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INTERSTITIUM A POSSIBLE NEW ORGAN

Nicoară Nicolae ^{*}, Bucur Angela ^{*}, Teodorescu Andrei George ^{*}, Maghiar Adriana ^{*}, Holt Gineta ^{*}, Pop Alexandra ^{**}

* University of Oradea, Faculty of Medicine and Pharmacy, Department of Morphological Sciences, Oradea, Romania, nicduni@yahoo.com

** University of Oradea, Faculty of Medicine and Pharmacy, studentă Medicină, e-mail: alepop95@yahoo.com

Abstract

A recent study has noticed the existence of a new unknown structure distributed in connective tissue all over the body. This structure is made up of a network of fluid-filled spaces that haven't been noticed before. The method of preparing slides for histology involves preserving the histological parts in formaldehyde and the dehydration of them in the following steps. The freezing section keeps those spaces that can be viewed microscopically. The histological structure of this new extracellular fluid circulation system remains to be clarified by further research. Understanding this new structure could provide another vision of the pathophysiology of some poor understood diseases, such as Chron's disease and ulcerative colitis. It could also help to understand the metastasis process. The new discovered organ located in connective tissue has a sponge-like structure with a network of channels in which there is extracellular fluid.

Key words: interstitium, fluid extracellular, confocal laser endomicroscopy

INTRODUCTION

The connective tissue is considered to be the seat of the third space where body fluids accumulate (Aukland, K.,1984,). Following the study of 12 pancreatic-biliary ducts obtained surgically and prior to arterial ligation and resection, the patients were given intravenous fluroscein and the pCLE in situ visualization microscopy technique observed a cross-linked pattern. Then the pieces were resected and scanned again with pCLE ex vivo, confirming the cross linked pattern, fluorescein still present in the resected parts. The samples were introduced into the cold section and serial sections were made perpendicular to the lumen of these spaces. Longitudinal sections were also performed and visualized with the fluorescence microscope, the pattern again correlating with the fluorescein observed with pCLE. In the final sections, the absence of fluorescein was observed due to freezing, air-drying, fixation and

washing processes, causing fluid to drain from the final samples. Parallel sections with frozen samples, stained with trichrome masson, confirmed the presence of collagen bands that maintained an open space. This suggests that previous descriptions of the dense structure of the submucosa represent an artifact due to fluid loss during excision and fixation due to the collapse of normally separated colagen fibers adhering to each other. It was noticed that the reticular pattern appeared in 30 seconds after intravenous fluorescein administration. Approximately at the same time to visualize lymph nodes, but less than to visualize vascular structures (Benias, P.C et al, 2018), (Benias, P. C. et al., 2016). Ultrasound investigation of the submucosa of some viscera of the dermis and fascia occurs heterogeneously, while the tendons and ligaments appear dark, indicating in the first situation the presence of fluid or adipose tissue(Chung, I. K. & Hawes, R. H. ,2007), (Patil, P. & Dasgupta, B. ,2012)(Sharma, M. et al ,2015,). Also, studies on ultra structure of the skin, vermiform appendix, and periaortic adventists confirmed the existence of these spaces but were not exactly characterized (Smith, L. T. & Holbrook, K. A. 1982)(Ohtani, O. et al ,1986). At the level of the liver, was identified the Mall space in the portal area, which is likely to represent this interstitium (Niiro, G. K. & O'Morchoe, C. C., 1986,) (Mall, F. P. ,1906,). Immunohistochemical tests have shown the presence of CD34positive fibroblasts or even mesenchymal stem cells(Sidney, L. E., 2014).

MATERIAL AND METHOD

The use of a new type of microscopy called confocal laser endomicroscopy provides a real-time image of human tissue up to a depth of 60-70 micrometers during endoscopy. Applying fluorescein injections into the bile duct showed a reticular pattern of sinuses that do not have anatomically known correspondence, and also the cold section keeps the pattern of these structures. The cold cut method reveals spaces in connective tissue of the skin, submucosa of the digestive tract and other organs containing connective tissue.

RESULT AND DISCUSSION

The human body is made of 70% water that has a relatively well-known circuit (Siri, W.E., 1956). According to current information, several types of circulation of aqueous solutions are known: blood circulation, venous

circulation, lymphatic circulation, cerebrospinal fluid circulation, circulation of secretions from the digestive tract and the urinary system. The new data have shown the existence of another type of circulation in the connective tissue of extracellular fluid in a sponge-like network. The role of this system seems to be anti-shock, but may also have a pathological implication. Other hypotheses support the involvement of this space in the formation of keloid scars that have different distribution depending on the applied skin pressure (Huang, C. *et al.*, 2017). The histological structure of this new extracellular fluid circulation system remains to be clarified by further research (Rennels, M.L., 1985). Understanding this new structure could provide another vision of the pathophysiology of some poor understood diseases, such as Chron's disease and ulcerative colitis(Sartor, R.B., 2006). It could also help to understand the metastasis process.

CONCLUSIONS

- 1. It has been observed the existence of a new anatomical structure not yet described by the anatomy and histology textbooks.
- 2. The new discovered organ located in connective tissue has a sponge-like structure with a network of channels in which there is extracellular fluid.
- 3. This new structure could be the missing link in understanding the spread of cancer cells that avoids lymph nodes.
- 4. Pathology in the digestive sphere may be explained by the existence of this anatomical structure.
- 5. Previous studies have noticed the existence of this space, but no detailed description has been made.

REFERENCES

- 1. Aukland, K. ,1984, Distribution of body fluids: local mechanisms guarding interstitial fluid volume. J. Physiol. (Paris) **79**, 395–400.
- Benias, P. C. *et al.*, 2016, Needle-based confocal Endomicroscopy for evaluation of malignant lymph nodes - a feasibility study. *Endoscopy* 48, 923– 928.
- Benias, P.C., Wells, R.G., Sackey-Aboagye, B., Klavan, H., Reidy, J., Buonocore, D., Miranda, M., Kornacki, S., Wayne, M., Carr-Locke, D.L. and Theise, N.D., 2018. Structure and distribution of an unrecognized interstitium in human tissues. Scientific reports, 8(1), p.4947.

- 4. Chung, I. K. & Hawes, R. H. ,2007. Advantages and limitations of endoscopic ultrasonography in the evaluation and management of patients with gastrointestinal submucosal tumors: a review. *Rev. Gastroenterol. Disord.* 7, 179–192.
- 5. Huang, C. et al. ,2017 Keloid progression: a stiffness gap hypothesis. Int Wound J. 14, 764–771.
- 6. Mall, F. P. ,1906, A study of the structural unit of the liver. *Amer. J. Anatomy* **5**, 1–82.
- 7. Niiro, G. K. & O'Morchoe, C. C. ,1986, Pattern and distribution of intrahepatic lymph vessels in the rat. *Anat. Rec.* **215**, 351–360.
- 8. Ohtani, O., Ohtsuka, A. & Owen, R. L. ,1986, Three-dimensional organization of the lymphatics in the rabbit appendix. A scanning electron and light microscopic study. *Gastroenterology*. **91**, 947–955.
- 9. Patil, P. & Dasgupta, B. ,2012, Role of diagnostic ultrasound in the assessment of musculoskeletal diseases. *Ther. Adv. Musculoskelet. Dis.* **4**, 341–355.
- Rennels, M.L., Gregory, T.F., Blaumanis, O.R., Fujimoto, K. and Grady, P.A., 1985. Evidence for a 'paravascular'fluid circulation in the mammalian central nervous system, provided by the rapid distribution of tracer protein throughout the brain from the subarachnoid space. Brain research, 326(1), pp.47-63.
- 11. Sartor, R.B., 2006. Mechanisms of disease: pathogenesis of Crohn's disease and ulcerative colitis. Nature Reviews Gastroenterology and Hepatology, 3(7), p.390.
- Sharma, M., Rai, P., Rameshbabu, C. S. & Senadhipan, B. ,2015, Imaging of peritoneal ligaments by endoscopic ultrasound (with videos). *Endosc. Ultrasound.* 4, 15–27.
- Sidney, L. E., Branch, M. J., Dunphy, S. E., Dua, H. S. & Hopkinson, A. ,2014, Concise review: evidence for CD34 as a common marker for diverse progenitors. *Stem Cells.* 32, 1380–1389.
- 14. Siri, W.E., 1956. The gross composition of the body. Adv Biol Med Phys, 4(239-279), p.513.
- 15. Smith, L. T. & Holbrook, K. A. 1982 Development of dermal connective tissue in human embryonic and fetal skin. *Scan. Electron. Microsc.***4**, 1745–1751.