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Case report

Autoimmune meningitis and encephalitis in adult-onset still disease – Case report

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ABSTRACT

Introduction: Adult-onset Still disease (AOSD) is a rare systemic inflammatory disease of unknown cause. Its symptoms usually include persistent fever, fugitive salmon-colored rash, arthritis, sore throat (not specific), but it may also lead to internal organs' involvement, which presents with enlargement of the liver and spleen, swollen lymph nodes, carditis or pleuritis – potentially life-threatening complications. In rare cases, AOSD can cause aseptic meningitis or/and encephalitis.

Case presentation: We report a case of 31-year-old male patient, who was referred to neurological department for extending diagnostics of frontal lobes lesions with involvement of adjacent meninges. Abnormalities have been revealed in brain MRI, which was performed due to persistent headaches, visual disturbances, fever, fatigue and cognitive decline. Wide differential diagnosis was performed including laboratory findings, contrast enhanced MRI, MR spectroscopy, flow cytometry and finally brain biopsy to exclude neoplastic or infectious origin. Final diagnosis of autoimmune meningoencephalitis in adult-onset Still disease has been made.

Conclusion: Adult-onset Still disease is a rare cause of inflammatory changes in central nervous system, which if diagnosed, may be treated successfully with steroids (commonly available agent), intravenous immunoglobulins or more specific immunomodulating regiments.

1. Introduction

Meningoencephalitis is a condition that simultaneously involves both meninges and brain parenchyma [1]. Clinical manifestation and severity depend on several factors, such as etiology, lesion's location (diffuse vs focal), potential complications etc. Prodrome symptoms usually include fever, headache, nausea and vomiting, lethargy, fatigue, and usually they can be followed by altered mental status, behavioral and personality changes, hypersomnolence, language difficulties, focal neurological deficits (e.g., hemiparesis, cranial nerves palsies). If not treated, may lead to seizures, increased intracranial pressure, coma and death. Patient's history may

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give clues concerning etiology (e.g., mosquito tick bites, certain animal bites, comorbidities including coexisting systemic autoimmune disorder, exposure to certain chemical, toxic or intoxicating substances or drugs etc.). Physical examination is also of great importance (e.g., rash, lymphadenopathy, hepatosplenomegaly, herpetic skin lesions) [2].

Differential diagnosis is complex especially if there is no history of preceding protozoans, viral or bacterial infection or travel health problems. But even the obvious infectious etiology requires infectious agent identification with meticulous serological testing, lesions smear, blood or CSF cultures [2].

Autoimmune encephalitis is a complex disease related to diverse immunologic response to coexisting neoplastic or non-neoplastic condition, or resulting from central nervous system vasculitis (primary or secondary). Autoimmune encephalitis can be suspected if there is evidence of serologic autoimmunity and intrathecal inflammation in the cerebrospinal fluid sometimes combined with diffused brain lesions [3].

As autoimmune causes of encephalitis are less common, diagnosis is usually made by an exclusion of other, more probable causative factors (infectious, toxic, metabolic, vascular or structural damage). Therefore, while diagnosing a patient with symptoms suggestive of meningoencephalitis several laboratory, neuroimaging and serological investigations must be carried out. Apart from typical laboratory evaluation (including complete blood counts, erythrocyte sedimentation rate, C-reactive protein, renal, liver and thyroid function, vitamin B complex deficiency), the markers of underlying systemic autoimmune disease should be obtained (e.g. anti-nuclear antibodies [ANA], anti-neutrophil cytoplasmic antibodies [ANCA], lupus anticoagulant [LA]). Cerebrospinal fluid analysis is crucial for exclusion of infectious and neoplastic background, moreover it can provide an evidence of intrathecal inflammation [4–6]. Magnetic resonance imaging is the method of choice for identification of vascular, demyelinating or neoplastic lesion. Due to increasing number of patient with antibodies-specific encephalopathies, the presence of some autoantibodies should be assessed (e.g. anti-NMDA receptor, anti-CASPR2 or anti-LGI1) [3–6].

Autoimmune encephalitis can produce a wide range of symptoms, that may mimic other neurological or psychiatric disorders, (e.g. limb or cranial nerve palsies, ataxia, involuntary movements, cognitive impairment, agitation, hallucinations or delirium, severe anxiety). Immunomodulating therapy may give improvement and it may include steroids, plasmapheresis or intravenous immunoglobulin (IVIG) [5,6] Removal of triggering factor (if present, such as coexisting neoplasm) is also effective [5,6]. In case of known cause that triggers immune response guided treatment methods may be required [5,6].

2. Case report

31-Year-old male patient was admitted to the neurological department due to frontal lobes lesions involving meninges of unknown etiology. Abnormalities have been revealed in brain MRI, which was performed due to persistent headaches, visual disturbance, fever, sleepiness, cognitive decline and weight loss. Previously the patient was hospitalized in other neurological ward and infectious disease department, where tuberculosis and bacterial meningitis have been excluded. As a 6-month-old baby the patient was diagnosed with phenylketonuria. He also reported that he had been treated for a long time because of Still disease diagnosis, but he stopped this treatment because long remission.

At admission the neurological examination was normal, apart for slowness of movements and apathy.

Contrast-enhanced MRI showed bilateral frontal lobes abnormalities, including poorly marginated cortical and subcortical hyperintensities on T2 weighted and FLAIR images with lobes swelling, little mass effect and absence of parenchymal enhancement (Fig. 1a and b). Abnormal meningeal thickening and enhancement especially prominent in both frontal regions including anterior part of falx cerebri was detected on gadolinium-enhanced T1-weighted image (Fig. 1c and d). Brain MRI was assessed by a neuroradiologist as non-specific localized hypertrophic pachymeningitis with frontal brain edema. Lesions location was not typical for tuberculosis.

Basic laboratory findings (such as complete blood counts, liver and renal testing, electrolytes, coagulation, CRP, serum protein electrophoresis) were normal apart from increased sedimentation rate (16 mm/h). HBV, HCV and HIV1/HIV2 antibodies were negative. Lupus antigen was present, unlike anticardiolipin (aCL) antibodies, which were absent. Serum rheumatoid factor and anti-nuclear antibodies were not performed as they were negative in several previous measurements. Ferritin was normal (75.1 ng/ml with normal range of 22–322 ng/ml). The serum level of glycosylated ferritin was not measured as the test was not available in author's research center.

Lumbar puncture was performed. General CSF analysis exhibited normal results except for slightly increased number of white cells (6 cells in mm^3 with normal range of 0–5 cells in mm^3, 82% of lymphocytes). The cerebrospinal fluid immunoglobulin index revealed several abnormalities: IgG CSF 6.70 mg/dl (normal range: 0.63–3.35), IgG CSF/protein CSF 19.1% (normal range: 0.0–12.0), IgG Index 1.11 (normal range: 0.00–0.70), IgG daily synthesis 3.11 mg/24 h (normal range: 0.00–3.30) and local IgG synthesis 2.78 mg/dl (normal range: <0.01). Oligoclonal bands were also present. CSF cytologic examination did not reveal any abnormal (neoplastic) cells.

Both serum and CSF testing for HSV DNA were negative. Serum Toxoplasma gondi antibodies were positive (which is probably an accidental finding as seroprevalence of Toxoplasma gondi antibodies in a healthy population is 20–24%) [7,8]. CSF Toxoplasma gondi antibodies were negative (0 IU/ml with normal range of <4 IU/ml). Serum and CSF ACE levels were normal.

The patient's case was consulted with infectious disease specialist, who advised anti-viral therapy – acyclovir was administered intravenously, but clinical improvement was not achieved.

To help identify a nature of brain lesions MR spectroscopy was performed (not shown). The conclusion suggested active neoplastic or inflammatory process with decrease NAA/Cr ratio and increased Cho/Cr ratio.

During second hospitalization – a month later, contrast enhanced MRI revealed further progression of frontal lesions

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