Possible association between immunoglobulin a vasculitis and the development of schizophrenia: A case study

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SUMMARY

This case report describes a 41-year-old woman with a history of childhood immunoglobulin A vasculitis and adult-onset schizophrenia, to the best of our knowledge, representing the first clinical observation suggesting a potential link between these conditions. Although current serological evaluations showed no active vasculitis, the case highlights a possible association, in line with research indicating an increased risk of schizophrenia in individuals with autoimmune disorders, including vasculitis. Mechanistically, immunoglobulin A vasculitis could hypothetically influence neuroimmune processes through transient effects on the blood-brain barrier or microvascular function, potentially contributing to pathways relevant to psychosis. Certain antipsychotic treatments are also known to interact with immune responses, supporting the rationale for further investigation. While causality cannot be inferred from a single case, this report underscores the importance of exploring immunoglobulin A vasculitis as a factor in schizophrenia pathogenesis and encourages longitudinal and mechanistic studies to better understand the potential neuroimmune mechanisms involved.

Key words: Schizophrenia, immunoglobulin A, IgA vasculitis, autoimmune diseases, mental disorders, blood-brain barrier

INTRODUCTION

Schizophrenia is a serious mental disorder marked by psychosis and significant disability (1). Genetic and environmental aspects (2) and immune responses (3) are believed to play a significant role in the development of schizophrenia. (3)

Vasculitis encompasses a diverse group of disorders characterized by inflammation of blood vessel walls. As the index case had a pediatric onset, it is important to note that epidemiological data on childhood vasculitis remains limited and insufficiently defined (4). Immunoglobulin A vasculitis (IgAV) formerly Henoch Schönlein Purpura (HSP) is an IgA-mediated autoimmune vasculitis that impacts multiple organs (5).

Increasing evidence of immune involvement in schizophrenia has prompted research on its links to autoimmune diseases and infections (6,7). Evidence from cerebrospinal fluid analyses indicates an association between blood-brain barrier (BBB) impairment and psychosis (8). Circulating autoantibodies are enabled to penetrate the damaged BBB and influence the central nervous system (7). The immune system's broader role in antipsychotic treatment response is key research. Medications like clozapine (for treatment-resistant schizophrenia) are linked to lower serum immunoglobulin levels (6). The dysregulation of immune-related genes plays a significant role in schizophrenia (9,10).

Although studies link autoimmune diseases like vasculitis to schizophrenia (11–13), the potential correlation with IgAV has not been specifically examined. Our study aims to explore this possible relationship.

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CASE REPORT

We present a case of a 41-year-old single woman with a high school education, no employment history, and a diagnosis of schizophrenia. She lives with her family and has been under regular psychiatric follow-up. Premorbid irritability and poor social adjustment were noted. Her first psychotic symptoms appeared at age 16, including persecutory and referential delusions, social withdrawal, and self-neglect, which persisted for two years. She has no history of hospitalization, suicide attempts, or substance use, and no family history of psychiatric illness.

The patient meets the diagnostic criteria for schizophrenia according to the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th edition). Current Positive and Negative Syndrome Scale positive, negative, and total scores were 9, 16, and 52, respectively. Global Assessment Scale score was 60. She maintains basic self-care, shows restricted affect with euthymic mood, and has goal-directed thoughts. While some referential ideation persists, no active delusions or hallucinations were noted. Insight is partial. She continues to live with family support. She was initially treated with risperidone but experienced partial symptom control and poor adherence to adjunctive treatments. Olanzapine was discontinued due to side effects. A combination of risperidone 8 mg/day and quetiapine XR 150 mg/day has since provided clinical stability. Despite occasional subthreshold symptom increases, the patient has not experienced a significant relapse or required hospitalization since the initial psychotic episode.

The patient has a significant medical history, including a diagnosis of HSP at age 7, which was found incidentally after purpuric lesions appeared on her hips. She was admitted for three weeks of inpatient care, resulting in full remission. Since then, there have been no recurrences of similar symptoms, and no other major illnesses have been reported during her childhood. About two years ago, she was diagnosed with Hashimoto's thyroiditis and is currently under regular follow-up and treatment with levothyroxine.

Physical examination revealed a BMI of 38.1 kg/m^2 (Class II obesity). Orientation and cooperation were intact. Vital signs were normal, and systemic examinations of cardiovascular, respiratory, abdominal, and dermatological systems were unremarkable.

The neurological exam showed intact cranial nerve functions. Muscle strength was normal in all extremities, with no focal neurological issues found. Sensory testing also showed normal results. Deep tendon reflexes were normal and symmetrical. Cerebellar assessments, specifically the finger-to-nose and heel-to-shin tests, were conducted and yielded no abnormalities in performance. Gait appeared normal.

Initial neuroimaging (cranial MRI and cervical-cranial angiography, 2017) showed no evidence of parenchymal, atrophic, or vascular pathology. Routine laboratory tests, including complete blood count, fasting blood glucose, lipid profile, electrolytes, renal and liver function tests, were within normal limits.

Although the patient currently reports no symptoms suggestive of vasculitis, a vasculitis panel was conducted to investigate potential autoimmune or inflammatory conditions. The results were negative (Table 1). Comprehensive serologic testing showed no evidence of vasculitis, with negative anti-neutrophil cytoplasmic antibodies (ANCA), including both myeloperoxidase (MPO) and proteinase 3 (PR3) subtypes, effectively ruling out ANCA-associated vasculitides such as granulomatosis with polyangiitis and microscopic polyangiitis. Negative antinuclear antibody (ANA) and anti-double-stranded DNA (anti-dsDNA) results argue against systemic lupus erythematosus (SLE)-related vasculitis. Complement levels revealed normal C3 and low-normal C4, indicating no significant complement consumption suggestive of immune complex-mediated vasculitis. The erythrocyte sedimentation rate (ESR) was within normal limits, and although D-dimer was mildly elevated, this finding is non-specific in the absence of supporting clinical features. Finally, a comprehensive antiphospholipid

Table 1: Vasculitis panel results for the patient

Test Name	Result	Reference Range
Anti-beta-2 glycoprotein IgG	<2 RU/mL	≤ 20 RU/mL
Anti-beta-2 glycoprotein IgM	Negative, 7.68 RU/mL	≤20 RU/mL
MPO ANCA	<2 RU/mL	≤ 20 RU/mL
PR3 ANCA	<2 RU/mL	≤ 20 RU/mL
Anti-cardiolipin IgM	Negative, 3.03 PL-IgM-U/mL	<12 PL-IgM- U/mL
Anti-cardiolipin IgG	Negative, 2.53 PL-IgG-U/mL	<12 PL-IgG-U/mL
Anti-ds DNA IFA	Negative	IIF (Crithidia luciliae) <1:10 titre (Negative)
Anti-nuclear antibody (ANA)	Negative	IIF <1/100
Erythrocyte Sedimentation Rate (ESR)	18 mm/hr	2- 20 mm/hr
Anti-phospholipid IgM	Negative, 1.44 IU/mL	Negative <12
Anti-phospholipid IgG	Negative, 4.45 IU/mL	Negative <12
C4	0.15 g/L	0.10- 0.40 g/L
C3	1.47 g/L	0.90- 1.80 g/L
D-dimer	0.61 µg/mL	0- 0.5 µg/mL

Autoimmune and inflammatory markers assessed in the patient. ANA: Anti-nuclear antibody, ANCA: Anti-neutrophil cytoplasmic antibody, dsDNA: Double-stranded DNA, ESR: Erythrocyte sedimentation rate, IFA: Indirect immunofluorescence assay, IgG: Immunoglobulin G, IgM: Immunoglobulin M, MPO: Myeloperoxidase, PR3: Proteinase 3, RU: Relative Units, PL: Phospholipid, IU: International Units.

antibody panel was negative, providing no evidence for antiphospholipid syndrome (APS) as a potential vasculitis mimic.

DISCUSSION

This study aimed to explore the underlying mechanisms of schizophrenia, offering new insights that may enhance our understanding of this complex disorder. Growing evidence suggests that immune dysregulation, particularly in autoimmune conditions, may play a role in schizophrenia's pathogenesis. This case report adds to the growing body of observations suggesting a possible association between schizophrenia and immune system dysfunction, particularly in the context of autoimmune vasculitis such as IgAV.

A Danish population study (N=7,704) of schizophrenia cases diagnosed between 1981-1998 revealed a 45% increased risk of schizophrenia among individuals with any autoimmune disorder, suggesting broader autoimmune associations (11). Another study from the National Health Insurance Research Database included a total of 118,921 participants (10,811 schizophrenia; 108,110 control) shows that there is a significant positive association between hypersensitivity vasculitis and schizophrenia with an ODD ratio of five (12). A follow-up study using the same database of 64,817 patients with autoimmune diseases and an equal number of age-matched controls investigated the association between autoimmune diseases and the development of schizophrenia. Over a maximum follow-up period of 10 years, autoimmune vasculitis (polyarteritis nodosa, hypersensitivity angiitis, Wegener's granulomatosis, giant cell arteritis, thromboangiitis obliterans, Takayasu's disease, acute febrile mucocutaneous lymph node syndrome, Behçet's syndrome) was linked to a significantly elevated risk of schizophrenia development in individuals with autoimmune diseases in the study (13).

Several recent case reports illustrate the clinical intersection of psychosis and autoimmune vasculitis. Gasparinho et al. reported a 42-year-old man with no prior psychiatric history who presented with a first manic episode with psychotic symptoms; subsequent work-up revealed ANCA-negative granulomatosis with polyangiitis (GPA) with central nervous system involvement. Immunosuppressive therapy achieved complete remission of psychiatric symptoms within one year. (14). Another report by Castle et al. detailed a 29-year-old male with schizophrenia who was ultimately diagnosed with c-ANCA-positive GPA initially presenting at the petrous apex (15), and Latvala et al. reported giant cell arteritis presenting with manic-psychotic symptoms (16), highlighting the diagnostic challenges and potential delays in autoimmune detection in psychiatric patients.

While aforementioned autoimmune diseases are associated with an increased risk of schizophrenia, the timing of immune events appears to be crucial. Compelling evidence shows a longitudinal dose-response association between childhood IL-6 levels

and future risk for depression and psychosis (17), coupled with elevated adolescent CRP predicting adult schizophrenia (18). However, the impact of specific entities like IgA vasculitides remains a gap this case aims to address. Though our patient lacked acute neurologic symptoms du-ring IgAV, retrospective studies suggest that headache and behavioral changes (31% of cases) may signify subtle CNS involvement. (19). Indeed, our patient showed premorbid irritability and poor social adjustment during school years, features often linked to EEG abnormalities and transient neurovascular dysfunction (19,20). In our patient, subclinical inflammation from IgAV may have caused lasting blood–brain barrier disruption, faci-litating neuroimmune mechanisms in schizophrenia. EEG, neurocognitive, and CSF assessments were not performed, representing a study limitation; future reports should include these. Although diagnosed with Hashimoto's thyroiditis two years ago, data on initial thyroid tests are lacking, but no psychotic episodes occurred before this diagnosis.

The deposition of IgA1-containing immune complexes in vessel walls is a key pathogenic event that promotes the development of IgAV (21). One study suggests that IgA antibodies may cross-react with host cardiolipin- a mitochondrial phospholipid (22), with increased levels of anticardiolipin antibodies also reported in patients' serum with schizophrenia (23), leading to the formation of immune complexes that contribute to vascular injury (24). Moreover, complement activation has been shown to mediate microvascular injury in IgAV and IgA nephropathy, supporting a mechanism by which IgA-containing immune complexes induce endothelial damage (25). Nailfold videocapillaroscopy has shown significant microvascular abnormalities, including architectural disarrangement and edema, during acute IgAV, with capillary edema persisting at 6-month follow-up despite symptom resolution (26). Analogous processes in childhood IgAV could transiently affect cerebral microvasculature, potentially disrupting the blood-brain barrier and priming long-term neuroimmune effects relevant to psychosis.

The nine-year gap between IgAV onset and psychosis suggests possible coincidence or shared genetic–immune risks that cannot be excluded. Yet, the case meets several of Hill's causality criteria: the immune event preceded psychosis, IgAV's inflammation could affect neurodevelopment, and the link aligns with epidemiological evidence. Though causation remains unproven, this case proposes that childhood IgAV may increase schizophrenia risk, warranting further longitudinal and mechanistic studies.

Another case study correlated IgAV and methylphenidate (27), a stimulant that increases dopamine release (28). These findings suggest a potential metabolic pathway linking IgAV to psychosis, possibly mediated by blood-brain barrier disruption and subsequent neuroinflammation (29).

Patient's D-dimer elevation is unlikely due to inactive childhood IgAV. The elevation may instead be explained by schizophrenia, referencing Geng et al. who reported elevated D-dimer in this disorder (30).

This case may be among the first to suggest a link between IgAV and schizophrenia, supported by biological plausibility and prior evidence on immune-related psychosis. However, as a single report with recall bias and unmeasured variables, it cannot confirm causality. The proposed mechanism of autoantibody passage across a damaged blood–brain barrier is limited by unmeasured factors such as exposure duration, antibody levels, and individual susceptibility. Larger epidemiological and molecular studies are needed to validate these findings. If confirmed, this link could inform precision diagnostics and immunomodulatory strategies for psychosis spectrum disorders.

Consent to participate

Written informed consent for the publication was obtained from the patient and her legal representative.

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REFERENCES

1. Shao L, Li Y, Yuan Z, Guo X, Zeng G, Liu J. The effect of clozapine on immune-related biomarkers in schizophrenia patients. Brain Res Bull 2024; 218:111104.

2. Kiltschewskij DJ, Reay WR, Geaghan MP, Atkins JR, Xavier A, Zhang X, Watkeys OJ, Carr VJ, Scott RJ, Green MJ, Cairns MJ. Alteration of DNA Methylation and Epigenetic Scores Associated with Features of Schizophrenia and Common Variant Genetic Risk. Biol Psychiatry 2024; 95:647-61.

3. Nielsen PR, Benros ME, Mortensen PB. Hospital Contacts with Infection and Risk of Schizophrenia: A Population-Based Cohort Study with Linkage of Danish National Registers. Schizophr Bull 2014; 40:1526-32.

4. Bouhuys M, Armbrust W, van Rheenen PF. Case Report: Systemic Small-Vessel Vasculitis in an Adolescent with Active Ulcerative Colitis. Front Pediatr 2021; 9:617312.

5. Zhou W, Zheng M, Hu Z, Zhang B, Zhao M, Lu Q. Single-cell transcriptomics reveals the alteration of immune cell profile in peripheral blood of Henoch-Schonlein purpura. Clin Immunol 2025; 272:110443.

6. Griffiths K, Mellado MR, Chung R, Lally J, McQueen G, Sendt KV, Gillespie A, Ibrahim M, Richter A, Shields A, Ponsford M, Jolles S, Hodsoll J, Pollak TA, Upthegrove R, Egerton A, MacCabe JH. Changes in immunoglobulin levels during clozapine treatment in schizophrenia. Brain Behav Immun 2024; 115:223-8.

7. Liu D, Jin Z, Wei H, Zhu C, Liu K, You P, Ju J, Xu J, Zhu W, Xu Q. Anti-SFT2D2 autoantibodies alter dendrite spine and cause psychotic behavior in mice. J Psychiatr Res 2024; 171:99-107.

8. Jeppesen R, Orlovska-Waast S, Sørensen NV, Christensen RHB, Benros ME. Cerebrospinal Fluid and Blood Biomarkers of Neuroinflammation and Blood-Brain Barrier in Psychotic Disorders and Individually Matched Healthy Controls. Schizophr Bull 2022; 48:1206-16.

9. Noto MN, Maes M, Vargas Nunes SO, Ota VK, Cavalcante D, Oliveira G, Rossaneis AC, Verri WA Jr, Cordeiro Q, Belangero SI, Gadelha A, Noto C, Bressan RA. BDNF in antipsychotic naive first episode psychosis: Effects of risperidone and the immune-inflammatory response system. J Psychiatr Res 2021; 141:206-13.

10. Yu S, Qu Y, Du Z, Ou M, Lu R, Yuan J, Jiang Y, Zhu H. The expression of immune related genes and potential regulatory mechanisms in schizophrenia. Schizophr Res 2024; 267:507-18.

11. Eaton WW, Byrne M, Ewald H, Mors O, Chen CY, Agerbo E, Mortensen PB. Association of schizophrenia and autoimmune diseases: Linkage of Danish national registers. Am J Psychiatry 2006; 163:521-8.

12. Chen SJ, Chao YL, Chen CY, Chang CM, Wu EC, Wu CS, Yeh HH, Chen CH, Tsai HJ. Prevalence of autoimmune diseases in in-patients with schizophrenia: Nationwide population-based study. Br J Psychiatry 2012; 200:374-80.

13. Wang LY, Chen SF, Chiang JH, Hsu CY, Shen YC. Autoimmune diseases are associated with an increased risk of schizophrenia: A nationwide population-based cohort study. Schizophr Res 2018; 202:297-302.

14. Gasparinho R, Fernandes N, Martins M, Santos N, Ferreira LP, Alho A. Psychosis as the first manifestation of granulomatosis with polyangiitis-A case report. Psychiatr Danub 2022; 34:315-7.

15. Castle MS, Carter MM, Poulakis A, Man LX, Schmale IL. Diagnostic Quandary of Granulomatosis with Polyangiitis Presenting First in the Petrous Apex. Case Rep Otolaryngol 2025; 2025(1).

16. Latvala HM, Reitan SK, Vaaler AE. Giant Cell Arteritis Presenting with Mania, Psychosis, and Cognitive Dysfunction: A Case Report. Case Rep Psychiatry 2023; 2023:7989712.

17. Khandaker GM, Pearson RM, Zammit S, Lewis G, Jones PB. Association of Serum Interleukin 6 and C-Reactive Protein in Childhood with Depression and Psychosis in Young Adult Life: A Population-Based Longitudinal Study. JAMA Psychiatry 2014; 71:1121-8.

18. Metcalf SA, Jones PB, Nordstrom T, Timonen M, Mäki P, Miettunen J, Jääskeläinen E, Järvelin MR, Stochl J, Murray GK, Veijola J, Khandaker GM. Serum C-reactive protein in adolescence and risk of schizophrenia in adulthood: A prospective birth cohort study. Brain Behav Immun 2017; 59:253-9.

19. Bérubé MD, Blais N, Lanthier S. Neurologic manifestations of Henoch–Schönlein purpura. Handb Clin Neurol 2014; 120:1101-11.

20. Ostergaard JR, Storm K. Neurologic Manifestations of Schönlein-Henoch Purpura. Acta Paediatr 1991; 80:339-42.

21. Xu S, Han S, Dai Y, Wang L, Zhang X, Ding Y. A Review of the Mechanism of Vascular Endothelial Injury in Immunoglobulin A Vasculitis. Front Physiol 2022; 13:833954.

22. Bradshaw PC, Aldridge JL, Jamerson LE, McNeal C, Pearson AC, Frasier CR. The Role of Cardiolipin in Brain Bioenergetics, Neuroinflammation, and Neurodegeneration. Mol Neurobiol 2025; 62:7022-40.

23. Chang SH, Chiang SY, Chiu CC, Tsai CC, Tsai HH, Huang CY, Hsu TC, Tzang BS. Expression of anti-cardiolipin antibodies and inflammatory associated factors in patients with schizophrenia. Psychiatry Res 2011; 187:341-6.

24. Yang YH, Huang MT, Lin SC, Lin YT, Tsai MJ, Chiang BL. Increased transforming growth factor-beta (TGF-β)-secreting T cells and IgA anti-cardiolipin antibody levels during acute stage of childhood Henoch–Schönlein purpura. Clin Exp Immunol 2000; 122:285-90.

25. Chua JS, Zandbergen M, Wolterbeek R, Baelde HJ, van Es LA, de Fijter JW, Bruijn JA, Bajema IM. Complement-mediated microangiopathy in IgA nephropathy and IgA vasculitis with nephritis. Mod Pathol 2019; 32:1147-57.

26. Zampetti A, Rigante D, Bersani G, Rendeli C, Feliciani C, Stabile A. Longitudinal study of microvascular involvement by nailfold capillaroscopy in children with Henoch-Schönlein purpura. Clin Rheumatol 2009; 28:1101-5.

27. Küçükdağ M, Ünal N. Methylphenidate-Induced Henoch Schönleın Purpura: A Case Report. Mathews J Case Rep 2023;8(1).

28. Moran LV, Ongur D, Hsu J, Castro VM, Perlis RH, Schneeweiss S. Psychosis with Methylphenidate or Amphetamine in Patients with ADHD. N Engl J Med 2019; 380:1128-38.

29. Fanous N, Clarke E, Levy ML. Posterior reversible encephalopathy syndrome in the setting of IgA vasculitis. Pediatr Dermatol 2024; 41:728-30.

30. Geng Y, Zhang P, Pan Y, Wang H, Chen Y, Lai J, Hu S. Clinical Characteristics of Asymptomatic Thromboembolism in Psychiatric Inpatients: A Retrospective Study. Neuropsychiatr Dis Treat 2024; 20:515-25.