Suicidal Iron and Paracetamol Overdose: A Case Report

Vandoorne, Carmen Zenda MBChB(Pret), DA(SA), Dip for Med (SA) Path

Medical Registrar, Department of Forensic Medicine, University of Pretoria, Prinshof Campus, Pretoria, South Africa.

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Correspondence to: Carmen Zenda Vandoorne, MBChB(Pret), DA(SA), Dip for Med (SA) Path, Medical Registrar, Department of Forensic Medicine, University of Pretoria, Prinshof Campus, Pathology Building, Level 4 Room 4-39, Pretoria, South Africa. E-mail: carmen.weyers@up.ac.za.

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Case Summary

A woman presented to a hospital complaining of drowsiness and body weakness. The patient reported intentionally ingesting about 30 ferrous sulfate tablets and about 10 paracetamol tablets after an argument with a loved one. The ingestion occurred within 24 hours of presentation to hospital. Blood samples taken before any treatment was given demonstrated severe metabolic acidosis, leukocytosis, and liver impairment with raised aspartate transaminase (244 U/L), alanine transaminase (140 U/L), alkaline phosphatase (130 U/L) and conjugated bilirubin (9 µmol/L), and an international normalized ratio of 4.61 seconds. Serum paracetamol levels more than 12 hours after ingestion confirmed paracetamol toxicity at 433 µmol/L (reference range, >264 µmol/L). Serum iron studies showed raised transferrin at 5.07 g/L (reference range, 2.50–3.80 g/L) and normal ferritin at 58 µg/L (reference range, 10–291 µg/L); however, serum iron testing was rejected due to insufficient specimens. The patient underwent treatment including iron chelation therapy with desferrioxamine and acetylcysteine therapy for paracetamol overdose. Later, an upper gastrointestinal bleed was suspected due to a rapid drop in hemoglobin level from 10.5 g/dL to 5.1 g/dL. Despite appropriate medical treatment and cardiopulmonary resuscitation, the patient died approximately 24 hours after admission.

As per the provisions of the Inquests Act (Act 58 of 1959), the death was considered unnatural and referred for medicolegal autopsy, performed by the author four days after the death occurred.

External examination showed a well-nourished adult female with conjunctival and oral mucosal pallor, and signs of medical intervention.

Internal examination revealed approximately 100 mL of brown fluid within the stomach with no definitive medicinal residue identified. There were diffuse, patchy, brown, raised plaques adherent to the gastric mucosa, predominantly overlying the gastric rugae, suggestive of iron deposits. No gastric hemorrhage, ulceration, or perforation was noted. The large bowel contained thick, black, tarry content, suggestive of melena stool. The liver was soft and diffusely hemorrhagic, in keeping with the macroscopic appearance of acute liver injury. In addition, pulmonary edema and hemorrhage and generalized visceral pallor were observed (Figs. 1, 2).

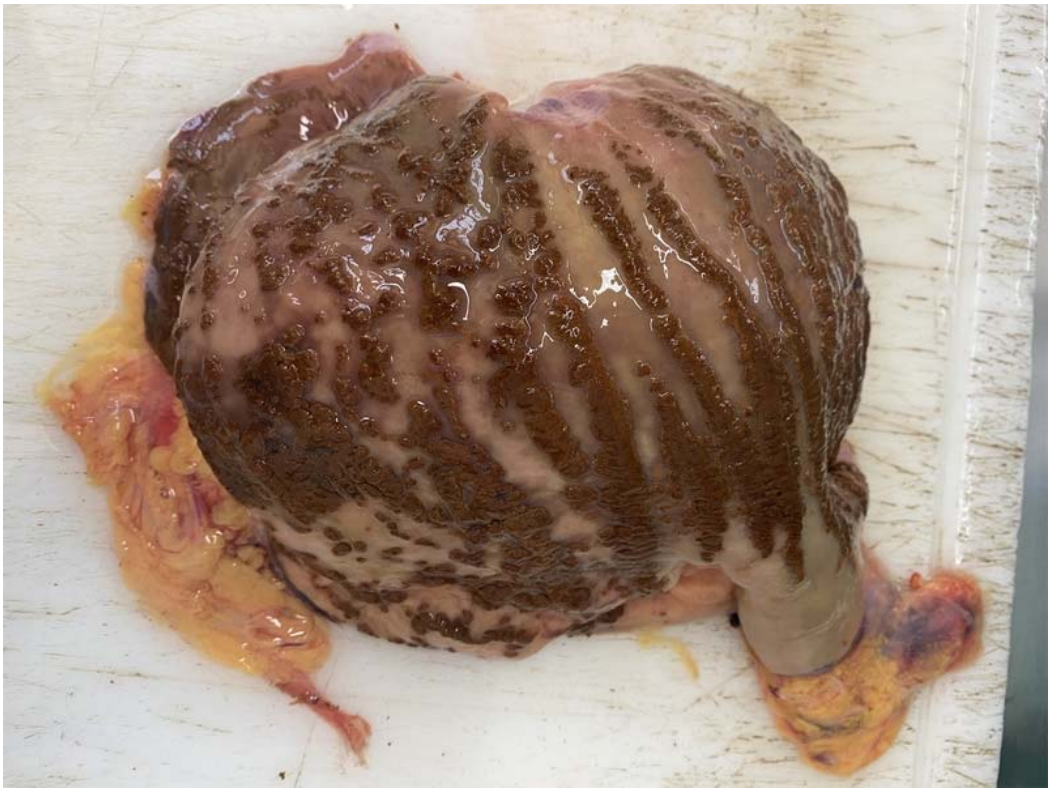

FIGURE 1: Gross image of iron deposits adherent to the gastric rugae.

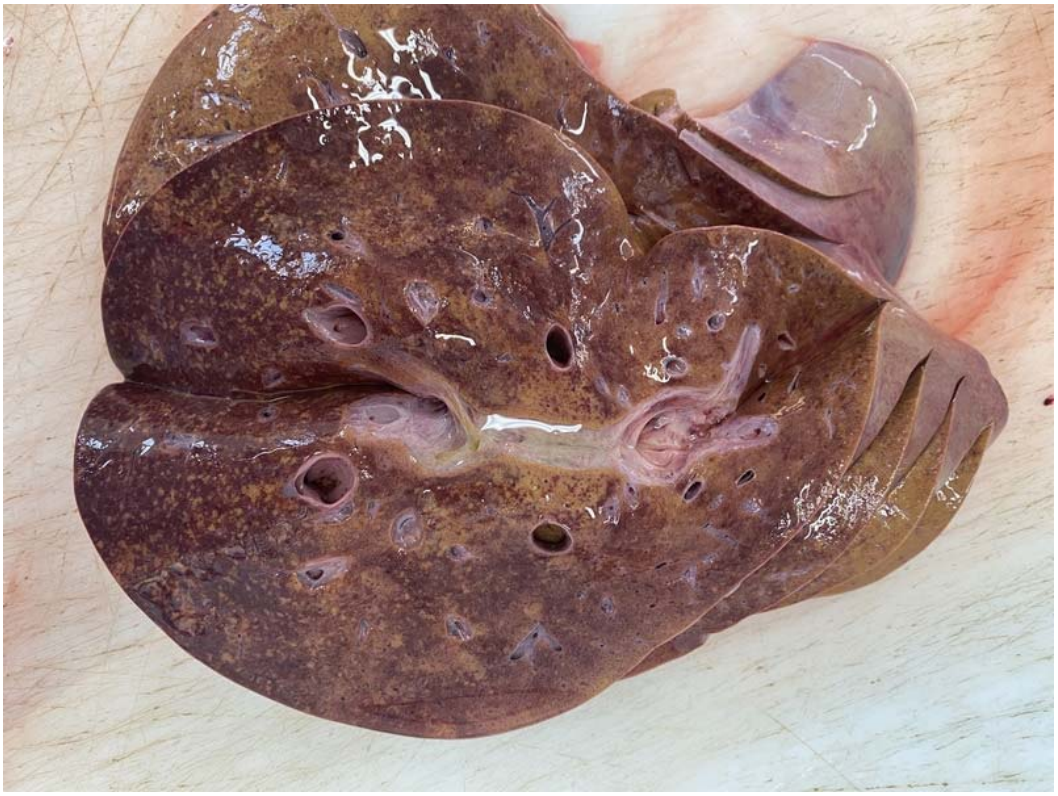

FIGURE 2: Gross image of diffusely hemorrhagic liver parenchyma.

Histopathologic examination on hematoxylin-eosin staining of gastric tissue showed diffuse deposition of fine brown pigment within the gastric mucosa and brown foci within the perivascular submucosal regions. There were foci of superficial mucosal ulceration, a neutrophilic transmural infiltrate with loose-lying red blood cells and focal full-thickness necrosis, in keeping with severe acute gastritis. Liver tissue showed diffuse, massive hepatocyte necrosis with hemorrhage, in keeping with acute liver failure, as well as patchy brown pigment deposition. The aforementioned features were noted in the presence of autolysis. Further findings showed signs of mild cerebral edema and patchy intra-alveolar hemorrhage Figs. 3–5.

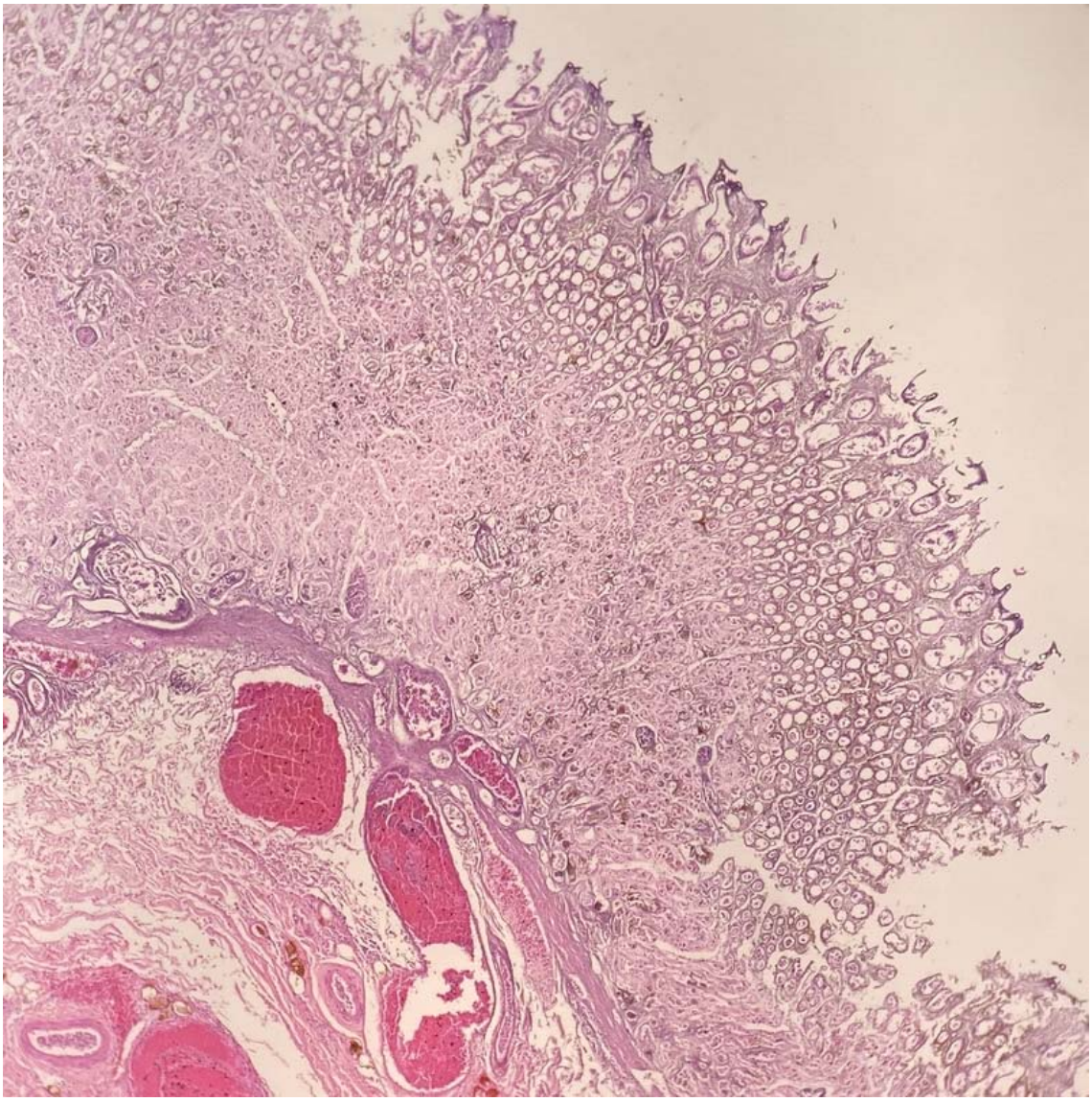

FIGURE 3: Iron deposition within the gastric mucosa (hematoxylin-eosin staining, original magnification ×4).

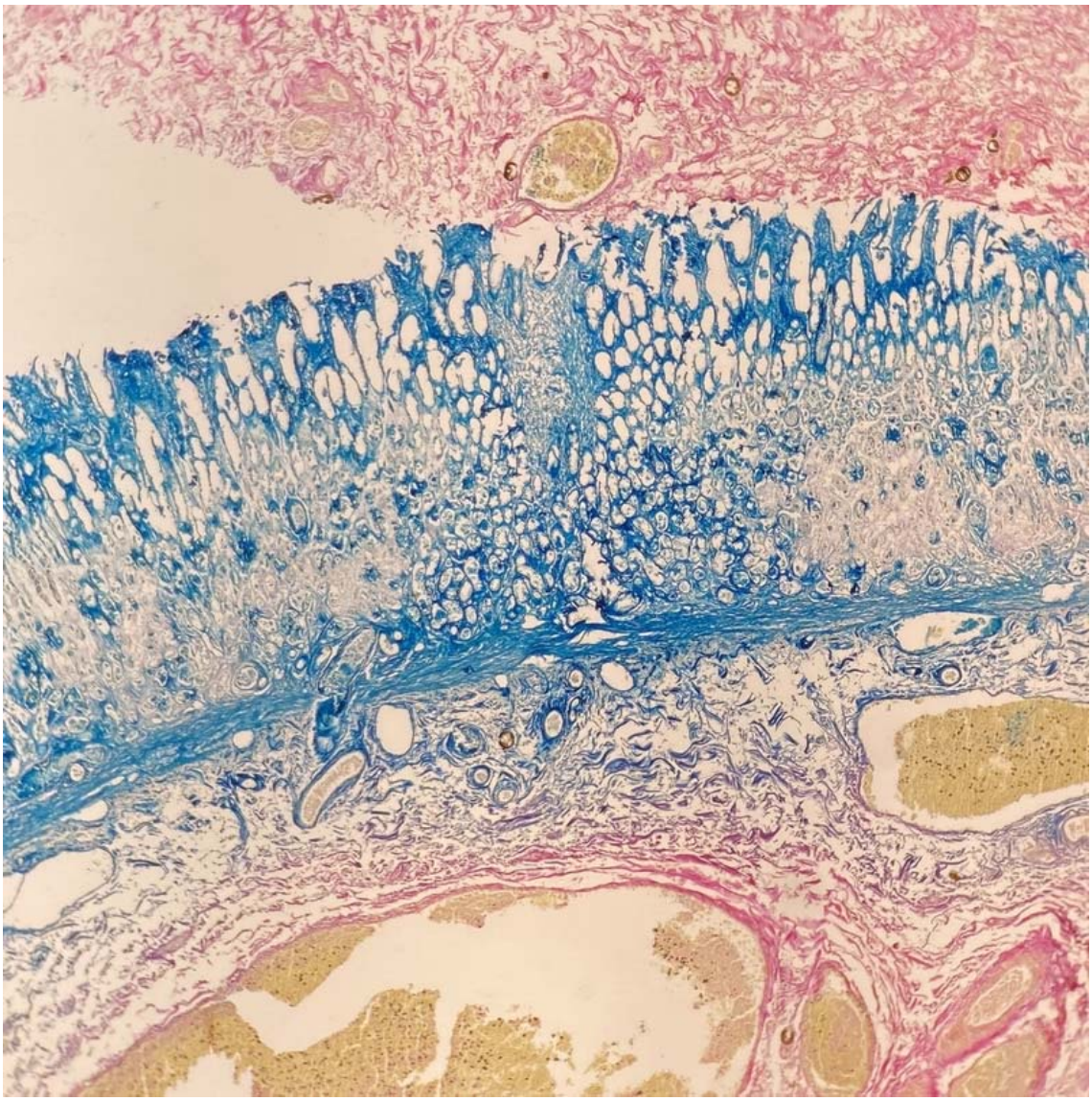

FIGURE 4: Positive iron staining within the gastric mucosa and submucosal blood vessels (Prussian blue staining, original magnification ×4).

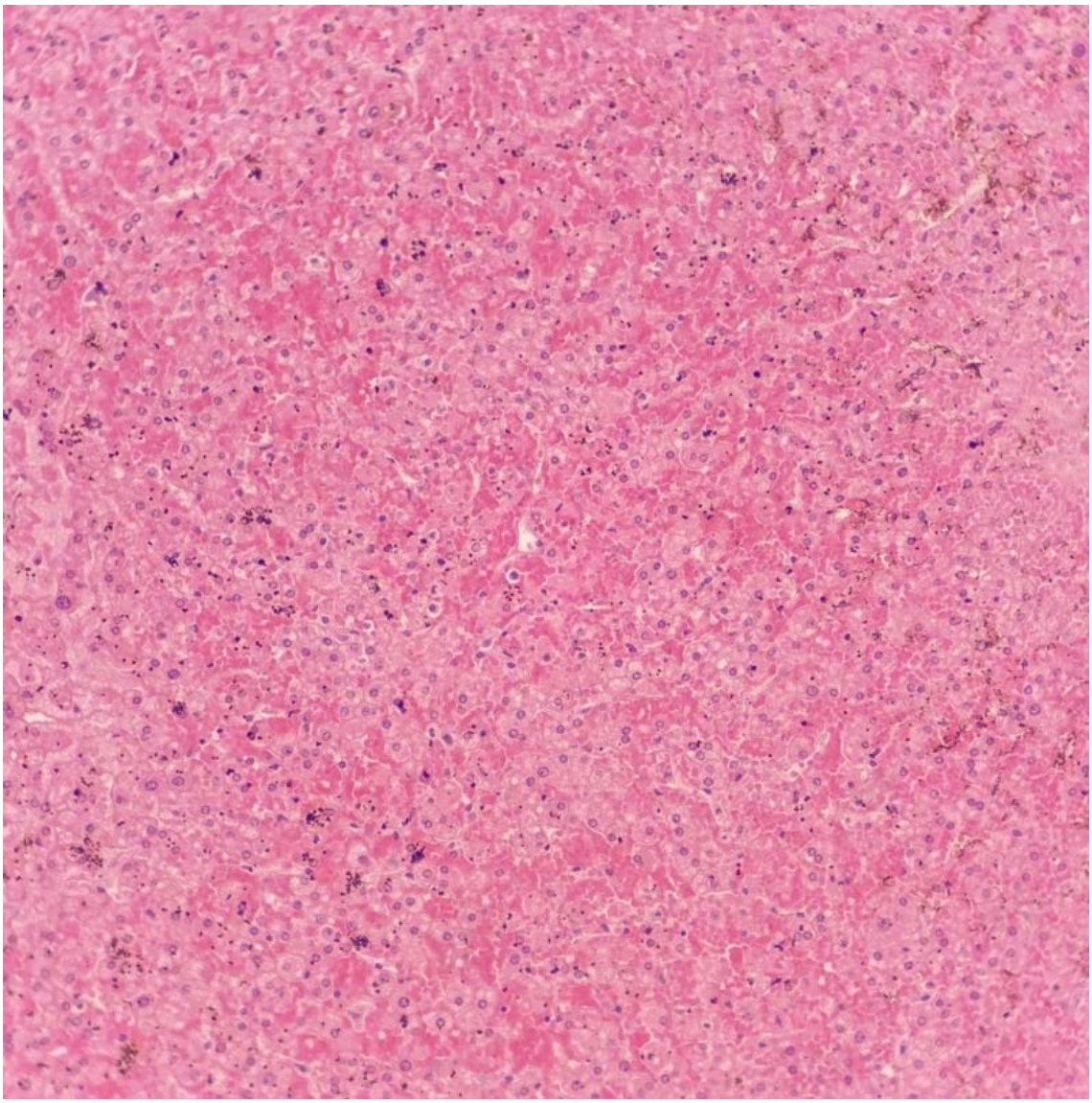

FIGURE 5: Massive hepatocyte necrosis with hemorrhage (hematoxylin-eosin staining, original magnification ×20).

Prussian blue staining showed significant iron deposition within the gastric mucosa. There was also staining of the submucosa, including submucosal blood vessels, chiefly at sites subjacent to areas of mucosal staining (also noted on additional cut levels). There was no stainable iron within the liver, suggesting the visualized brown pigment was artefactual, likely formalin pigment (Figs. 3–5)..

The cause of death was described as iron and paracetamol toxicity.

Discussion

The purpose of this article is to document the finding of iron and paracetamol overdose and present an overview of the related research.

Acute iron toxicity in adults is uncommon and few cases regarding the clinical and/or autopsy findings are described in the literature, however, acute paracetamol toxicity is common and extensively

researched. [1] A review of the literature yielded one publication regarding a fatal combination of paracetamol and iron. [2]

Acute iron toxicity is typically seen in the paediatric population due to accidental ingestion. [3] In adults, acute iron toxicity usually occurs due to intentional ingestion during a suicide attempt. The minimum lethal dose of iron is not established with certainty but doses ranging from 60 mg/kg-300 mg/kg of elemental iron have been reported. Ferrous sulfate is the most commonly used iron supplement and contains approximately 20 % elemental iron. [1]

Iron toxicity typically affects the gastrointestinal tract and causes iron encrustation of the gastric mucosa. [4] Microscopically, it causes iron staining of the gastric mucosa and submucosal blood vessels. [1] [5] Peak serum iron levels may help make the distinction between acute iron toxicity and a chronic state of iron overload. [3] Acute iron toxicity also causes acute liver failure, typically resulting in necrosis of the periportal regions. [1] [4] Unlike serum paracetamol levels, iron levels do not show any linear correlation with the risk of hepatotoxicity. [4]

Paracetamol toxicity typically occurs in accidental ingestion in children and intentional ingestion in adults. [6] The minimum lethal dose is approximately 10 g or 200 mg/kg in those under 50 kg. [6] [7] Paracetamol poisoning is classically associated with centrilobular hepatocyte necrosis which progresses to massive hepatic necrosis in the setting of acute liver failure. [8] Paracetamol overdose may also result in myocardial injury and renal failure. [2] [7]

This case demonstrates the rare finding of combined iron and paracetamol overdose in an adult where hepatotoxicity occurred at seemingly sub-lethal doses of the drugs. Allegedly 5 g of paracetamol was ingested but toxicity was proven on serum levels. This discrepancy could be due to factors such as understatement of the dose ingested or the potential additive toxic effect from concomitant iron ingestion. The total dosage of iron ingested is undetermined as the ferrous sulfate dose per tablet is unknown and the serum iron level was not obtained. However, the clinical history and autopsy findings support the diagnosis of iron toxicity. It is postulated that the rapid progression to acute liver failure is due to a double-hit mechanism, with centrilobular and periportal necrosis from paracetamol and iron respectively, causing massive necrosis with no potential for hepatic regeneration. [2] The presence of melena stool supports the clinical suspicion of an upper gastrointestinal bleed with the presumed source being severe acute gastritis with ulceration.

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Conflict of interest

The author reports no conflict of interest. No funding was received for this study.

References

[1] D. Yu and M. Griffen, "Suicidal iron overdose: A case report and review of literature," *J Forensic Sci.,* vol. 66, pp. 1564-1569, 2021.

[2] V. Audimoolam, J. Wendon, W. Bernal, N. Heaton, J. O'Grady and G. Auzinger, "Iron and acetaminophen a fatal combination?," *Transpl Int,* vol. 24, no. 10, pp. 85-88, 2011.

[3] M. Sane, K. Malukani, R. Kulkarni and A. Varun, "Fatal Iron Toxicity in an Adult: Clinical Profile and Review," *Indian J Crit Care Med.,* vol. 22, no. 11, pp. 801-803, 2018.

[4] S. Daram and P. Hayashi, "Acute Liver Failure Due to Iron Overdose in an Adult," *South. Med. J.,* vol. 98, no. 2, pp. 241-244, 2005.

[5] J. Pestaner, K. Ishak, F. Mullick and J. Centeno, "Ferrous Sulfate Toxicity A Review of Autopsy Findings," *Biol Trace Element Res,* vol. 69, pp. 191-198, 1999.

[6] A. Chidiac, N. Buckley, F. Noghrehchi and R. Cairns, "Paracetamol (acetaminophen) overdose and hepatotoxicity: mechanism, treatment, prevention measures, and estimates of burden disease," *Expert Opin Drug Metab Toxicol,* vol. 19, no. 5, pp. 297-317, 2023.

[7] A. Feola and B. Della Pietra, "Acute liver failure caused by paracetamol toxicity: a case report," *Acta Med. Mediterr.,* vol. 33, pp. 55-58, 2017.

[8] V. Kumar, A. Abbas and J. Aster, "Robbins and Cotran Pathologic Basis of Diseases," vol. 11, Amsterdam, Elsevier, 2020, pp. 826-827.

[9] A. Howle, M. Nott and I. Baguley, "Aspiration Pneumonia Following Severe Traumatic Brain Injury: Prevalence and Risk Factors for Long-Term Mortality," *Brain Impairment,* vol. 12, no. 3, pp. 179-186, 2011.