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Neuroradiological manifestations of neuroinflammatory diseases; A concept for rare cases and neuro-COVID-19

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Abstract

Uncommon neurological diseases make for roughly half of all rare diseases. As one of the key players in the diagnostic process, neurologists require guidelines on the types of screening tests that can be done. In this sense, biomarker research has been very active. By minimizing the chance of misdiagnosis and improper therapy, diagnostic biomarkers may help reduce the risk of disease progression. Also, Neurological complications and associated radiological findings have been reported in an increasing number of patients with COVID-19 infection. Despite improved methods, diagnosing CNS inflammatory diseases is still difficult and time-consuming. Although MRI is essential in this procedure, it might be confusing in some circumstances due to overlapping radiological results. Considering the above facts, the necessity for specialized biomarkers seems to be paramount. Serological markers appear to merit special consideration. Peripheral blood samples, unlike CSF, are easily obtained in routine ambulatory care for many periods, allowing noninvasive monitoring of therapy response. A complete combination of clinical examination, radiographic assessment, laboratory tests, and often a multidisciplinary approach is required to make an accurate diagnosis.

Keywords: Neurocovid; Neuroinflammatory diseases.

Introduction

Neuroinflammatory illness of the CNS has a wide differential diagnosis that encompasses, but is not limited to, rare neurological conditions [1]. MS must be distinguished from rare MS variants, Acute Disseminated Encephalomyelitis (ADEM), a variety of Neuromyelitis Optica Spectrum Disorders (NMOSDs), Myelin Oligodendrocyte Glycoprotein (MOG) antibody disease, other inflammatory diseases such as primary angiitis of the CNS, systemic lupus erythematosus, Behcet's disease, and neurosarcoidosis.

Neuroinflammation refers to a variety of humoral and cellular reactions. They let the CNS fight against unpleasant events, such as infections and trauma, and play an important role in autoimmune and neurodegenerative illnesses [2]. To be properly examined in vivo, the intricate interactions of immunological, endothelial [3], and neural cells during inflammation necessitate an analogous complexity of imaging approaches.

Long-term mild inflammation, mostly associated with microglial activation, can damage brain cells, promoting neuroinflammation, providing a possible basis for the bidirectional reinforcement of neuroinflammatory and neurodegenerative phenomena [4].

MRI: MRI may be used to study various features of neuroinflammation, allowing researchers to examine the mechanisms

underlying the brain/immune interaction at the vascular, cellular, and interstitial levels. In the clinical setting, Dynamic contrast-enhanced MRI is used for BBB permeability. For Myeloid/glial cells activation, we can use the Spectroscopy of Creatine, Myoinositol, Lactate, Choline, Lipids/macromolecules; and Magnetization transfer.

For finding sequeled, we can look forward to 1-Demyelination Diffusion: Radial diffusivity; 2-Neuronal loss: Spectroscopy: NAA (neuronal loss/dysfunction) 3-Axonal loss: Diffusion: Axial diffusivity 4-Axonal loss: Conventional MRI segmentation: Black holes load, and 5-Demyelination/gliosis Conventional MRI segmentation: T2w lesion load [4].

Molecular imaging of neuroinflammation: Molecular imaging can help understand essential features of the dynamic interaction of numerous inducers, sensors, transducers, and effectors of the coordinated inflammatory response in vivo in animal models and people. Most neurologic conditions have a neuroinflammatory response. Thus, precise and consistent neuroinflammation detection is critical from both a scientific and clinical perspective. To comprehend the complex interplay of various cellular and molecular players in neuroinflammation, molecular imaging can be used. Two-photon microscopy (e.g., T cells) and MRI (macrophages) allow direct observation of peripheral cells into the brain, whereas PET and SPECT imaging allow microglia activation [24]. It may be possible to modify the neurotoxic inflammatory cascade, minimize tissue damage, and improve tissue healing using molecular imaging indicators for neuroinflammation [25]. An important aspect of success is identifying "neurotoxic" versus "neuroprotective" microglia and the effects of treatments that inhibit the former while boosting the latter for enhanced tissue outcome [5].

The Neuro-COVID-19: Coronavirus disease 2019 (COVID-19) causes inflammatory neurological and neuropsychiatric disease, has a wide neuroradiological manifestations that vary depending on the severity of the infection. Mild infection with a high degree of olfactory tract involvement appears to be associated with cranial nerve abnormalities, whereas severe infection is associated with hemorrhagic events. Ischemic infarction was found to be equally common in both mild and severe COVID-19 infection.

Cerebrovascular events in COVID-19 patients are becoming more common. These include hemorrhagic necrotizing encephalopathy, Guillain-Barré and Miller-Fisher syndromes, acute demyelinating encephalomyelitis (ADEM,) and encephalitis. The number of patients with psychosomatic disorders manifesting as memory loss, cognitive dysfunction, depression or other affective disorders is increasing after COVID-19 recovery. Some of these symptoms responded to immunotherapies [6]. Radiological imaging can distinguish many of these neurological manifestations of infection, and also it is vital in determining the course of COVID-19, diagnosing respiratory complications, and managing infected patients. Similarly, radiological techniques are crucial in determining the cause of neurological symptoms associated with SARS-CoV-2 infection. Using radiological imaging techniques to monitor the onset of various symptoms is critical when assessing the severity and scope of involvement. Rapid diagnosis and identification of complications can help avoid long-term secondary conditions and speed up recovery [7]. COVID-19-related neurological illness is challenging to diagnose, investigate, and treat [23]. More clinical, neuroradiological, biomarker and neuropathological research is required to establish underlying pathobiological mechanisms [8]. So radiology biomarkers can be essential for neurocovid diagnosis.

In one Neurocovid investigation, Fallmar et al. quantified the MRI findings by developing an a priori semi-quantitative neuroradiological severity scale and applying it to the MR images by two neuroradiology specialists. The severity scale score was substantially linked with blood biomarkers of CNS injury (glial fibrillary acidic protein, total-tau, ubiquitin carboxyl-terminal hydrolase L1) and inflammation (C-reactive protein), Glasgow Coma Scale score, and the number of days spent in intensive care. Inter-rater agreements for the underlying radiological assessments were 90.5 percent /86 percent (for assessments with 2/3 alternatives). The sum of the interclass correlations was 0.80. The degree of findings in an MRI examination of the brain, assessed using a structured report, is correlated with important biomarkers in this investigation [9].

Diagnostic Biomarkers for rare neuroinflammatory disorders: Rare neurological illnesses are diverse groups that account for nearly half of all rare diseases [10]. Neurologists are one of the most important professionals involved in their diagnostic process, and they also require guidelines on the kind of screening tests that can be performed. Biomarker research has been a particularly active topic in this regard. Diagnostic biomarkers may help with timely diagnosis and good illness management, reducing the risk of disease worsening due to misdiagnosis and incorrect therapy. Although autoimmune demyelinating illnesses of the Central Nervous System (CNS) emerge due to organ-specific autoimmunity, the disease's pathology is organized across multiple anatomical and functional compartments. Rare neurological illnesses are included in the differential diagnosis, but they are not the only ones. Rare MS variations, Acute Disseminated Encephalomyelitis (ADEM), the range of Neuromyelitis Optica Spectrum Disorders (NMOSDs), Myelin Oligodendrocyte Glycoprotein (MOG) antibody illness, and other systemic inflammatory diseases must all be differentiated.

Rare diseases of neuroinflammation, the specific concept for Radiology: Several rare neurological diseases of neurometabolic origin (Leber hereditary optic neuropathy, Leigh syndrome, Kearns–Sayre syndrome, biotin-responsive basal ganglia disease, acute necrotizing encephalopathy, and various leukodystrophies), which are either hereditary or have a strong genetic predisposition, frequently mimic neuroinflammatory diseases of the CNS [11].

Certain uncommon diseases should be considered specifically in neuroinflammation radiology. For instance, primary central nervous system vasculitis (PCNSV) is a poorly understood neuroinflammatory disease of the central nervous system (CNS) that primarily affects the intracranial vascular. While PCNSV is typically manifested by a multifocal beaded constriction of the intracranial arteries, some patients may present with no angiographic abnormalities. A small fraction of PCNSV patients manifests with masslike brain lesions that mimic neoplasms. Suthiphosuwan et al. conducted a retrospective study of 0 biopsy-confirmed cases of tumefactive PCNSV (t-PCNSV) who had CTA or MRA [12]. They suggested that normal vascular imaging

does not rule out the possibility of t-PCNSV infection. Although advanced imaging techniques such as MR perfusion and MR spectroscopy could not reveal specific findings for t-PCNSV, they aided in removing neoplasm from the differential diagnosis. The biopsy is still required for a conclusive diagnosis. Mortezazadeh et al. described another unusual case, an unusual Ankylosing spondylitis (AS) with unique neuroinflammation radiological manifestations. Although the distribution of AS involvement in joints and bones varies, it is typically ascending from the sacroiliac, lumbar, and thoracic regions. They reported an undiagnosed case of AS that lasted five years. Despite the sacroiliac joint's typical look, substantial spinal column involvement in the thoracic area known as the "bamboo spine" was observed. In that patient, the time sequence of SPINE involvement is reversed from what is often observed [13].

Imaging in rare neuroinflammatory disorders: The CNS is an inaccessible organ that reflects disease processes poorly in the peripheral blood. Clinical and radiological heterogeneity in rare demyelinating neuro-inflammatory diseases necessitates more precise phenotypic characterization and frequent update of diagnostic and therapeutic consensus guidelines [14,15]. It also needs rigorous, evidence-based clinical outcome definition. For example, rare MS variations are still diagnosed using historical clinical, pathological, and radiological descriptions. Despite laboratory data, it is uncertain if these entities are MS. However, universal standards addressing patient selection eligible for long-term immunotherapy and associated treatment protocols are still absent [16]. Rare and ill-defined entities in particular necessitate customized treatment and long-term maintenance. Large collaborations and network development are required to fully describe these disorders' clinical, radiological, biological, and pathological spectrum [17].

Conclusion

Despite improved methods, diagnosing CNS inflammatory diseases is still difficult and time-consuming. Although MRI is essential in this procedure, it might be not very clear in some circumstances due to overlapping radiological results. Considering the above facts, the necessity for specialized biomarkers seems to be paramount. Serological markers appear to merit special consideration. Peripheral blood samples, unlike CSF, are easily obtained in routine ambulatory care at many time periods, allowing noninvasive monitoring of therapy response [18]. Healthcare providers treating COVID-19 patients should be aware of these potential complications and, if necessary, consider neurological assessments and neuroimaging studies [19]. A complete combination of clinical examination, radiographic assessment, laboratory tests, and often a multidisciplinary approach is required to make an accurate diagnosis. Observing the progression of neuroinflammation and clinical indicators and imaging findings in several regions would assist clinicians in accurately and swiftly diagnosing neuroinflammatory disorders. Additionally, the radiologic manifestations of neuro-rheumatology illnesses may arise randomly.

Future research

Artificial intelligence (AI) advances have enabled computer algorithms to surpass human interpretation of medical pictures in very specialized areas. It may be appropriate to focus on the implications for clinical imaging in neuro-rheumatology after this shock wave. Artificial intelligence has long been used in neurology and rheumatology imaging. These approaches have been used sparingly in clinical practice. Deep learning's recent breakthroughs will change this, where AI will augment human picture interpretation and clinical reasoning [20]. About the advance of Imaging-guided treatment, many neuroinflammation may be future signals of neuromodulation or intervention [21]. They can be paired with neuroimaging and used on any nerves or organs. For example, radiofrequency can ablate or modify different inflammation-producing components to alleviate pain and inflammation [22].

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