

SPECIFIC COMMENTS TO AUTHORS

Congratulation to the authors for the great work done. This case report is important, and the manuscript is well-written. Thank you for the opportunity to review this work. This manuscript is a case report presented with a localized Menetrier's disease with an underlying lipoma. -1 Title. Does the title reflect the main subject/hypothesis of the manuscript? -Yes -2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? -Yes -3 Key words. Do the key words reflect the focus of the manuscript? -Yes -4 Background. -Menetrier's disease is also characterized by protein-losing gastropathy and hypoalbuminemia. The authors stated in the case presentation section that serum protein or albumin levels were not tested due to no suspicion of Menetrier's disease at that time point. However, I believe a liver function test, including serum protein, might be obtained before the operation (pre-operative laboratory evaluation). Please report the serum protein result in this case if data is available. If no data is available, please discuss this limitation in the discussion section, such as the importance of serum protein in alerting the physician about this disease. -5 Methods. -Not applicable. -6 Results. -There were good results. -7 Discussion. -Although the pathophysiology of Menetrier disease is not fully elucidated, increased production of TGF-alpha and increased signaling of the epidermal growth factor receptor (EGFR), which stimulates the growth of epithelial cells, is proposed to be the pathophysiology of this disease. Please provide the investigation of TGF-alpha and EGFR using immunohistochemistry in this case. If not done in this case, please discuss when this investigation should be done in a patient with suspected Menetrier's disease. -8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? -Yes -9 Biostatistics. -Not applicable. -10 Units. Does the manuscript meet the requirements of use of SI units? -Yes -11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? -Yes -12 Quality of manuscript organization and presentation. -Yes -13 Research methods and reporting. -Yes -14 Ethics -Yes

Dear Sir/Madam

Thank you very much for the thorough review as you brought up important points that can help enrich our paper.

Unfortunately serum protein or albumin level was not tested during preoperative laboratory examinations, so we cannot provide the results. The importance of hypoalbuminaemia in Menetrier's disease is further discussed in Discussion section as you requested.

During the diagnostic process we did not perform immunohistochemical reactions using TGF α and EGFR, therefore we cannot provide the results. The diagnostic process of Menetrier's disease was based on pathological changes characteristic for the disease such as foveolar hyperplasia, tortuous foveolar epithelium and cystically dilated deeper glands, decreased number of parietal and chief cells, scattered strands of smooth muscles and mild inflammation(1). Directions using TGF α and EGFR are not routinely performed during the diagnostic process as they are not a requirement for the diagnosis of Menetrier's disease. However, the definite pathophysiology of Menetrier's disease is still researched and one of the theories is linked to increased production of TGF-alpha and as a consequence increased signaling of the epidermal growth factor receptor (EGFR). One of consequences of TGF α overexpression is cellular proliferation which in consequence may trigger neoplastic transformation. One of the studies on mice has proven that TGF α overexpression in the mices' stomach mucosa shows changes characteristic of Menetrier's disease(2,3,4). Furthermore, studies on Menetrier's disease patients proved a similar mechanism(5,6). Increased overexpression of TGF α causes increased signaling of EGFR, transmembrane receptor with tyrosine kinase activity which further triggers intracellular signaling cascade, expanding the cell's proliferation. The EGFR oversignaling proved to be an important feature from a clinical point of view as it allowed for alternate therapy using monoclonal antibodies (eg. cetuximab)(7,8). However as there are various approaches to treating Menetrier's disease using antibodies is still not used as a first choice. Due to ongoing research we routinely do not perform those immunohistochemical reactions. We did perform H.pylorii reaction- infection which is also connected with symptoms of Menetriers'

disease patients and which is treated to alleviate the symptoms of Menetriers' disease as well. In the future studies it is worth to focus on the study of TGF α and EGFR pathways in order to understand its pathophysiology and consequences.

The extensive information on the role of TGF α and EGFR overexpression in Menetrier's disease was added to the Discussion section.

On behalf of the Authors

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