Manuscript NO: 83436 - Answering Reviewers

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

Please see and discuss two recent articles about the same subject

a. https://casereports.bmj.com/content/13/10/e235103

b. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9283822/</u>

Thank you for mentioning these two recent articles. We have updated our discussion to add the additional risk factors for formation of primary vaginal stones described in the case reports, including neurogenic bladder dysfunction as in the multiple sclerosis patient (case report "a"above) and paralysis (case report "b" above). We have additionally further emphasized the more typical struvite composition of vaginal stones as the aforementioned case reports also highlight.

Discussion can be reshaped in a more organized manner. The authors mentioned nephrolithiasis and the suddenly continued to discuss about the vaginal stone. The relationship between these entities should be more clearly stated.

The text has been edited to more clearly explain that the reason for discussing kidney stones is to highlight that the hydroxyapatite composition of our patient's vaginal stone is unusual. Hydroxyapatite composition is more typical of kidney stones. Previously published cases of vaginal stones report predominantly struvite composition. We propose that our patient's stones were primarily composed of hydroxyapatite, which again is more typical of kidney stones, due to her underlying hyperaldosteronism which causes urinary changes that are known to predispose individuals to kidney stone formation. The text is as follows: "The predominantly hydroxyapatite composition of our patient's vaginal stones is unusual since most published cases of vaginal stones report a struvite composition. Hydroxyapatite is more common for kidney stones. Our patient has no history of nephrolithiasis; but she does have hyperaldosteronism. We propose that this patient's history of hyperaldosteronism is responsible for the atypical composition of the secondary vaginal stones. Hyperaldosteronism causes hypercalciuria, phosphaturia, and hypocitraturia. These urinary changes are risk factors associated with kidney stone formation and recurrence[11]. In our patient's case, these urinary changes secondary to hyperaldosteronism likely contributed to the atypical composition of her vaginal stones, which more closely resemble that of the most common types of kidney stones rather than the typical struvite composition of vaginal stones. Therefore, it is prudent for clinicians to be aware of medical conditions that increase the risk of kidney stones because patients with such conditions may be at increased risk for forming vaginal stones."

The known risk factors for vaginal stones should be clearly and separately discussed. The risk factors are now more clearly reviewed and the text has been updated to the following:

"Primary stones typically result from urinary stasis within the vagina allowing for deposition of urinary salts. Some causes of primary stones include vaginal outlet obstruction, neurogenic bladder dysfunction, prolonged recumbent positioning such as in bedridden or paralyzed patients, and vesicovaginal, urethrovaginal, or ureterovaginal fistulae.^{4,5,6,7} Secondary stones form in the vagina in the presence of a foreign body, such as contraceptive devices or exposed vaginal mesh, which acts as a nidus for urinary crystallization and subsequent stone formation.^[1]"

The relatively unique part of the case- the relation with mesh- must be emphasized.

The discussion has been edited to highlight that the expectant management of this patient's mesh exposure created a nidus for vaginal stone formation. Expectant management of the mesh exposure allowed for reaccumulation of the vaginal stones after the initial removal due to persistent contact of the mesh with urine. The text is as follows: "In addition to the unusual hydroaxyapatite composition of this patient's vaginal stones, this patient's rapid reaccumulation of stone material overlying the mesh exposure after the initial stone removal is unique to this case. The reaccumulation suggests that patients with vaginal mesh exposure who are at increased risk of kidney stones may not be optimal candidates for expectant management, even if they have asymptomatic mesh

exposure. This is particularly pertinent for individuals with risk factors for persistent contact of the mesh exposure to urine, such as significant urinary incontinence as with our patient. In addition, the short-interval reaccumulation of stones in this patient favors recommending excision of exposed mesh rather than temporizing measures, such as removal of the stone material only. Leaving exposed mesh is likely to result in reaccumulation of the vaginal stones."

If possible please add one or picture of two imaging such as X ray, Ultrasound and/or CT images.

The only images obtained were taken at the time of vaginoscopy and have been included with submission. There are no radiographic images available for this patient's case.

Reviewer #2: Scientific Quality: Grade C (Good) Language Quality: Grade B (Minor language polishing) Conclusion: Accept (General priority) Specific Comments to Authors: Dear author thank you for submitting your findings.