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Case Series

Organic Psychiatric Syndromes: A Critical Analysis of Secondary Psychosis and Treatment Resistance—Lessons from Five Clinical Case Reports

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Abstract:

Introduction: Treatment-resistant psychiatric disorders remain a clinical challenge. Emerging evidence links occult brain lesions to poor therapeutic response.

Methodology: We report five patients, two schizophrenia, dissociative disorder, severe depression, and delusional disorder, all showing inadequate response to treatment. MRI brain was performed.

Results: Imaging revealed pituitary adenoma, tubercular granuloma, partially calcified granuloma, chronic small vessel ischemic changes and cerebellar convexity meningioma.

Conclusion: Neuroimaging is crucial in evaluating refractory psychiatric cases, warranting further research for better diagnosis and management.

Keywords: Neuroimaging, treatment-resistant psychiatric disorder, schizophrenia, depression, dissociative disorder, delusional disorder.

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Introduction

The distinction between primary psychiatric disorders and secondary psychiatric manifestations resulting from organic pathology remains a fundamental challenge in clinical psychiatry. While primary psychiatric illnesses such as schizophrenia, major depression, and bipolar disorder are widely recognized and extensively studied, secondary psychiatric syndromes—those arising from demonstrable organic, neurological, endocrinological, or infectious etiologies—are frequently overlooked, leading to prolonged diagnostic delays, inappropriate pharmacological management, and preventable morbidity. The five case reports presented herein exemplify the critical importance of maintaining a high index of suspicion for organic etiology in patients presenting with treatment-resistant psychiatric manifestations. These cases span diverse pathophysiological mechanisms, including endocrine dysfunction (pituitary adenoma with hyperprolactinemia), infectious disease (CNS tuberculosis and old neuroinfectious sequelae), cerebrovascular pathology (small-vessel ischemic changes), and structural intracranial lesions (meningioma), each demonstrating significant psychiatric symptomatology that initially mimicked primary psychiatric illness. This analysis synthesizes the clinical presentations, diagnostic investigations, and outcomes of these five cases to illuminate the essential role of comprehensive medical evaluation in the approach to apparent treatment-resistant psychiatric disease.

Case Series

The five cases under analysis demonstrate remarkable diversity in both presentation and underlying etiology. Case 1 presents a 28-year-old female with a 10-year history of schizophrenia refractory to multiple antipsychotics, ultimately revealing a large pituitary adenoma measuring 11.5 × 10 × 9.5 cm with severe hyperprolactinemia (prolactin 4000 IU). Case 2 describes a 42-year-old female initially diagnosed with dissociative disorder who presented with recurrent episodes of loss of consciousness and subsequently was found to harbor a 2.5 cm tubercular granuloma in the left parietal lobe consistent with CNS tuberculosis. Case 3 involves a 40-year-old male with treatment-resistant depression who developed headaches and dizziness, revealing a partially calcified granuloma in the right

frontal lobe likely representing sequelae of prior neuroinfection. Case 4 presents a 55-year-old female with delusional parasitosis unresponsive to antipsychotics, whose neuroimaging demonstrated chronic small-vessel ischemic changes in subcortical white matter and deep gray structures. Finally, Case 5 describes a 64-year-old female with treatment-resistant schizophrenia who developed neurological symptoms and was found to have a 3.5 cm cerebellar convexity meningioma [5]. These diverse presentations underscore the principle that organic pathology can masquerade as primary psychiatric disease and that diagnostic complacency in the face of treatment resistance represents a fundamental clinical error [6].

Observation Chart

Table 1: Comprehensive Clinical and Diagnostic Comparison

Case	Demographics	Initial Psychiatric Diagnosis	Presenting Psychiatric Symptoms	Associated Medical Symptoms	Organic Etiology Identified
1	28F	Treatment-resistant Schizophrenia (10 years)	Psychosis, treatment resistance	Amenorrhea, weight gain, lethargy	Pituitary adenoma with hyperprolactinemia (prolactin 4000 IU)
2	42F	Dissociative disorder	Recurrent loss of consciousness (10 min episodes)	Speech difficulty, right-sided weakness, positive Hoover's sign	CNS tuberculosis—left parietal tubercular granuloma (2.5 cm, central necrosis)
3	40M	Treatment-resistant depression	Anhedonia, sleep disturbance, fatigue, low mood	Headaches, dizziness, fatigue	Partially calcified granuloma—right frontal lobe (sequelae of neuroinfection)
4	55F	Delusional parasitosis	Fixed false belief of infestation, compulsive skin checking	Gradual cognitive decline, executive dysfunction	Chronic small-vessel ischemic changes—subcortical white matter and deep gray structures
5	64F	Treatment-resistant schizophrenia	Psychosis, poor antipsychotic response	Blurred vision, ataxia, imbalance	Cerebellar convexity meningioma (3.5 cm, mass effect on adjacent structures)

Table 2: Neuroimaging Findings and Diagnostic Characteristics

Case	Neuroimaging Modality	Lesion Location	Lesion Size and Characteristics	Associated Features	Diagnostic Certainty
1	MRI brain	Pituitary gland	11.5 × 10 × 9.5 cm hyperplasia	Prolactin 4000 IU (200-400x normal); mass effect	High—confirmed adenoma with biochemical abnormality
2	MRI brain with contrast	Left parietal lobe	2.5 cm granuloma with central necrosis and rim enhancement	T2-hyperintense lesion; T1-hypointense; classic TB imaging pattern	Very high—imaging highly suggestive of CNS TB
3	MRI brain	Right frontal lobe	Partially calcified granuloma	No significant surrounding edema; inactive chronic lesion	Moderate—consistent with old neuroinfection sequelae
4	MRI brain	Subcortical white matter and deep gray structures	Chronic small-vessel ischemic changes (multiple punctate and linear foci)	Diffuse pattern; age-appropriate changes; no focal mass	High—classic small-vessel disease pattern

5	MRI brain	Cerebellar convexity	3.5 cm meningioma	Mass effect on adjacent structures; cerebellar compression	Very high—characteristic meningioma appearance

Table 3: Pharmacological Management and Therapeutic Response

Case	Failed Psychiatric Medications	Disease-Specific Intervention	Additional Supportive Management	Psychiatric Symptom Response	Overall Outcome
1	Clozapine 300 mg/day (minimal response)	Cabergoline 0.25 mg BID × 1 month + neurosurgical evaluation	Tumor-directed therapy; clozapine reintroduction after stabilization	Significant improvement post-intervention	Excellent—psychiatric recovery following prolactin control
2	Sertraline 50-100 mg + clonazepam + mood stabilizer + low-dose antipsychotic (maximal treatment failure)	Anti-tubercular therapy (ATT) + adjunctive corticosteroids	Supportive neurological management; infection control	Marked improvement in both psychiatric and neurological symptoms	Excellent—resolution with appropriate anti-TB therapy
3	Sertraline 50 mg + mirtazapine 15 mg + CBT; augmented with olanzapine 5 mg + lamotrigine 50 mg × 4-6 weeks	Prednisolone 20 mg/day (tapered over 4 weeks) + anti-inflammatory management	Acetaminophen for headaches; acetyl-L-carnitine 500 mg/day × 3 months; continued antidepressants	Gradual improvement in mood; reduction in neurological complaints	Good—partial recovery with anti-inflammatory and nutritional support
4	Olanzapine 20 mg + haloperidol 10 mg (delusional parasitosis refractory)	Aspirin 81 mg daily + atorvastatin 40 mg daily + antihypertensive agents	Continued antipsychotic therapy; vascular risk factor optimization	Delusions reduced; cognitive performance improved	Good—improvement with vascular risk modification
5	Risperidone, olanzapine, aripiprazole (initial failures); clozapine up to 300 mg/day (minimal benefit)	Neurosurgical resection of meningioma	Clozapine tapering post-resection; enhanced psychotherapy engagement	Significant improvement in both psychiatric and neurological symptoms	Excellent—recovery post-neurosurgical intervention

Discussion

The case of the 28-year-old female with pituitary adenoma and severe hyperprolactinemia exemplifies the complex interplay between endocrine dysfunction and psychiatric symptomatology. Prolactin, primarily synthesized and secreted by lactotroph cells of the anterior pituitary, exerts multifaceted effects throughout the central and peripheral nervous systems beyond its well-recognized role in lactation. This finding suggests that the patient's psychiatric manifestations were, at least in part, secondary to prolactin excess rather than representing primary idiopathic schizophrenia. The psychiatric literature has documented associations between hyperprolactinemia and various mood disturbances, anxiety states, and psychotic symptoms, though the precise neurobiological mechanisms remain incompletely understood. Proposed mechanisms include alterations in dopaminergic neurotransmission in mesolimbic and mesocortical pathways (the same pathways implicated in the pathophysiology of schizophrenia), effects on hypothalamic-pituitary-adrenal axis function, and modulation of reproductive hormone signaling with secondary effects on mood and behavior. The clinical implication is unambiguous: in all patients

presenting with apparent treatment-resistant psychosis, particularly those with concomitant reproductive or metabolic symptoms, endocrinological evaluation including prolactin measurement should be performed, and if markedly elevated, imaging of the pituitary gland should be obtained.

The case of the 42-year-old female with dissociative disorder symptoms who harbored CNS tuberculosis exemplifies the diagnostic challenges posed by infectious etiologies of psychiatric disease. CNS tuberculosis represents one of the most serious complications of Mycobacterium tuberculosis infection, occurring in approximately 10% of patients with active tuberculosis, though the global epidemiology varies significantly by region, with higher prevalence in immunocompromised populations. The imaging characteristics—a 2.5 cm lesion with central necrosis and rim enhancement—are highly suggestive of CNS tuberculosis, representing a classic radiological finding. MRI typically demonstrates TB-related granulomas as hypointense lesions on T1-weighted imaging, with variable enhancement patterns depending on inflammation and vascularity, while T2-weighted imaging shows predominantly hyperintense lesions. The subsequent initiation of anti-tubercular therapy (ATT) combined with adjunctive corticosteroids resulted in marked improvement in both neurological and psychiatric symptoms over subsequent months.

The case of the 40-year-old male with treatment-resistant depression and a partially calcified granuloma in the right frontal lobe represents a more subtle but equally important diagnostic consideration. This case differs from Case 2 in that the infectious lesion appears to be sequelae of prior infection rather than active infection at the time of psychiatric presentation. The patient had failed multiple antidepressants (sertraline, mirtazapine) and augmentation strategies (olanzapine, lamotrigine) without significant response, fitting criteria for treatment-resistant depression. His symptomatology—anhedonia, sleep disturbance, fatigue, and persistent low mood—represents the classic depressive syndrome. Over subsequent months, psychiatric symptoms improved gradually with reduction in neurological complaints. The gradual improvement in depressive symptoms following anti-inflammatory management and nutritional support suggests that these interventions may have addressed ongoing inflammatory or metabolic derangements related to the old lesion. This case emphasizes the importance of comprehensive neuroimaging evaluation in all patients with treatment-resistant depression, particularly when onset is relatively abrupt or when neurological symptoms are present or develop.

The case of the 55-year-old female with delusional parasitosis represents a distinct pathophysiological pathway to psychiatric symptomatology: cerebrovascular disease and associated vascular brain injury. This patient presented with delusional parasitosis—a chronic fixed false belief about infestation with parasites or small organisms, often accompanied by compulsive skin checking, excoriation, and repeated dermatological consultation—unresponsive to standard antipsychotic medications. The presence of cognitive decline and executive dysfunction provided a crucial clinical clue pointing toward an organic etiology. The management approach—continuation of antipsychotic therapy while adding vascular risk factor interventions reflects a pragmatic strategy of simultaneously addressing both the psychiatric symptomatology and the underlying cerebrovascular pathology. The subsequent reduction in delusions and improvement in cognitive performance supports the hypothesis that optimizing cerebrovascular disease management addresses the root cause of the psychiatric manifestations. This case underscores the critical importance of neuroimaging evaluation in late-onset psychosis where the likelihood of organic etiology is significantly elevated compared to early-onset psychosis.

The final case, a 64-year-old female with treatment-resistant schizophrenia who harbored a 3.5 cm cerebellar convexity meningioma, exemplifies the category of space-occupying lesions presenting with psychiatric symptoms. Meningiomas represent the most common benign intracranial tumor in adults, typically arising from the meningeal coverings of the brain and spinal cord. While meningiomas are typically associated with focal neurological deficits corresponding to their location and mass effects (headache, seizures, focal weakness), they can also present with neuropsychiatric symptoms, particularly when located in areas affecting frontal or temporal lobes, or when mass effect produces increased intracranial pressure and brain edema The neurosurgical resection of the meningioma, followed by significant improvement in both psychiatric and neurological symptoms, represents perhaps the most direct evidence among these cases for a causal relationship between organic pathology and psychiatric manifestations. The fact that clozapine could subsequently be tapered, and the patient engaged more effectively in psychotherapy, suggests that the previous apparent "treatment resistance" reflected the uncorrected underlying structural lesion rather than true pharmacological resistance to antipsychotics. This case emphasizes the principle that in patients with first-episode psychosis or apparent treatment resistance accompanied by neurological signs, neuroimaging must be obtained as part of the diagnostic evaluation.

All five patients received psychiatric diagnoses (schizophrenia, treatment-resistant depression, dissociative disorder, delusional parasitosis) based on their presenting psychiatric symptoms, yet all had demonstrable organic pathology as primary contributors to their psychiatric manifestations. This phenomenon is well-documented in the psychiatric literature, with systematic reviews consistently demonstrating that 10-15% of patients presenting with apparent primary psychiatric illness have secondary psychiatric syndromes that explain their presentation. The implications are profound: a psychiatric diagnosis, while useful for descriptive and prognostic purposes, should never preclude investigation for underlying medical causes, particularly in cases of treatment resistance, atypical presentation, or associated neurological symptoms.

In psychiatry, "treatment resistance" typically refers to failure to achieve adequate response after adequate trials of at least two antipsychotics or antidepressants at therapeutic doses for adequate durations. However, as these cases demonstrate, apparent treatment resistance may not reflect true pharmacological resistance but rather misidentification of the underlying condition. When the true etiology is endocrine (Case 1), infectious (Case 2), inflammatory (Case 3), cerebrovascular (Case 4), or structural (Case 5), standard psychiatric pharmacotherapy will predictably fail because it addresses the wrong pathophysiological process. The recognition of pseudo resistance and identification of the true underlying condition can fundamentally transform patient outcomes.

Conclusion

The five case reports presented herein offer compelling evidence that organic psychiatric syndromes—secondary psychiatric manifestations arising from identifiable medical, neurological, infectious, or structural causes—represent a clinically significant phenomenon that demands systematic diagnostic attention in modern psychiatric practice. While the psychiatric diagnostic and classification systems continue to evolve, they remain predominantly symptom-based, creating inherent vulnerability to misidentification of secondary psychiatric syndromes as primary psychiatric illness. The consequences of such misidentification are substantial: delayed appropriate treatment, exposure to unnecessary psychiatric medications with their attendant side effects and risks, prolonged suffering and disability, and preventable morbidity and mortality in cases where the underlying condition is progressive or life-threatening. Conversely, the correct identification of organic etiology can transform patient outcomes through disease-specific therapy that addresses root causes rather than merely treating psychiatric symptoms. These cases collectively argue for a paradigm shift in psychiatric practice toward more systematic, comprehensive evaluation of medical etiologies as integral components of psychiatric assessment, rather than as an optional or secondary consideration. The integration of medical and neurological investigation into standard psychiatric practice represents not an impediment to psychiatric care but rather an essential enhancement that honors the complexity of human neurobiology and the multiple pathways through which the brain can produce psychiatric symptomatology. Future psychiatric training and practice must emphasize this biopsychosocial understanding and ensure that all patients presenting with psychiatric symptoms receive appropriate evaluation to identify and appropriately treat underlying organic causes.

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