Peer Review File

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Reviewer A

I congratulate with you for this interesting case presentation, that augment the body of evidence on the utility of NIR technology for the treatment of chylothorax. However, there are some points that need to be further elucidated and some imperfections that need to be addressed.

- pag. 4, line 92: "The most common etiology of the non traumatic chylothorax is idiopathic." I would better rephrase this sentence as idiopathic etiology makes sort of non-sense.
Reply: Thank you for your comment. I have rephrased it in the text.
Changes in the text: Most non-traumatic chylothoraxes are idiopathic

- pag 4, line 94-101: line all this sentences require a proper bibliography reference
There are two references that I have updated- line 100 and 102

- pag 5, line 119: the Authors refer to a paraspinal lymphatic mass that is described again all along the manuscript. However, no mention is made as to the nature of this mass, which might have a relevant importance: first, if the mass is the cause of chylothorax, I would not consider this case as idiopathic, but rather secondary to a lymphatic obstruction. This would change the therapeuthic approach as treatment of the underlying cause is the mainstay of secondary chylothorax, In addition, if this mass was a tumor that could not be excised or reduced in mass by standard treatments, I would have considered a pleuro-peritoneal shunt as a viable palliative option. Could the Authors comment on that and give further details on the paraspinal mass nature?
Reply: Thank you for this very important question. At the time the scan was done, it was unclear what the mass was and on pathology only appeared as normal lymphatics. We had our patient assessed by our genetics team to identify the etiology of the mass as a potential abnormal congenital lymphatic collection but the pathology came back as normal lung lymphatics. As such, we rephrased the report to reflect that and instead of a lymphatic mass denoted it as abnormal lymphatics. A pleuro- peritoneal shunt was considered however given how refractory she was to thoracoscopic drainage, our main concern was source control as our previous palliative measures failed to resolve the refractory chylothorax.
Changes in the text: instead of lymphatic mass parasapinal lymphatic enhancements p6 line 126-127

- pag 6, line 136: could the Authors explain why they opted for lung decortication instead of a parietal pleurectomy for obtaining pleurodesis? I also wonder why, when disposing of a NIR camera, the surgery was performed by thoracotomy,

while many papers report high rates of success when TD ligation was performed by VATS.
Reply: Thank you for the interesting point and question.
When it comes to parietal pleurectomy vs lung decortication, we performed a pleurectomy and decortication. Given the angulation of the area of concern and after discussing with interventional radiology, we opted to convert to a mini thoracotomy for better visualization especially with the multiple failed embolization attempts. The location of the lesion was in a fold that we did not believe we would be able to easily visualize using minimally invasive approaches. Also, once we start the injection with ICG, if we are unable to immediately visualize, the fluorescent chyle will then start pooling. As such, upon converting to a thoracotomy, we would have lost time and exacerbated the pooling.
Changes: page 6, line 134-138

- pag 6, line 139: how was the dose of ICG determined? Many publications report a dose in mg/kg. Was the injection unilateral or bilateral?
Reply: 5 mg/kg is the dose of ICG used and that has been added to the paper. The injection was unilateral and on the same side of the pleurectomy and thoracic duct ligation.
Changes in the text: we have added the dose and site of injection to the manuscript on p7, line 143

- pag 6, line 141: why a ligation of the TD, once identified by fluorescence, was not performed? I ca barely imagine that a simple glue injection on the leakage point would be sufficient to close the fistula (as actually later described in line 146…)
That is a very valid point. The reason no direct ligation was performed was because we could identify the general area from which fluorescence was leaking but could not localize a unique enough spot to identify a leaking duct and addressed, We first applied multiple clips to whatever appeared to be safe intraop and possible sites from where the leakage was coming. Once we saw a dramatic decrease in fluorescence accumulation, we then added glue over a wider area and ensured that the entire area of concern was covered and addressed. This has been further clarified in the text.
Changes: p7 line 144-145

- page 7, line 145: what do you mean with “her diet was advanced”?
Diet advancement was originally changing her diet from NPO to clear liquids to full liquids and then fat free diet.
Changes int eh text: This has been clarified in the text.p7, lines 150-151

- there are several abbreviations along the manuscript that need to be expressed in their full form when cited for the first time
Thank you for pointing that out. Indocynaine green (ICG) line 103 has been

corrected, TB was explained as tuberculosis on line 108, NPO and TPN on line 115, line 1129 computed tomography for CT,)

- when reading the conclusions paragraph, after the description of the overall course of this patient, I raise some concerns regarding the comprehensive sense of this experience and the relevance given to the use of ICG. From the case description ICG was used only to identify the spillage point, but no ligation was performed and glue application resulted in a substantial failure of the procedure. I would therefore rather focus the main message of the paper on the importance of the multidisciplinary approach more that on the effectivenes of ICG-guided identification of the TD.
Thank you for your clarification. Indeed, in the initial manuscript, we did not mention that we actually performed an intraoperative ligation with clips that was guided by ICG. This was explained further and as such the conclusion now reflects the diagnostic and therapeutic component of this imaging technology. Secondly, we believe that the multidisciplinary approach is a very important takeaway from out case report.
Changes in text: Lines 191-193 p 9

Considering the already available literature on the issue describing better results with a less invasive approach I think that the contribution of this paper in the present form would not add any relevant information on the topic and therefore I do not think it can be accepted for publication.

Reviewer B

Great solution. An advice. To identify the thoracic duct it is easier to inject green into the subcutaneous tissue as I have amply demonstrated:

Int J Med Robot
. 2022 Jun;18(3):e2380. doi: 10.1002/rcs.2380. Epub 2022 Feb 9.
Fluorescent lymphography for thoracic duct identification: Initial experience of a simplified and feasible ICG administration
Giuseppe Barbato 1, Francesca Cammelli 1, Giovanni Braccini 1, Fabio Staderini 1, Fabio Cianchi 1, Francesco Coratti 1
Thank you for your valuable feedback. Indeed, we have come across reports of injecting subcutaneously. However, given the multiple procedures they patient had underwent, we had opted to go the more guaranteed, fluorescence-guided approach of direct inguinal injection. There are patients who would certainly benefit from the simpler approach of subdermal injection.
Changes in text: line 175-177 p8

Reviewer C

I read with interest the manuscript entitled “Fluorescence-Guided Surgery with Indocyanine Green to Identify an Idiopathic Chyle Leak-Case Report”. The authors report a complex case of refractory idiopathic chylothorax treated after Fluorescence-Guided Surgery with indocyanine green.
The topic is interesting. In fact, the role of ICG in idiopathic chylothorax is still controversial and this report may help a wider diffusion of this technique.
English language is straight and correct. Figures can be improved in quality.
However there are some major issues that should be addressed:
1- Doing a quick search on PubMed matchin the therms Inocyanine Green AND idiopathic chylothorax, the treatment of spontaneous chylothorax with ICG is already well described in 2020 by Bassi et al. So your case does NOT represent the first described case of ICG use in idiopathic chylothorax. Please correct and add the previously reported case in your discussion

- Bassi M, Vannucci J, Venuta F, De Giacomo T. Effectiveness of indocyanine green fluorescence for the identification of thoracic duct in recurrent idiopathic chylothorax. Interact Cardiovasc Thorac Surg. 2020 Aug 1;31(2):284. doi: 10.1093/icvts/ivaa080. PMID: 32706031.
Thank you for your comment. We made sure to remove the terms first. However, we have in our study provided in addition to identifying the duct, the use of this technology to confirm the condition has been addressed and that the leak is resolved. The reference is included in the test as reference number 2.
Changes in text: page 8 line169

2- In the manuscript, the authors describe a paraspinal lymphatic mass and it is not clear if there is an underlying lymph node disease. In this case, it cannot be classified as idiopathic chylothorax.
Thank you for the comment and question. The term mass has been replaced by paraspinal lymphatic enhancements. On pathology it was identified as normal lymphatics and such is rather idiopathic.
Changes in text: instead of lymphatic mass we used parasapinal lymphatic enhancements p6 line 126-127

Reviewer D
I would describe with more detail the procedure during ICG visualization! Why you did not legate the duct? What is the second procedure?
Why not a minimally invasive porcedure in thoracoacopy?
I propose to add more references

Thank you for this valuable review.
The procedural visualization of ICG was explained in lines 133-143. The duct was actually ligated and that has been added to the manuscript. This was the first procedure done followed by a second interventional radiology thoracic duct

ligation. There was no separate surgical procedure.

Changes in text: p6, line 128-134
The minimally invaseive approach has been addressed in reviewer A

Given the angulation of the area of concern and after discussing with interventional radiology, we opted to convert to a mini thoracotomy for better visualization especially with the multiple failed embolization attempts. The location of the lesion was in a fold that we did not believe we would be able to easily visualize using minimally invasive approaches. Also, once we start the injection with ICG, if we are unable to immediately visualize, the fluorescent chyle will then start pooling. As such, upon converting to a thoracotomy, we would have lost time and exacerbated the pooling.

Changes: page 6, line 134-138

References were changed accordingly.