We are grateful to the reviewers for the valuable and helpful comments of our manuscript ID # [82475] with the title **"An Idiopathic Steno-Occlusive Disease in a Child: A Case Report of bilateral Internal Carotid Artery Occlusion"** which we are submitting as an original article to World Journal of Clinical Cases. We have addressed all editor's and reviewers' comments (point-by-point), as indicated in the attached pages and considered their corrections within the main text. We hope that the explanations and revisions of our work are satisfactory. We have highlighted the changes in the revised manuscript (yellow color).

Response to Editorial comments:

Editor:

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Author:

The manuscript has been polished for type and grammar correction by a colleague who naïve language is English. A new language certificate has been submitted along with the manuscript.

Editor:

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition.

Author:

The basic rules on abbreviations were followed as indicated.

Editor:

Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Author:

The figures are original. We added "Copyright ©The Author(s) 2023" to the bottom right-hand side of the picture in PowerPoint (PPT)

Editor:

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Author:

We did supplement the highlights for the latest cutting-edge research results

Editor:

- Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as "**82782-Figures.pptx**" on the system.

Author:

Figures were formatted and submitted as asked.

Response to reviewer's # 1 comments

The authors describe the first case of a pediatric Moyamoya disease in their country (to their knowledge). The manuscript is well written. This case report may add information on the incidence of pediatric moyamoya disease around the globe and keep the pediatricians aware of this rare condition among children. Several questions arose: -

Reviewer:

- Was the child prescribed with calcium channel blockers? if no, why, as both aspirin and calcium channel blockers may play a supportive role especially when surgical treatment is not available locally; if yes, which meds and what dosage

Author:

No we did not prescribed calcium channel blockers as the recommended drug for MMD is not available in suitable formulation for the child age. However, we add this information to the text in the introduction section as follow:

Page 5, last paragraph:

It has been reported that calcium channel blockers (as nicardipine) can be used for secondary prevention from ischemic insults. Nicardipine (in a dose of 0.25-0.5 mg/kg/day every 12 hours by oral route) may .improve the hemodynamics in patients with MMD by optimizing the collateral circulation[16].

Reviewer:

- did the child undergo genetic testing for Moyamoya? If not, do the doctors plan to withdraw blood and isolate DNA for further analysis in order to promote knowledge and awareness of the condition;

Author:

We did not do genetic testing as this service is not locally available. However, we added a paragraph related to the genetic testing for cases of MMD in the introduction and also as a recommendation for future investigatory workup as follow:

Introduction, page 4, lines 6-12:

"The ring finger protein 213 or the p.4810K variant in the RNF213 gene has been identified by both genome-wide association studies and whole exome sequencing in 95.0% for familial and 75.0% for sporadic cases with MMD. RNF213 gene has been suggested to be the most frequent susceptibility gene in MMD. However, there are other genes, allelic heterogeneity and ethnic specific variants that also has been thought to contribute rarely to the susceptibility, clinical characteristics and outcomes of MMD. Also some studies emphasized the effect of genetic variants on risk stratification and clinical presentation, follow-up of patients and surgical outcomes of MMD[4-6]."

Case presentation, page 8:

FURTHER DIAGNOSTIC WORK-UP

This will include genetic testing with special emphasis to RNF213 gene variants.

Reviewer:

- did the child have any other concomitant conditions?

Author:

There we no other conditions or associated diseases. This has been clarified in many sections of the text even in the old version of the manuscript. As follow:

Page 4, line 6-8:

"There was no comorbid medical or surgical condition. There was no history of risk factors in temporal relation with disease onset (e.g. infection/inflammation, vaccination, etc). There was no family history of similar condition."

Page 7, line 19-24:

"Her detailed history, comprehensive investigations (hematological and metabolic laboratory testing) and medical and cardiac evaluations excluded an underlying diseases or predisposing factors as a cause of stroke. Investigations included: complete blood cell count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), erythrocyte sedimentation rate (ESR), antinuclear (ANA), anticardiolipin and antiphospholipid antibodies, protein C and S, serum lactate and pyruvate, sickle cell preparation, serum amino acids, triglycerides, cholesterol, electrocardiogram and echocardiogram. No genetic testing was done."

Page 9, line 4-8:

"She had no family history of similar condition. There were no risk factors (e.g. infection, vaccination, etc) in temporal relation to the disease onset. There were no comorbid other neurological or extra-neurological manifestations. Her comprehensive laboratory investigations did not reveal an identifiable cause for the ischemic attacks. Her MRI, MRA and CTA findings are highly supportive for the diagnosis of MMD."

Reviewer:

- what kind of vaccinations did the child undergo before being diagnosed with Moyamoya? this seems like a very important issue.

Author:

- This is the compulsory and additional recommended vaccines given according the patients age:

The compulsory vaccination schedule in Egypt:
At 18 months:
NMR (2nd dose)
OPT (Booster dose)
DPT (Booster dose)
At 4-6 years:
OPT and DT (Booster doses)
Additional recommended vaccines in Egypt:
At 18 months:
Hib and PCV (Booster doses)
At 2 years:
Meningococcal (one dose)
Hepatitis A (2nd dose)
At 4-6 years:
BCG (Booster dose)
Chicken box (2nd dose)
Meningococcal (Booster dose)

- We know that infection/inflammation might be associated with the onset of MMD, however, as we mentioned in the text (as we mentioned in our response to the authors above), that there were no history of risk factors in temporal relation with disease onset (e.g. infection/inflammation, vaccination, etc".
  We also read that some authors associated the onset of MMD after chicken box vaccine, however, large sample sized or meta-analysis studies did not support this information. We prefered not to discuss this point in details in the text as it did not really exist in our case report.

Response to reviewer's # 2 comments

The authors described a case of a child patient with bilateral internal carotid artery occlusion, and the follow-up results of MDCT and MRI images from 2019 to 2021 year. The MDCT and MRI images from 2019 to 2021 year showed the increased collateral circulation of intracerebral vessels, which may contribute to the clinical improvement and the stabilization of the child's condition over the 3 years of follow-up. This is the merit and innovation of the manuscript.

Reviewer:

1 Title: It is suggested to add "Bilateral internal carotid artery occlusion" to the title;

Author:

We have changed the title as recommended as follow: "An Idiopathic Steno-Occlusive Disease in a Child: A Case Report of bilateral Internal Carotid Artery Occlusion"

Reviewer:

CORE TIP: It is suggested to simplify this section;

Author:

We simplified the core tip section as follow:

"Stroke in children is a significant cause of long-lasting morbidity. The advances in neuroimaging and laboratory investigations serve an important role in proper evaluation of stroke in children and identification of its potential etiologies, risk factors and outcomes. Moyamoya disease (MMD) is a rare progressive non-inflammatory steno-occlusive arteriopathy of the large cerebral blood vessels. It is a rare cause of ischemic stroke and recurrent transient attacks in children. The disease is very under-recognized in different areas of the world except East Asia, predominantly Japan. MMD can be sporadic or familial. The Japanese term "moyamoya" refers to the puff of smoke morphology of the dilated basal collateral vessels within the brain tissue seen on cerebral angiography. Compared to other arteriopathies, MMD is unique as its treatment solely relies on surgical revascularization. Therefore, increasing reporting and evaluation of cases with MMD from different ethnicities may help in better understanding of its causes and proper management.**"**

Reviewer:
In the Page7, 2nd paragraph, line 8, the word, "porthion", should be revised "portion";
Author:
Corrected

Reviewer:
7 Discussion: The first paragraph of the discussion section lacks logic and clear hierarchy. It is suggested that this part be divided into two parts.
Author:
We have revised the first paragraph of the discussion as follow and the text related to previous studies about the value of imaging for diagnosis in MMD was shifted to a next part of the discussion as follow:
Discussion (first paragraph):
"We present a younger female child with epilepsy (right and left focal seizures and generalized tonic-clonic convulsions (GTC) and TIAs. She developed left sided hemiparesis after an attack of ischemic cerebrovascular stroke. A common child behavior which triggered the TIA was crying (i.e. hyperventilation or hyperpnea excitement). She had no family history of similar condition. There were no risk factors (e.g. infection, vaccination, etc) in temporal relation to the disease onset. There were no comorbid other neurological or extra-neurological manifestations. Her comprehensive laboratory investigations did not reveal an identifiable cause for the ischemic attacks. Her MRI, MRA and CTA findings are highly supportive for the diagnosis of MMD."
Page 9, line 5-15:
"However, CT is less sensitive than MRI for visualization of deep brain infarcts[12] Previous studies indicated that CTA is non-invasive technique. It captures snapshots in different contrast bolus phases and provides more relevant data regarding secondary collateral flow, which significantly correlates with the neurological outcome. They also indicated that combined MRI, MRA and MRV, non-invasive imaging tests, are enough for the diagnosis of suspected MMD in a child with sensitivity of 92% and a specificity of 100%[8]. It has been found that MRA is beneficial for diagnosis of large basal intracranial vessels and Willisian, leptomeningeal, and transdural collaterals[17,18], whereas conventional angiography is better for diagnosis of smaller moyamoya collaterals and extracranial distal collateral networks[8]. MRI and MRA also differentiate MMD from the mimicking conditions including vascular dissection, inflammatory vasculitis and cystic medial necrosis[8]."

With this manuscript, there are 5 figures which we wish to be published.

I certify that the materials of this work **"An Idiopathic Steno-Occlusive Disease in a Child: A Case Report of bilateral Internal Carotid Artery Occlusion"** have not been submitted simultaneously elsewhere and that no part of the text or any of the tables has been copyrighted, published, or reproduced elsewhere. I certify that all individuals included as authors of papers have contributed substantially to the scientific process leading up to the writing of the paper and its revised version.

Thank you for accepting reviewing our manuscript.