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PSYCHOSIS AS THE FIRST MANIFESTATION OF GRANULOMATOSIS WITH POLYANGIITIS - A CASE REPORT

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INTRODUCTION

Granulomatosis with Polyangiitis (GPA) is a rare multisystemic autoimmune disease of unknown aetiology, 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 (Comarmond et al. 2014). Aetiology is linked to environmental and infectious triggers inciting disease onset in genetically predisposed individuals (Lutalo et al. 2014). Anti-neutrophil cytoplasmic antibodies (ANCAs) play an important role in the pathogenesis (Comarmond et al. 2014, Lutalo et al. 2014, Woywodt et al. 2006), they're present in most cases (often directed against proteinase 3 – PR3) (Chen et al. 2018), but aren't essential for a clinical diagnosis (Chen et al. 2018). Although GPA has been defined and diagnostic criteria have been pinpointed (Jennette et al. 2013, Leavitt et al. 1990), diagnosis is still based on clinical manifestations of systemic vasculitis and evidence of target organ damage (Lutalo et al. 2014). Histological evidence of necrotizing or granulomatous inflammation greatly helps diagnosis but it isn't essential (Comarmond et al. 2014, Jennette et al. 2013, Leavitt et al. 1990).

Here we report a case of GPA diagnosed following psychiatric symptoms present at disease onset.

CASE REPORT

A 42-year-old man was brought to the emergency department for behavioural changes over the last 3 weeks. He had past medical history of Type 2 Diabetes treated with metformin 500 mg daily. He didn't have past psychiatric history. He had smoking habits (42 packs-year) and drinking habits (3 alcohol units daily). He had no history of recreational drug use. He had family history of suicide (his sister and his paternal grandfather).

His mental state examination didn't find consciousness or orientation disturbances. He was agitated, distracted, with pressured speech. He had grandiose and persecutory delusions. There was flight of ideas and irritable mood. He had insomnia in the last few days and total insomnia the night before. He lacked insight for his situation.

Further assessment concluded that behavioural changes had started 4 months before and incoherent speech started in the last month. He had lost around 20 kg in 4 months.

His work-up at admission showed hyperglycaemia (247 mg/dl), elevated Gamma-glutamyl transferase (92 U/L). No other clinically relevant abnormalities were found (including hemogram, cobalamin, folate, urea, creatinine, serum electrolytes, remaining liver enzymes, C-reactive protein, Free Thyroxine (FT4), Thyroid-stimulating hormone (TSH), Anti-Treponema pallidum antibody, serologic screening for Hepatitis B, Hepatitis C and for Human immunodeficiency virus (HIV), urine analysis, toxic screening and brain Computed tomography [CT] scan).

He was voluntarily admitted to a psychiatric ward and medicated with a mood stabilizer (valproic acid) and an antipsychotic (risperidone). The diagnostic hypothesis was a first manic episode with psychotic symptoms (F30.2, accordingly with the International Classification of Diseases, Tenth Revision – ICD-10). Since day 2 after admission, he presented with cough and rhinorrhea. His chest x-ray showed bilateral pulmonary nodules. His Chest CT scan showed multiple bilateral nodular lesions. His percutaneous CT guided pulmonary biopsy showed histology compatible with granulomatous disease and vasculitis affecting small and medium vessels. His brain Magnetic Resonance Imaging (MRI) showed white matter lesions suggestive of central nervous system vasculitis and a possible granuloma (Figure 1). Immunohistochemistry was non-specifically positive (titer of 1:160) for antinuclear antibodies (ANA) and didn't show any other relevant findings: it was negative for ANCA-PR3, ANCA-myeloperoxidase (ANCA-MPO), Anti–citrullinated protein antibody (Anti-CCP), Anti-centromere antibodies (ACA), Lupus anticoagulant, anti-cardiolipin (aCL) antibody and anti-beta2-glycoprotein (GP) 1 antibodies, anti-double stranded DNA (anti-dsDNA). Complement component 3 (C3) and C4 values were normal (respectively 116 mg/dL and 28 mg/dL). When evaluated by Internal Medicine he referred complaints compatible with polyarthralgias

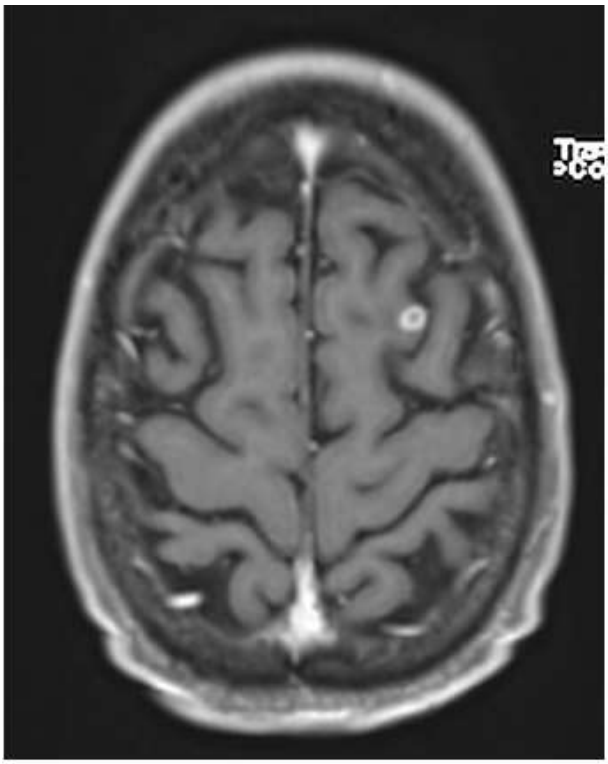

Figure 1. Brain showing a possible granuloma

with inflammatory rhythm with 15-year evolution course affecting coxofemoral, wrists and metacarpophalangeal joints bilaterally. Involvement of other organs was excluded. During the entire admission period (65 days), the patient showed grandiose and erotomania delusions resistant to treatment (valproic acid, risperidone, olanzapine, benzodiazepines). Further complete work-up didn't show any relevant findings (including serum protein electrophoresis, anti–thyroid peroxidase and antithyroglobulin antibodies, cerebrospinal fluid analysis). Through cooperation with Internal Medicine and Pulmonology the diagnosis of GPA *de novo* with CNS vasculitis was established. He started treatment with prednisolone 60 mg daily and cyclophosphamide (6 cycles, consisting on 500 mg every fortnight). After one month prednisolone was cross-switched to azathioprine (titrated up to 100 mg daily). He progressively and consistently showed an improvement in psychiatric symptoms, and after 1 year of treatment there was complete remission of psychotic symptoms. Treatment was progressively tapered and during the entire follow-up (24 months) he stayed completely and consistently asymptomatic.

DISCUSSION

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 (Chen et al. 2018). GPA with CNS involvement is also rare (Holle et al. 2011) and ANCA negative GPA with initial CNS symptoms is even rarer (Chen et al. 2018). 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 (Holle et al. 2011, Seror et al. 2006). Cerebral vasculitis has been associated with haemorrhage, 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) (Holle et al. 2011).

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 (Chen et al. 2018, Lee et al. 2018, Rogaczewska et al. 2019, Seror et al. 2006).

CONCLUSIONS

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.

When facing a first episode psychosis and possible neuropsychiatric symptoms a strict differential diagnosis is crucial. In this case a thorough work-up, a high clinical suspicion and a multidisciplinary approach were vital to achieve an accurate diagnosis.

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Ricardo Gasparinho: diagnosis, patient follow-up (inpatient and outpatient), first draft, draft review.

Nuno Fernandes: patient follow-up (inpatient), draft review.

Marisa Martins, Núria Santos, Liliana P. Ferreira & António Alho: draft review.

All authors approval of the final version.

References

1. *Chen Z, Miao Y, Wu H, et al: Anti-Neutrophil Cytoplasmic Antibody-Negative Central Nervous System Granulomatosis With Polyangiitis and Its Clinical Characteristics. The Journal of craniofacial surgery 2018; 29:449-51*
2. *Comarmond C, Cacoub P: Granulomatosis with polyangiitis (Wegener): clinical aspects and treatment. Autoimmunity reviews 2014; 13:1121-5*
3. *Holle JU, Gross WL: Neurological involvement in Wegener's granulomatosis. Current opinion in rheumatology 2011; 23:7-11*
4. *Jennette JC, Falk RJ, Bacon PA, et al: 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis and rheumatism 2013; 65:1-11*
5. *Leavitt RY, Fauci AS, Bloch DA, et al: The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis and rheumatism 1990; 33:1101-7*
6. *Lee E, Park J, Choi SH, et al: Seronegative granulomatosis with polyangiitis presenting with multiple cranial nerve palsies. Neuropathology: official journal of the Japanese Society of Neuropathology 2018; 38:192-7*
7. *Lutalo PM, D'Cruz DP: Diagnosis and classification of granulomatosis with polyangiitis (aka Wegener's granulomatosis). Journal of autoimmunity 2014; 48-49:94-8*
8. *Rogaczewska M, Puszczewicz M, Stopa M: Exclusively ocular and cardiac manifestation of granulomatosis with polyangiitis - a case report. BMC ophthalmology 2019; 19:139*
9. *Seror R, Mahr A, Ramanoelina J, et al: Central nervous system involvement in Wegener granulomatosis. Medicine. 2006; 85:54-65*
10. *Woywodt A, Haubitz M, Haller H, et al: Wegener's granulomatosis. Lancet 2006; 367:1362-6*

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