

A Case of Ankylosing Spondylitis Overlapped by Presenile Dementia and Epilepsy

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Abstract:

This was a female (64-year-old) with cognitive decline for nearly 7 years, based on her ankylosing spondylitis (sacroiliitis, AS), accompanied with her hippocampal atrophy and sclerosis on the left side on MRI and the CT scan of her brain showed a large-sized demyelination on her left cortex of cerebrum, but not committant with a hemiplegia correspondingly. Her mother suffered from “humpback” (compression fracture of thoracic spine), and this lady had experienced persistent backache for many years prior to her dementia; and now, a severe pain emerged at her right hip with a difficult walking. During her stay in ward, the patient had an episode of epilepsy (grandmat), and her CD4/CD8 ratio was 4.33 higher than normal, with a positive result of HLA-B27 (an immunological mark for AS). A diagnosis of sacroiliitis due to her family history of ankylosing spondylitis (humpback) was established according to a classical morphological findings on her pelvic X-ray. Finally, integrating the current dementia with her sacroiliitis and family history of AS, the essential etiology of her presenile dementia was thought to be autoimmune dementia (AiD); in short, her ankylosing spondylitis (AS) had been overlapped by a presenile dementia (AiD).

Keywords:

Autoimmune Dementia, Ankylosing Spondylitis, Sacroiliitis Hippocampal Atrophy, CD4/CD8 Ratio, Overlap Syndrome

1. Introduction

This was a 64-year-old female, admitted with a complaint of dementia for nearly 7 years, alongside with her hippocampal atrophy and sclerosis on the left side on MRI. There was a history of persistent backache for many years before her cognitive decline seven years ago, and now severe pain occurred in her right hip with a difficult walking. Tracing back to her family history, her mother suffered from “humpback”. Also, the CT scan of this lady showed an irregular demyelination on the left cortex of brain, but not complicating a hemiplegia correspondingly. During her stay in ward, the patient experienced an episode of “grand mat” (epilepsy), and her CD4/CD8 ratio

(lymphocyte subpopulation) was 4.33, together with a positive result of HLA-B27 (an immunological mark for AS). A diagnosis of sacroiliitis was then made on the basis of her family history of ankylosing spondylitis (AS) according to a classical morphological findings on her pelvic X-ray. As a result, integrating the current dementia with her sacroiliitis, the causative factor of her present presenile dementia at that time, was considered as autoimmune dementia (AiD); that is, her ankylosing spondylitis (AS) had been overlapped by a presenile dementia (AiD). It has been emphasized in this case that the elders' conditions, such as dementia, emerged almost in their "late stage", and less effective in their treatment. By comparison, preventive screening and detection of autoimmune diseases for their offspring might be more significant sociologically.

2. Case Report

This was a female (64-year-old) who had a chief complaint of cognitive decline (dementia) for 7 years, associated with her hippocampal atrophy and sclerosis on the left side on MRI; also showing an irregular demyelination on the left cortex of her cerebrum on CT, not presenting a hemiplegia correspondingly; but remaining a severe pain in her right hip, alongside with the difficulties in doing with a bath. During her stay in ward, the patient experienced an episode of "grand mat" (epilepsy) before dawn—a rollover of both eyes, white bubbles in her mouth, and positive signs of arm clonus on her both were seen. A clinical expert believed that "the demyelination" on her left cortex pointed to "cerebral infarction", and relevant therapy was then given intravenously, but fewer effects were achieved. As an immunological study, her negative results of anti-nuclear antibody spectrum (ANAs) were observed; but her CD4/CD8 ratio (lymphocyte subpopulation) was 4.33 higher than normal (reference ranges: 0.58-2.56), indicating to immune function disturbance, together with a positive result of HLA-B27 (an immunological mark for ankylosing spondylitis, AS). The son of this lady had been inquired of some details about her family history and learned that his grandma suffered from "humpback" (compression fracture of thoracic spine caused by ankylosing spondylitis). The patient had been allergic to penicillin and had gotten ever-lasting backache; and recently she acquired an intense pain in her right hip and difficulty in walking. Furthermore, her son has "perovskitis" (an autoimmune disease for sweat glands). Compared with the left sacroiliac joint (clear structure), the right one was a little blurred on her pelvic X-ray (see Figure 1), indicating to sacroiliitis on the right (yellow arrow).

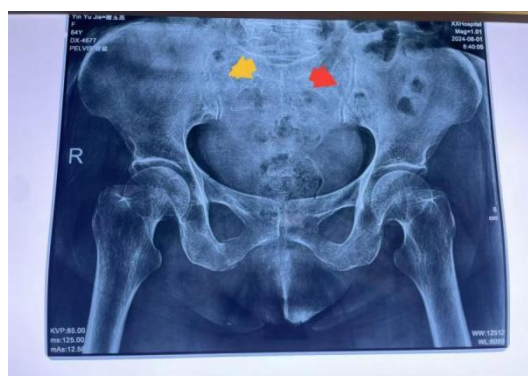


Figure 1. A 64-years-old female(No.20183414).

Comparatively, the red arrow (as a reference) showing normal sacroiliac joint, but the yellow one (on the right) looked obscure, indicating to sacroiliitis. Combined the

current status of “presenile dementia” with the essential history of “ankylosing spondylitis (sacroiliitis)”, the causative factor of presenile dementia was thought to be AiD(autoimmune dementia); that is, her ankylosing spondylitis (AS) had already been overlapped by presenile dementia (AiD) and later epilepsy.

3. Pathophysiology of Overlap Syndrome

3.1. Inflammatory Mechanisms in Ankylosing Spondylitis

Ankylosing spondylitis (AS) is a debilitating chronic inflammatory disease primarily affecting the axial skeleton, including the sacroiliac joints and the spine. It is characterized by persistent inflammation leading to pain, stiffness, and progressive spinal fusion. The pathophysiology of AS involves an aberrant autoimmune response where the body’s immune system mistakenly targets its own tissues. This autoimmune reaction is predominantly driven by pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α) and interleukin-17 (IL-17). These cytokines play a crucial role in mediating the inflammatory processes that contribute to the disease. TNF- α is a key cytokine involved in AS. It promotes inflammation by stimulating the production of other inflammatory mediators and recruiting immune cells to the sites of inflammation. Elevated levels of TNF- α in the serum and synovial fluid of AS patients reflect the chronic inflammatory state associated with the disease. Similarly, IL-17, a cytokine produced by T-helper 17 (Th17) cells, is implicated in driving inflammation and bone remodeling. IL-17 stimulates osteoclastogenesis, leading to bone erosion and new bone formation, which contributes to the fusion of spinal vertebrae. A critical genetic factor associated with AS is the presence of the HLA-B27 antigen. HLA-B27 is a major histocompatibility complex (MHC) class I molecule that is highly prevalent in individuals with AS. The antigen is believed to influence the immune response by presenting self-antigens to T-cells, which may lead to an autoimmune attack on the body’s own tissues. The interaction between HLA-B27 and other environmental factors triggers a cascade of immune responses that exacerbate inflammation and disease progression. In AS, chronic inflammation leads to the formation of syndesmophytes, which are bony growths bridging the spinal vertebrae. This results in the characteristic spinal stiffness and reduced mobility observed in patients. Beyond the spine, the systemic inflammation associated with AS can impact other organs, including the eyes (e.g., uveitis), heart (e.g., aortic regurgitation), and lungs (e.g., pulmonary fibrosis). The systemic effects of AS highlight the importance of comprehensive management strategies to address not only the spinal symptoms but also the potential extra-articular manifestations of the disease. Overall, understanding the inflammatory mechanisms underlying AS is essential for developing effective treatment strategies. Targeting key cytokines like TNF- α and IL-17 with biologic therapies has shown promise in reducing inflammation and halting disease progression, thereby improving the quality of life for patients with AS.

3.2. Neuroinflammatory Processes in Presenile Dementia

Presenile dementia, also known as early-onset dementia, encompasses a range of neurodegenerative disorders that manifest with cognitive decline and functional impairment at an earlier age than typical age-related dementias. The neuroinflammatory processes underlying presenile dementia involve complex interactions between various brain cells and inflammatory mediators. A key feature of these processes is the activation of microglia and astrocytes, the primary immune cells

within the central nervous system (CNS). Microglia, the resident macrophages of the brain, play a crucial role in monitoring and responding to pathological changes. In the context of presenile dementia, microglial activation leads to the release of inflammatory cytokines such as interleukin-1 β (IL-1 β) and tumor necrosis factor- α (TNF- α). These cytokines contribute to a pro-inflammatory environment that exacerbates neuronal damage. IL-1 β is known to influence synaptic function and plasticity, and its elevated levels can disrupt normal cognitive processes. TNF- α , on the other hand, is involved in promoting inflammation and apoptosis, further contributing to neuronal loss. Astrocytes, another type of glial cell, also become reactive in the setting of neuroinflammation. Reactive astrocytes release a variety of neurotoxic factors that can exacerbate neuronal injury. This glial activation contributes to a vicious cycle of inflammation and neuronal damage, leading to progressive cognitive decline. Imaging studies, such as magnetic resonance imaging (MRI) and computed tomography (CT) scans, are essential tools in assessing the structural changes associated with presenile dementia. MRI can reveal hippocampal atrophy, which is a hallmark of early neurodegenerative changes. The hippocampus is crucial for memory formation, and its atrophy correlates with the cognitive impairments observed in dementia. CT scans may show cortical demyelination, indicating widespread neuronal damage and disruption of normal brain function. The overlap of neuroinflammation with cognitive decline highlights the critical role of systemic inflammation in accelerating the onset and progression of dementia. Conditions like ankylosing spondylitis (AS) that involve systemic inflammation can potentially exacerbate neuroinflammatory processes in the brain. In individuals with pre-existing neurodegenerative conditions, the presence of chronic systemic inflammation may further compromise cognitive function and accelerate the progression of dementia. Understanding these interactions is essential for developing targeted therapies that address both the local neuroinflammatory changes in the brain and the systemic inflammatory conditions that may contribute to cognitive decline. In summary, the neuroinflammatory processes in presenile dementia involve intricate interactions between glial cells and inflammatory cytokines, leading to neuronal damage and cognitive impairment. The role of systemic inflammation, particularly in the context of comorbid conditions like AS, underscores the need for a comprehensive approach to managing and potentially mitigating the impact of neuroinflammation on cognitive health.

4. Therapeutic Approaches and Preventive Measures

4.1. Management of Ankylosing Spondylitis and Autoimmune Dementia

The management of ankylosing spondylitis (AS) and autoimmune dementia involves distinct but complementary approaches, each tailored to the specific needs of the patient and aimed at improving their quality of life. For AS, the primary goals are to reduce inflammation, alleviate pain, and preserve spinal mobility. Non-steroidal anti-inflammatory drugs (NSAIDs) are typically the first-line treatment for managing pain and inflammation. Common NSAIDs used include ibuprofen and naproxen, which work by inhibiting the production of prostaglandins, thereby reducing inflammation and pain. However, long-term use of NSAIDs may have adverse effects, including gastrointestinal issues and cardiovascular risks. When NSAIDs are insufficient in controlling symptoms or when there is a need for more aggressive treatment, biologic agents are introduced. Tumor necrosis factor (TNF) inhibitors, such as etanercept, infliximab, and adalimumab, are among the most effective

biologics used in treating AS. These agents specifically target and neutralize TNF- α , a key cytokine involved in the inflammatory process. By blocking TNF- α , these drugs help reduce inflammation, slow disease progression, and improve functional outcomes. Another class of biologics, interleukin-17 (IL-17) inhibitors, has also shown promise in managing AS by targeting IL-17, another crucial cytokine involved in inflammation. In addition to pharmacological treatments, physical therapy plays a crucial role in managing AS. Regular exercise and stretching routines are designed to maintain spinal flexibility and strength, which are essential for preserving mobility and reducing stiffness. Patient education on proper posture and ergonomics can also help manage symptoms and prevent exacerbations. For presenile dementia, therapeutic strategies are aimed at supporting cognitive function and slowing the progression of the disease. Cholinesterase inhibitors, such as donepezil and rivastigmine, work by increasing the levels of acetylcholine, a neurotransmitter involved in memory and learning. These medications can help improve cognitive symptoms and delay the progression of dementia. Another commonly used medication, memantine, is an NMDA receptor antagonist that helps regulate glutamate activity, which is implicated in neurodegenerative processes. Addressing neuroinflammation through lifestyle modifications is also beneficial. A balanced diet rich in antioxidants, omega-3 fatty acids, and anti-inflammatory foods can support brain health and potentially mitigate the effects of both AS and dementia. Regular physical activity, including aerobic exercises and strength training, can help improve overall health, reduce inflammation, and enhance cognitive function. Engaging in cognitive stimulation activities, such as puzzles and memory exercises, may also contribute to better cognitive outcomes. In summary, managing AS and autoimmune dementia requires a multifaceted approach that includes pharmacological treatments, physical therapy, lifestyle modifications, and ongoing patient education. Tailoring the treatment plan to individual needs and regularly monitoring disease progression are essential for optimizing outcomes and improving the quality of life for patients with these challenging conditions.

4.2. Preventive Strategies and Future Research

Preventive strategies play a crucial role in managing the risk and progression of autoimmune and neurodegenerative diseases. Early detection and intervention are key to improving patient outcomes and quality of life. Genetic screening, particularly for markers such as HLA-B27, can identify individuals at increased risk of developing conditions like ankylosing spondylitis (AS). This proactive approach allows for early monitoring and management, potentially delaying the onset of symptoms and mitigating disease severity. Additionally, individuals with a family history of autoimmune or neurodegenerative diseases might benefit from more frequent health check-ups and early screening measures to identify any early signs or predisposing factors. Preventive measures should encompass a holistic approach, including regular health assessments, lifestyle modifications, and proactive management of risk factors. Lifestyle adjustments such as adopting a balanced diet rich in anti-inflammatory foods, maintaining regular physical activity, and managing stress levels can have a significant impact on overall health and disease risk. For individuals at risk of autoimmune diseases, managing chronic inflammation through diet, exercise, and medication can help reduce disease incidence and severity. Stress management techniques, such as mindfulness and cognitive behavioral therapy, can also play a role in reducing the impact of stress on immune system function and disease progression. Future research is essential to deepen our understanding of the

mechanisms linking autoimmune diseases like AS with neurodegenerative conditions. Investigating the intersection of these diseases could reveal shared pathways and common factors that contribute to their development. Research should focus on elucidating the role of autoimmune responses in neurodegenerative processes, such as how inflammation and immune system dysregulation may contribute to cognitive decline and neurodegeneration. Studies exploring the genetic, environmental, and immunological factors that link AS with conditions like autoimmune dementia could lead to the development of more effective targeted therapies. Advancements in research will also benefit from integrating interdisciplinary approaches, combining insights from immunology, neurology, and genetics to develop comprehensive strategies for prevention and treatment. Novel biomarkers and imaging techniques could improve diagnostic accuracy and enable more precise monitoring of disease progression. Moreover, identifying new therapeutic targets and developing innovative treatments tailored to the specific needs of patients with overlapping autoimmune and neurodegenerative conditions will enhance treatment efficacy and patient outcomes. In summary, implementing preventive strategies through early detection and lifestyle modifications, combined with ongoing research into the mechanisms linking autoimmune and neurodegenerative diseases, will be pivotal in managing these complex conditions. Advancements in understanding these interactions will lead to better diagnostic tools, targeted therapies, and ultimately, improved quality of life for affected individuals.

5. Discussion

Overall, Alzheimer's disease (AD) is a degenerative disorder of the central nervous system (CNS), but some people believe that AD is characteristic of "heterogeneity", in which there is a minor proportion of them is overlapped by some kinds of autoimmune diseases [1], e.g. a few inpatients with Sjogren's syndrome (SjS) and vitiligo were treated in our ward, and their brains might be attacked by the toxic T-lymphocytes due to the inflammation inside their hippocampus and cortex of cerebrum; resulting in a premature decline in their cognitive function. In other words, is there a possibility of "overlapping autoimmune diseases" in the patients with presenile dementia [2]? Once suspicious of "autoimmune factors" in the research of etiology, it is less likely to obtain "valuable clues" from the inpatients with dementia themselves; it's necessary to find an insider at this time, who can provide with detailed family history, including their relatives to outline a complete "family tree" to aid in diagnosis [3]. Knowing of the insider's grandma in this case, who had suffered from "humpback"; a diagnosis of ankylosing spondylitis (AS) was then made for this lady by means of comparatively observing the differences in both sacroiliac joints on her pelvic X-ray. Film reading about arthritis should be related with the "clues" available in clinic in order to recognize the abnormalities of unknown origin and put forward a new diagnosis [4]. The diagnostic breakthrough in this case just began with: a. family investigation of the maternal grandma's "humpback"; b. the patient was allergic to penicillin and had a history of persistent backache. The attending doctor kept an eye on "her spine and sacroiliac joints" (central axis system of joints) on iconography, and finally discovered something wrong on her pelvic X-ray (Figure 1), which was soon confirmed immunologically. Beside focusing on the patient's own treatment, our attention should also be paid to the "early protection" of their descendants [5]. Generally, the elders' conditions occur almost in their "late stage", and the efficacy less achieved; by comparison, preventive screening and earlier detection of autoimmune diseases for their offspring might be much more significant

sociologically. The physicians of rheumatic team in our hospital, therefore, are taking actions to reduce the number of patients with AiD by giving the effective intervention of TCM Compounds, such as total glycosides of peony capsule (oral use). Not only using “Rating Scale of Mental Cognition” (MMSE), but also observing the titre fluctuation of “antinuclear antibody spectrum” (ANAs), both of them are applied to achieving our goal.

6. Conclusions

In short, systemic thinking (integrated with the other clinical information, such as family history and iconographic findings on bone X-ray), we think, is crucial to make a breakthrough in the diagnosis of overlap syndrome, in which, an ankylosing spondylitis (sacroiliitis) had been overlapped by presenile dementia (autoimmune dementia) and symptomatic epilepsy.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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