Peer Review File

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Reviewer Comment	Author Comments	Manuscript Revisions
Reviewer 1		
On physical examination, she had large, ptotic, heavy dense breasts with significant striae and shoulder grooving (Figure 1). Dear authors in the figure 1, I can not see clearly that the patients had a shoulder grooving; about breast size, the inferior pole of their breast are not lower than elbow flexures which is an indirect way to evaluate the breast size in a particular patient (it is an easy way to test Nicolete index which relates jugulum to nipple distance to patient high). I recommend change the figure or remove "with significant striae and shoulder grooving".	The photo has been reviewed to ensure alignment with the text.	"…with significant striae" was left, as striae across the shoulders and breasts is easily visible in the photo. "And shoulder grooving" was removed from this sentence, as it is not easily visible in this photo.
Please define the age range for "adolescent".	Thank you for pointing out the many different definitions of adolescent. We added the World Health Organization's definition.	Our definition of adolescent is in accordance with the World Health Organization's age range of 10 to 19 years old.
Reviewer 2		
The authors present a case of hEDS with bilateral inferior pedicled wise pattern reduction mammaplasty. Missing facts are, if there is already existing literature for hEDS in plastic surgery, especially in breast reduction. Is hEDS a contraindication in other surgery disciplines? Why was this stated in the beginning? this is absolutely UNCLEAR! there are existing publications on EDS in surgery, these should be added (Verdure et al. and Gerogiannis et al. in bariatric /obesity surgery e.g., Burcharth in gastrointestinal surgery, Elsisy et al in cardiovascular surgery, and others!	We agree that we can add more examples of the existing literature on EDS and emphasize the point that this case is the first reported case of breast reduction in a patient with hEDS. We added more, however, we are limited to 20 references.	Most of the published studies focus on surgery in adults with EDS.[3,10–12] However, there are few published studies describing cases of plastic surgery in patients with EDS.[2,4,6,13] There are even fewer studies describing surgery in pediatric and adolescent patients with EDS.[5,14,15] To our knowledge, this is the first report of breast reduction in an adolescent patient with Ehlers-Danlos Syndrome.
So far there is only one reference of EDS complications of surgery in	We also agree that we can establish more clarity regarding postoperative	However, surgeons may be hesitant to operate on these patients given

children, which is not enough! could hEDS be a relative contraindication? hEDS and its possible complications in surgery should be more clarified in introduction and discussion section. what are the scientific facts for an elevated risks for delayed wound healing? other publication to this topic?? what are the higher risks for surgical complications in hEDS and why?! what were blood analysis specimens and hormone analysis, clotting/coagulation blood analysis in the preop evaluation?	complications in patients with EDS. We added more examples of published literature on complications for these patients, and further explained why surgeons are hesitant to operate in patients with EDS. No Routine hormone or coagulation studies were performed.	their complex diagnosis and increased propensity to develop surgical complications, including wound dehiscence, severe bruising, and increased risk of hemorrhage and hematomas.[2–7] Due to the fragile connective tissue and blood vessels, delayed wound healing, and chronic pain, patients with EDS may have less favorable surgical outcomes compared to the general population.[8–10]
The breast measurements are missing. Sternal-notch-NAC distance (SN-NAC), NAC-IMF, breast width, NAC diameter, intermammary NAC distance! This case should be compared to other cases and publications in this field of plastic surgery. There should be more standard pictures added, from left/right 90 degrees, 45 degrees oblique left/right.		These measurements were added to the document. Standard pictures were also added; however, we are limited to 8 pictures only so we chose the 6 most important angles
There is only one 3 months postop picture, why not also 1 year or more after? these 1 year or longer postop pictures (as described from different angles) should definitely be added in this special case!		I agree with the desire for one year follow-up photos. Unfortunately, this patient did not follow-up at their one-year appointment. Attempts have been made to reschedule but the family is reporting "no issues" and would not like to come in.
Also there should be a Breast-Q questionnaire added regarding the patients satisfaction evaluation, especially due to the postoperative life quality change. The satisfaction of the lady was not scientifically		Thank you for the comments, this is correct, the results are subjective. Since this time, we have started initiating Breast Q for the patients however this patient was operate

presented. The reduction in pain was how preop vs. postop? VAS pain scale is missing!		done prior to this change in our protocol.
How was the scar treatment of the authors in this special case? was the suture removal 2 weeks postop or longer due to hEDS? what kind of suture did the authors use? the surgical method is so far not sufficiently described!		Excellent recommendation, the details have been added to the document.
So far there is no scientific evaluation of patient-related outcome measures (PROMs)! How was relief of joint and muscle pain evaluated? there are no results in numbers or measurements stated! significant reduction in pain? but how in measures? this should be clarified! Also, nipple sensitivity analysis should be added.		Reduction in pain was subjective based on patient reported outcomes. This has been edited in the document.
The postoperative course of wound healing and postop show-ups in the outpatient clinic should be clarified. When were the follow-ups? the follow-ups should be more frequently than other patients without hEDS! How did the authors state that the breast was form-stable in the postoperative course? did they measure the NAC-IMF distance direct postoperatively and 1year after compared to patients without EDS? there are no numbers or proven results measurements for this statement! The NAC-IMF distance would be a very nice indicator of hyperelasticity of the skin!		Post-operative follow-up timeline in our clinic has been added to the document. Measurements are not routinely made on post-operative patients but this is an excellent suggestion that will be looked at in the future. The main focus of this paper is to provide an example of a patient who underwent surgery who did not demonstrate the feared postoperative complications related to wound healing and bleeding risk in this patient population. Long term results, including 1,5,10 year f/u have not been established yet.
What was the result of the histological examination of the resected breast tissue specimens?		This has been added to the document.
The surgical technique with inferior pedicle should also be discussed, why not superomedial pedicle, as it is a more reliable pedicle, especially the risk for bottoming out is much lower than inferior pedicle. And in hyperelastic skin (hEDS) the risk for bottoming out is very high as in		This is a great topic of discussion. We understand that this is another technique for breast reductions. This is not routinely used in this practice, any may lead to better results, however this was not the focus of this discussion, rather that wound healing and immediate post-

this hEDS case. The patient case is very young (18y), so in elderly women the risk for bottoming out is much higher and the pedicle technique should be further discussed! In total a good example for a rare entity of eHDS in bilateral reduction mammaplasty but there is definitely a major revision needed!		operative complications can be mitigated in this patient population. It would be a very interesting study to follow these patients over the course of several years to be able to assess this.
Reviewer 3		
This case report describes a patient with hypermobile Ehlers-Danlos syndrome who underwent bilateral breast reduction for symptomatic macromastia with an uncomplicated recovery. The Authors proposed that hypermobile Ehlers-Danlos syndrome is not a contraindication to surgery in adolescents and acceptable outcomes can be achieved. The case is very interesting and should be of interest to the readers. It is hard to decide on non-life saving surgery in patients with rare diseases (e.g. I decided on breast reduction in a patient with Fabry Syndrome, which ended well, but decision-making process was hard). In this aspect the paper is worth publishing. However, I have some remarks: -first of all, I would rephrase the conclusion – it is not justified to conclude on the basis of one case that EDS "is not a contraindication to surgery" – I would suggest saying that "may not be" or sth less definite… (as you stated in limitations you cannot generalize)	Thank you for pointing this out. We changed this to "may not be" because we agree that one case is not a justification for a definite conclusion.	We propose that reduction mammoplasty in adolescents with hEDS may not be contraindicated, but instead may offer substantial improvement of the physical and psychological symptoms associated with macromastia.
- in introduction the reader would like to know how many cases /if any/ of breast reduction in women with EDS were reported and if problems with healing are common in the syndrome, what about face-lifting complications in these patients? – see: Rollett R, Bramhall RJ, Khan MA, Riaz M. Facelift for an Ehlers-Danlos Syndrome Patient: A Case Report. Aesthet Surg J. 2016 Mar;36(3):NP131-4. doi: 10.1093/asj/sjv214.	We agree that we can further clarify this so we added more references to the complications these patients face and added that this case, to our knowledge, is the first reported breast reduction in a patient with EDS.	However, surgeons may be hesitant to operate on these patients given their complex diagnosis and increased propensity to develop surgical complications, including wound dehiscence, severe bruising, and increased risk of hemorrhage and hematomas.[2–7] Due to the fragile connective tissue and blood vessels, delayed wound healing, and chronic pain, patients with EDS may have less favorable surgical

		outcomes compared to the general population.[8–10] To our knowledge, this is the first reported incidence of breast reduction in a patient with Ehlers-Danlos Syndrome.
- in the aim you should highlight that this is the first report of a patient with EDS who had breast reduction… and “We present the following case in accordance with the CARE reporting checklist” – should not be stated as the aim (is it needed?)	The phrase “CARE reporting checklist” was kept because the guidelines for submission of the case report on the AMJ AME website state “A statement like “We present the following case in accordance with the CARE reporting checklist” should be included at the end of the “Introduction”.” We highlighted this was the first report of breast reduction in a patient with EDS.	To our knowledge, this is the first report of breast reduction in an adolescent patient with Ehlers-Danlos Syndrome.
- Case presentation: at what age was the patient diagnosed with EDS? Did you use drainage after this breast reduction (any collection? When removed?), as I understand you performed the surgery when the patient was 18 years old (in EU this means being adult not adolescent) - you stated that “The patient attended appointments with the physical medicine and rehabilitation department for one year after the surgery.” – so why are you showing photographs 3 mo after surgery /with a silicone dressing on a scar…/, not a final one-year result? -“Surgical complications for patients with hEDS may consist of wound dehiscence, hypertrophic scarring, and hematomas, making surgeons reluctant to operate;” – please provide references.	We added references to provide evidence for this point. We added more, however, we are limited to 20 references.	This has been updated and clarified in the document. She continues to follow-up with PMNR but has been lost to follow-up in our clinic. Unfortunately, we have patients fill out the breast Q on the final follow-up and this was not completed. We understand these results are not long-term follow-up but they do demonstrate there there was no initial wound healing or bleeding increase in this patient with a diagnosis of EDS. Surgical complications for patients with hEDS may consist of wound dehiscence, hypertrophic scarring, and hematomas, making surgeons reluctant to operate.[5,8–10]