Psychosis as the first manifestation of Granulomatosis with Polyangiitis

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Background

Granulomatosis with Polyangiitis (GPA) is a rare multisystemic autoimmune disease of unknown etiology, characterized by necrotizing granulomatous inflammation and pauci-immune vasculitis in small- and medium-sized blood vessels. It has similar frequency between both genders and diagnosis is more common between 45 and 60 years (1). Aetiology is linked to environmental and infectious triggers inciting onset of disease in genetically predisposed individuals (2). Anti-neutrophil cytoplasmic antibodies (ANCA) play an important role in the pathogenesis (1-3), they are present in most cases (most frequently directed against proteinase 3 – PR3) (4), but they aren't essential for a clinical diagnosis (4, 5). Although GPA has been defined and diagnostic criteria have been pinpointed (6, 7), diagnosis is still based on clinical manifestations of systemic vasculitis and evidence of target organ damage (2). Histological evidence of necrotizing or granulomatous inflammation greatly helps diagnosis but it isn't essential (1, 6, 7).

Our objective is to report a unique case of GPA diagnosed following psychiatric symptoms present at disease onset.

Methods

Inpatient clinical assessment for 61 days, follow-up outpatient clinical assessment for 11 months and clinical file consultation. Pubmed search with key terms: "Granulomatosis with polyangiitis"; "Wegener's Granulomatosis"; "Vasculitis, Central Nervous System"; "Organic Psychosis"; "Psychiatric Symptoms". Search was restricted to articles written in English, without temporal limitations.

Discussion

This was an important case due to its severity, diagnostic complexity and rarity. Our patient clinically presented with a first manic episode with psychotic symptoms resistant to psychopharmacological treatment. After further assessment and with multidisciplinary cooperation, the diagnosis of GPA with central nervous system (CNS) vasculitis was established.

ANCA negative GPA is a rarely described entity (4, 5), GPA with CNS involvement is also rare (8) and ANCA negative GPA with initial CNS symptoms is even rarer (4). CNS involvement has three different pathogenic patterns: granulomatous tissue may contiguously invade adjacent structures; granulomatous lesions may develop in intracerebral tissues; vasculitis may affect the cerebral or spinal cord vessels (8, 9). Cerebral vasculitis has been associated with hemorrhage, transient ischemic attacks or ischemic infarction, and arterial or venous thrombosis. Manifestations include neurological and neuropsychiatric symptoms (e.g. altered consciousness, cognitive impairment or dementia) (8).

To our knowledge this is the first case of ANCA negative GPA with initial CNS symptoms which presented itself with such psychiatric symptoms. This case reminds us that GPA can affect any organ and that unusual rare presentations are possible, such as psychiatric manifestations at disease onset. Singular GPA phenotypes have already been described through disease's history but they're yet to be fully understood (4, 5, 9-11).

Conclusion

This rare and defying clinical case raises awareness for possible psychiatric manifestations of autoimmune diseases that may go unnoticed and emphasizes the importance of multidisciplinary team work. GPA is a highly polymorphous disease and its CNS involvement can be challenging.

Facing a first episode psychosis and possible neuropsychiatric symptoms a strict differential diagnosis is crucial. In this case a thorough work-up and high clinical suspicion were fundamental to achieve the right diagnosis.

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Case Report

Said: "I was in war from 1995 to 2003 (...) travelled for more than 45 countries (...) now I have to prepare myself for a rank promotion (...) I have no sleep... in war it's like this (...) last days I walked more than 70 km and that's nobody's business! (...) Lately I'm more irritated because I feel mistreated (...) like they mock me! (...) it bothers me that my father and my sister try to control me (...) sometimes I want to harm them (...) to calm myself I watch Egyptian movies".

Further questioning: first behavioral changes started 4 months ago and incoherent speech started in the last month. Two weeks ago he assaulted his father and 4 days ago his mother. He stocked cold weapons in his room and barricaded it "because he was afraid someone would attack him". **Lost around 20 Kg in the last 4 months.**

Mental state examination: No consciousness or orientation disturbances. Agitated. Pressured speech. Distracted. Grandiose and persecutory delusions. Flight of ideas. Irritable mood. Insomnia in the last few days and total insomnia last night. No insight.

Work-up: hyperglycemia (242 mg/dl), elevated GGT (92 U/L). No other clinically relevant abnormalities (including toxic screening and brain CT scan).

Voluntarily accepted admission to a psychiatric ward and started treatment with a mood stabilizer (valproic acid) and an antipsychotic (risperidone). **Diagnostic hypotheses:** first manic episode with psychotic symptoms.

Since day 2 he presents with **cough and rhinorrhea**. Chest x-ray – **bilateral pulmonary nodules** (fig.1). Chest CT scan – **multiple bilateral nodular lesions**. Percutaneous CT guided pulmonary biopsy – **histology was compatible with granulomatous disease and vasculitis affecting small and medium vessels**. Brain MRI – white matter lesions suggestive of **central nervous system vasculitis** (fig. 2) and a possible granuloma (fig. 3). Immunohistochemistry didn't show relevant findings: it was **negative for ANCA** and nonspecifically positive for antinuclear antibodies (ANA). Internal Medicine Evaluation – when questioned referred **polyarthralgias with inflammatory rhythm with 15 year evolution course affecting coxofemoral, wrists and metacarpophalangeal joints bilaterally**. Involvement of other organs was excluded.

During entire admission period (65 days) showed **grandiose and erotomania delusions resistant to drug therapy** (valproic acid, risperidone, olanzapine, benzodiazepines). **Further complete work-up didn't show relevant findings** (including cerebrospinal fluid analysis). Cooperation with Internal Medicine and Pulmonology - **diagnosis of GPA de novo with CNS vasculitis was established. Therapy with prednisolone and cyclophosphamide were initiated and an improvement of both systemic and psychiatric symptoms was consistently observed during follow-up.**