Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Transplantation*

Manuscript NO: 68157

Title: Diagnosis of acute intermittent porphyria in a renal transplant patient: A case report

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503026
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Assistant Professor
Reviewer's Country/Territory: Brazil
Author's Country/Territory: Italy

Manuscript submission date: 2021-08-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-11 20:49

Reviewer performed review: 2021-08-11 21:08

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The present article brings the first description of acute intermitent porphyria in a patient with renal transplantation. It is interesting and well written article. I suggest to remove the specific times (day monthyear) from the case description , since they become The case a little boring. Since there is a figure with all datas described, they may be removed from the text.

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Transplantation*

Manuscript NO: 68157

Title: Diagnosis of acute intermittent porphyria in a renal transplant patient: A case report

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05190615
Position: Editorial Board
Academic degree: MD
Professional title: Associate Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Italy

Manuscript submission date: 2021-08-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-12 01:19

Reviewer performed review: 2021-08-12 05:27

Review time: 4 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is the first report of new onset AIP symptomatology in a renal transplant patient. which provides new knowledge supplement for emergency doctors:an older subject with a common presentation of an uncommon disease. In patients with postoperative abdominal pain, we exclude common causes such as intestinal obstruction, and suspicion of AIP is also necessary.In short, this is a very rare and meaningful case.

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Transplantation*

Manuscript NO: 68157

Title: Diagnosis of acute intermittent porphyria in a renal transplant patient: A case report

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00006486
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: France

Author's Country/Territory: Italy

Manuscript submission date: 2021-08-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-17 08:24

Reviewer performed review: 2021-08-20 12:06

Review time: 3 Days and 3 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In the manuscript "Diagnosis of acute intermittent porphyria in a renal transplant patient: a case report", the authors report a patient who underwent deceased donor renal transplantation and subsequently developed acute porphyria. The patient developed diabetes mellitus and porphyria attacks two years after a renal transplantation that progressively remitted after a high carbohydrate diet and insulin administration to treat diabetes. The study is interesting and clearly sets a degree of novelty. The manuscript may be improved further with attention to the following: In the introduction section, page 3, the authors claim that "We found three previous reports describing renal transplantation4,5 or combined liver-renal transplantation6 in patients with a history of known AIP, but none reporting the diagnosis of AIP in a previously transplanted patient."….Although it has been reported that kidney transplantation improves the clinical outcomes of AIP (Lazareth et al. Mol Genet Metab. 2020), the development of acute attacks is not surprising because the disease has a hepatic origin. Thus, the liver of a patient with AIP can produce and accumulate heme precursors in case of post-transplant complications, excess of medications, recurrent infection due to immunosuppressive therapy, or reduction in carbohydrate intake. The methods used for measurement of urinary PBG and porphyrins should be described in more detail. The identification of the mutation would allow the identification of asymptomatic but porphyrin precursor excreters carriers whiting the family. It would be relevant to explore the PBGD gene more in deep to find the responsible mutation. According to the Human Gene Mutation Database (HGMD® Professional 2021.2), 527 mutations have already been reported in the PBGD gene and most of them are unique

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

[http://www.hgmd.cf.ac.uk/ac/index.php; Institute of Medical Genetics in Cardiff., last access on August 19, 2021]. Thus, it could be desirable to sequence the entire gene, also the intronic regions close to the exons and promoter. It can also be interesting to explore the variant of Peptide Transporter 2 (PEPT2). The gene variant PEPT2*1*1 is predictive of the severity and evolution of Porphyria-Associated Kidney Disease (as reported in Tchernitchko et al. J Am Soc Nephrol, 2017). In the discussion section, it would be helpful if the authors discuss whether long-term undiagnosed AIP could be the origin of the progressive renal insufficiency (as previous proposed in Pallet et al. Kidney Int 2015 and Unzu et al. PlosOne 2012). Potential toxicity of heme precursors by passing through the kidney, especially ALA, has been identified as responsible for progressive renal failure. Regarding the authors' comment "It is possible that the patient's diabetes (leading to low insulin secretion) combined with his low carbohydrate intake resulted in low uptake of glucose into the cells, mimicking the fasting state known to trigger AIP attacks". In this regard, in a recent publication including a case-control study including 44 patients with AIP presented evidences that patients with hyperinsulinemia showed clinically stable disease (Solares et al. Biomedicines 2021). Indeed, authors demonstrated that the combination of glucose and a liver-targeted insulin promoted partial but sustained protection against acute attack in a mouse model of the disease. In figure 1, please include the enzyme Protoporphyrinogen Oxidase that regulates the metabolic step of protoporphyrinogen IX to form protoporphyrin. This enzyme and the previous one, Coproporphyrinogen Oxidase, have mitochondrial emplacement, please correct it in the figure. The authors should write "ferrochelatase" instead of "ferochelatase". Porphobilinogen deaminase (PBGD) enzyme is also known as hydroxymethylbilane (HMB) synthase (as used in the figure). However, it seems more convenient to continue using the same nomenclature in the figure as in the text for this enzyme.