Meningeal lymphatic vessels

Dural lymphatics refer to the lymphatic vessels and system found within the dura mater.

The presence and significance of dural lymphatics have been the subject of scientific investigation and debate.

Traditionally, the central nervous system (CNS) was considered devoid of a traditional lymphatic system, which is responsible for the drainage of interstitial fluid, immune cell trafficking, and waste clearance in other tissues of the body. However, more recent research has suggested the existence of lymphatic vessels within the dura mater, which may play a role in CNS lymphatic drainage.

Studies in animals and human cadavers have provided evidence supporting the presence of dural lymphatics. These lymphatic vessels have been observed primarily in the meningeal layers adjacent to the superior sagittal sinus, a large vein in the brain. They have also been identified in the region of the cribriform plate, which separates the nasal cavity from the cranial cavity.

The dural lymphatic vessels may be connected to cervical lymph nodes, suggesting a potential pathway for cerebrospinal fluid (CSF) and waste clearance from the CNS. This drainage system has been proposed to be involved in immune surveillance, clearance of macromolecules, and the regulation of brain homeostasis.

The discovery of dural lymphatics has implications for our understanding of neurological disorders, including neuroinflammatory conditions, neurodegenerative diseases, and brain tumor metastasis. Dysfunction or impairment of dural lymphatic drainage may contribute to the accumulation of waste products, protein aggregates, and immune dysregulation in the CNS.

It's important to note that research on dural lymphatics is still evolving, and their exact functions and clinical implications are still being investigated. Further studies are needed to fully understand the significance of dural lymphatics in CNS physiology and pathology.

The lymphatic drainage system of the brain, composed of the glymphatic system and meningeal lymphatic vessels (MLVs), plays an essential role in the clearance of toxic waste after brain injury.

In 2015, the traditional view of the brain having no lymphatic vessels was challenged by evidence showing functional lymphatic vessels lining the cranial dural sinuses in rodents

The meningeal lymphatic vessels were discovered in 2015 as the drainage system involved in the mechanisms underlying the clearance of waste products from the brain. The blood brain barrier (BBB) is a gatekeeper that strongly controls the movement of different molecules from the blood into the brain.

There is extremely limited information on how the brain clears the substances that cross the BBB.

Using the model of the sound-induced opening of the BBB, Semyachkina-Glushkovskaya et al. clearly show how the brain clears dextran after it crosses the BBB via the meningeal lymphatic vessels. They first demonstrate the successful application of optical coherence tomography (OCT) for imaging of the lymphatic vessels in the meninges after the opening of the BBB, which might be a new useful strategy for noninvasive analysis of lymphatic drainage in daily clinical practice. Also, we give information about the depth and size of the meningeal lymphatic vessels in mice. These new fundamental data with the applied focus on the OCT shed light on the mechanisms of brain clearance and the role of lymphatic drainage in these processes that could serve as an informative platform for the development of therapy and diagnostics of diseases associated with injuries of the BBB such as stroke, brain trauma, glioma, depression, or Alzheimer disease [1].

The central nervous system (CNS) is considered an organ devoid of lymphatic vasculature. Yet, part of cerebrospinal fluid (CSF) drains into the cervical lymph nodes (LNs). The mechanism of CSF entry into the LNs has been unclear.

Aspelund et al. in 2015 reported the surprising finding of a meningeal lymphatic vessel network in the dura mater of the mouse brain. They show that dural lymphatic vessels absorb CSF from the adjacent subarachnoid space and brain interstitial fluid (ISF) via the glymphatic system. Dural lymphatic vessels transport fluid into deep cervical LNs (dcLNs) via foramina at the base of the skull. In a transgenic mouse model expressing a VEGF-C/D trap and displaying complete aplasia of the dural lymphatic vessels, macromolecule clearance from the brain was attenuated, and transport from the subarachnoid space into dcLNs was abrogated. Surprisingly, brain ISF pressure and water content were unaffected. Overall, these findings indicate that the mechanism of CSF flow into the dcLNs is direct via an adjacent dural lymphatic network, which may be important for the clearance of macromolecules from the brain. Importantly, these results call for a reexamination of the role of the lymphatic system in CNS physiology and disease [2].

Louveau et al. discovered functional lymphatic vessels lining the dural sinuses. These structures express all of the molecular hallmarks of lymphatic endothelial cells, are able to carry both fluid and immune cells from the cerebrospinal fluid, and are connected to the deep cervical lymph nodes. The unique location of these vessels may have impeded their discovery to date, thereby contributing to the long-held concept of the absence of lymphatic vasculature in the central nervous system. The discovery of the central nervous system lymphatic system may call for a reassessment of basic assumptions in neuroimmunology and sheds new light on the aetiology of neuroinflammatory and neurodegenerative diseases associated with immune system dysfunction [3].

A lack of research focused on understanding such a drainage system may be attributed to its location in a unique area of the brainless commonly investigated, the dura mater.Macromolecules and waste products in the brain were previously thought to be cleared by a system of glial cells and arterial pulsations that helped to recycle fluid and lipid transport throughout the brain, called the glial lymphatic or "glymphatic" system.

Although fluids were known to be exchanged between the brain interstitial fluid, cerebrospinal fluid, and the venous circulation via arachnoid granulations, the finding of subarachnoid fluid in the extracranial lymphatic vessels and lymph nodes suggested that there was more to the drainage system of the brain than solely the glymphatic system.

Both Aspelund et al and Louveau et al investigated the existence and functionality of these lymphatic vessels. Aspelund et al investigated a lymphatic vessel "network" in the meninges under the skull bones. They created K14-VEGFR3-IgTG knockout mice with a lack of dura mater lymphatic vasculature. After fluorescent dye was administered to the knockout mice, central nervous system macromolecules could not clear without the dural lymphatic vessels.

The newly found lymphatic vessels had attributes similar to the previously studied lymphatic vessels such as the peripheral lymphatic vessels. Louveau et al also alluded to the importance of the microenvironment surrounding the vessels because these vessels were larger and more complex, depending on the area of the brain. They used surgical removal of deep cervical lymph nodes in vivo to examine interactions between the meningeal lymphatic vessels and the deep cervical lymph nodes rather than the superficial lymph nodes.

The current analyses by Aspelund et al and Louveau et al reinforce the early description of a lymphatic system in the brain. This system could encompass immune cell trafficking, thereby explaining why primary brain tumors rarely metastasize into cervical lymph nodes.

A disrupted brain drain could also explain the misfolded amyloid β accumulation in Alzheimer disease and other neurodegenerative diseases. These publications may engender new investigations into the neuropathology of various central nervous system disorders and reinforce the relevance of neuroanatomy not only for neurosurgery but also for neuroscience [4].

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