to stop taking part will not affect my future relationships.
- I give permission to the use and disclosure of my de-identified information collected for use in this case study, as described in this form.
- I understand that by signing this document I do not waive any of my legal rights.
- I will be given a signed copy of this consent form.

Name of participant/patient (please print)

15/04/2023

Participant/patient signature — Date

RULE HUMAN

Name of investigator (please print)

Human — 15.06.2023

Investigator signature — Date

Annexure B:

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences

Institution: The Research Ethics Committee, Faculty Health Sciences, University of Pretoria complies with ICH-GCP guidelines and has US Federal wide Assurance.

- FWA 00002567, Approved dd 18 March 2022 and Expires 18 March 2027.
- IORG #: IORG0001762 OMB No. 0990-0279 Approved for use through June 30, 2025 and Expires 07/28/2026.

Faculty of Health Sciences **Research Ethics Committee**

9 October 2023

Approval Certificate
New Application

Dear Dr R Human

Ethics Reference No.: 567/2023
Title: Simultaneous Presentation of Isoniazid Toxicity and Eclampsia in a Pregnant Female

The **New Application** as supported by documents received between 2023-09-19 and 2023-10-09 for your research, was approved by the Faculty of Health Sciences Research Ethics Committee on 2023-10-09 as resolved by its quorate meeting.

Please note the following about your ethics approval:

- Ethics Approval is valid for 1 year and needs to be renewed annually by 2024-10-09.
- Please remember to use your protocol number (567/2023) on any documents or correspondence with the Research Ethics Committee regarding your research.
- Please note that the Research Ethics Committee may ask further questions, seek additional information, require further modification, monitor the conduct of your research, or suspend or withdraw ethics approval.

Ethics approval is subject to the following:

- The ethics approval is conditional on the research being conducted as stipulated by the details of all documents submitted to the Committee. In the event that a further need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

Approved on condition:

1. Written "consent" was obtained from a 17-year-old.

I suggest approval with the following note:

"The patient was below the age of 18 and could not legally consent to participation in research. Her assent was nonetheless noted and a waiver to obtain legal consent was granted."

2. Perhaps add an explanation on the role of POC tyrosine kinase 1 (sFlt-1): Placental growth factor (PLGF) ratio as biomarkers to distinguish pre-eclampsia/eclampsia vs other causes.

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Lefapha la Disaense tša Maphelo

Annexure C:

CARE case report guidelines

CARE Checklist of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Line
Title	1	The diagnosis or intervention of primary focus followed by the words "case report"	24
Key Words	2	2 to 5 key words that identify diagnoses or interventions in this case report, including "case report"	28
Abstract (no references)	3a	Introduction: What is unique about this case and what does it add to the scientific literature?	32–36
	3b	Main symptoms and/or important clinical findings	38–43
	3c	The main diagnoses, therapeutic interventions, and outcomes	45–49
	3d	Conclusion—What is the main "take-away" lesson(s) from this case?	51–55
Introduction	4	One or two paragraphs summarizing why this case is unique (**may include references**)	73–78
Patient Information	5a	De-identified patient specific information.	82
	5b	Primary concerns and symptoms of the patient.	86–88
	5c	Medical, family, and psycho-social history including relevant genetic information	82
	5d	Relevant past interventions with outcomes	n/a
Clinical Findings	6	Describe significant physical examination (PE) and important clinical findings.	90–95
Timeline	7	Historical and current information from this episode of care organized as a timeline	93–113
Diagnostic Assessment	8a	Diagnostic testing (such as PE, laboratory testing, imaging, surveys).	174 (table)
	8b	Diagnostic challenges (such as access to testing, financial, or cultural)	n/a
	8c	Diagnosis (including other diagnoses considered)	119–120
	8d	Prognosis (such as staging in oncology) where applicable	N/A
Therapeutic Intervention	9a	Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care)	103/112
	9b	Administration of therapeutic intervention (such as dosage, strength, duration)	118–122
	9c	Changes in therapeutic intervention (with rationale)	118–122
Follow-up and Outcomes	10a	Clinician and patient-assessed outcomes (if available)	n/a
	10b	Important follow-up diagnostic and other test results	n/a
	10c	Intervention adherence and tolerability (How was this assessed?)	n/a
	10d	Adverse and unanticipated events	n/a
Discussion	11a	A scientific discussion of the strengths AND limitations associated with this case report	177–183
	11b	Discussion of the relevant medical literature **with references**.	132–167
	11c	The scientific rationale for any conclusions (including assessment of possible causes)	171–175
	11d	The primary "take-away" lessons of this case report (without references) in a one paragraph conclusion	169–173
Patient Perspective	12	The patient should share their perspective in one to two paragraphs on the treatment(s) they received	n/a
Informed Consent	13	Did the patient give informed consent? Please provide if requested	Yes ☑ No ☐