CATATONIA IN THE GENERAL HOSPITAL: A CASE SERIES WADING THROUGH DIAGNOSTIC & MANAGEMENT CHALLENGES

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ABSTRACT
Catatonia is a cluster of affective, behavioral, and motor symptoms. Its causes are multifactorial ranging from severe and untreated psychiatric illnesses to neurological diseases and other general medical conditions. It is estimated that 20% of catatonia causes are due to medical conditions out of which two thirds are due to an underlying neurological condition which might include encephalitis, neural injury, developmental disorders, structural brain pathology, or seizures. Symptoms of catatonia can wax and wane, fluctuating between the retarded and the excited type within hours making it more difficult to identify and diagnose. If left untreated, catatonia can lead to multiple medical complications which can lead to significant long-term morbidity and mortality. The initial complications include dehydration, malnourishment, electrolyte imbalance, deep venous thrombosis, pulmonary embolism, pneumonia, urinary tract infection, and retention. In the long run, patients can have sepsis, rhabdomyolysis, DIC, decubitus ulcers, arrhythmia, renal failure, and liver dysfunction. This article will describe three patients (adolescent & adult) that presented to Aga Khan University Hospital (AKUH), Karachi with challenging presentations of catatonia. Their diagnostic and management difficulties will be discussed.

Keywords: Catatonia; Hyperthyroidism; Autoimmune encephalitis; Consultation Liaison Psychiatry; Medical education; Pakistan

INTRODUCTION
Catatonia is a cluster of affective, behavioral, and motor symptoms. Its causes are multifactorial ranging from severe and untreated psychiatric illnesses to neurological diseases and other general medical conditions.1,2 It is estimated that 20% of catatonia causes are due to medical conditions out of which two-thirds are due to an underlying neurological condition which might include encephalitis, neural injury, developmental disorders, structural brain pathology, or seizures.2 Solmi et al found the incidence of catatonia at around 9.2% among subjects with diverse psychiatric or medical conditions.3 A recent study conducted in India showed an incidence of 5.3-19%, in an acute inpatient psychiatry ward. Incidence has been shown to be as high as 37.2% in other studies.4,5

The motor symptoms of catatonia include increased or decreased activity compared to the patient’s baseline.6,7 The retarded type includes stupor, mutism, rigidity, posturing, mannerism, stereotypy, grimacing, immobility, negativism, catalepsy (and waxy flexibility or rigidity), and echo-phenomena. This presentation can be confused with hypoactive delirium. The excited catatonia type can present with excitement, aggression, and impulsivity along with above symptoms. This can be difficult to differentiate from hyperactive delirium, manic episode, and drug intoxication.8,9 In another type called malignant catatonia, autonomic instability can be present and be fatal if left untreated.10 Therefore, catatonia is a challenging clinical diagnosis.

Symptoms of catatonia can wax and wane, fluctuating between the retarded and the excited type within hours making it more difficult to identify and diagnose.10 If left untreated, catatonia can lead to multiple medical complications which can lead to significant long-term morbidity and mortality. The initial complications include dehydration, malnourishment, electrolyte imbalance, deep venous thrombosis, pulmonary embolism, pneumonia, urinary tract infection, and retention. In the long run, patients can have sepsis, rhabdomyolysis, DIC, decubitus ulcers, arrhythmia, renal failure, and liver dysfunction.11

It is important to take an extensive history and investigate for underlying medical and neurological causes, while dealing with this presentation. Treatment...
should be initiated immediately after the diagnosis. The first-line treatment recommended for catatonia, regardless of the cause, is benzodiazepine followed by electroconvulsive therapy (ECT). Patients can respond dramatically with both the treatments, hence early recognition and treatment can prevent long-term consequences.14,15

This article will describe three patients (adolescent & adult) that presented to Aga Khan University Hospital (AKUH), Karachi with challenging presentations of catatonia. Their diagnostic and management difficulties will be discussed.

CASE 1 (CATATONIA DUE TO HYPERTHYROIDISM)
A previously well-adjusted 26 years old lady presented to the AKUH ER, with a 12-day history of abrupt onset of behavioral changes, withdrawal & fearfulness. She developed decreased sleep, appetite and hygiene. She stopped participating in household chores and was always in bed. She was fearful and was having visual hallucinations. The family reported history of an undocumented fever. No history of fits, falls or head injury were reported. The family denied any stressful precipitant. No previous psychiatric history or substance abuse was reported. There was no history of disorientation to time, place or person. Her medical history was significant for primary amenorrhea. There was no family psychiatric history reported. She was seen by multiple physicians with antipsychotic treatment before being seen at AKUH.

On examination, she was noted to be slow to respond and crying during interview. She wasn’t maintaining eye contact. She was speaking incomprehensible words. She was afebrile & hemodynamically stable. Due to the acute presentation and absence of past history extensive workup including lumbar puncture with an autoimmune panel was sent. The initial impression was of a brief psychotic episode versus a mood disorder, if medical illness was ruled out. Her preliminary laboratory investigations were significant for hyperthyroidism (TSH<0.010 & diffuse toxic goiter on thyroid scan) & hypokalemia (K: 2.7 mg/dl). Her autoimmune panel was negative (ANA, PATTERN, ANAG-EET, ASMA, AMA). She was initially admitted under medicine with psychiatry consulting. Treatment for hyperthyroidism was initiated.

Next day, she became mute, started staring with no blinking and developed posturing (her hands were outstretched in mid-air while being assisted to finish her meal). Her movements had slowed down and she had a blunt affect, in contrast to her appearance in the ER. No spontaneous unpredictable movements nor hallucinatory behavior was seen. Her score on the Bush Francis Catatonia rating scale (BFCRS) was 13/69. A working diagnosis of Catatonia secondary to hyperthyroidism was made. Primary mood vs psychotic disorder was kept as a differential.

She was given Tablet lorazepam 1 mg every 12 hours, and was observed for clinical response. She started responding, eating, drinking & moving spontaneously within an hour of the 1st dose. Her BFCRS score then changed to 1/69. Tablet lorazepam was continued as her catatonic symptoms improved.

CASE 2. (CATATONIA DUE TO BIPOLAR DISORDER)
A 16-year-old boy, presented to the emergency room at AKUH. His presenting complaints were mutism, no appetite, generalized rigidity, immobility and decreased responsiveness for the past four days. He belonged to a rural area.

Symptoms started one month ago, when he initially developed disorganized behavior, started talking inappropriately, and was abusing people. He had decreased sleep and was talking excessively on multiple themes. Lability of mood was noticed by the family too. He was taking meals excessively and self-laughing/talking. He was admitted for a month at a local psychiatric facility where he was mostly kept sedated, and as his condition did not improve, he was shifted to AKUH. He had received multiple antipsychotics and antidepressants till then. He had a history of taking cannabis and tramadol tablets.

On examination he was not communicating. He had a staring gaze with no blinking. He was lying in bed and resisting movement. Intentional tremors were also seen. On neurological examination his GCS was 12/15, tone was increased, and reflexes were brisk. Left planter reflex was up going.

He was afebrile and hemodynamically stable. Extensive laboratory workup was sent. His CPK levels were 1131 (range: 46-171). Inj. midazolam 2.5 mg was given intra-muscularly in ER with no improvement in symptoms. He was initially admitted to Pediatric Special Care Unit (SCU). NG tube was passed and feed started. Lumbar puncture was done which showed increased proteins 68 mg/dl (15-40). MRI brain was done which showed no acute pathology. EEG showed mild slow posterior dominant rhythm (alpha internixed theta). Eye examination for KF rings was done which was unremarkable. Autoimmune work up showed raised ASO titers (normal < 200). Echocardiogram showed slightly reduced LV systolic function with mildly
depressed peak systolic LV GLS.

He was diagnosed with catatonia and benzodiazepines were started. Pulse steroids were given for five days due to suspicion of Autoimmune encephalitis. No improvement in symptoms were noted and finally ECT was planned.

Six ECT sessions were conducted and significant improvement was noted in symptoms after ECT number 3. He started making some conversation. He was blinking and his rigidity improved. Swallowing assessment was done and diet was gradually progressed as tolerated. As his catatonia improved, he was diagnosed with bipolar disorder and an antipsychotic was added. The patient was then discharged on Tab. Olanzapine 5 mg every night, after three weeks of admission.

On out-patient follow up visit after three weeks, he reported feeling well and was adhering to the medications. No symptoms of tremors, mutism or rigidity were present. Tab. olanzapine 5 mg HS was continued.

**CASE 3. (CATATONIA DUE TO AUTOIMMUNE ENCEPHALITIS)**

A previously well-adjusted 16 years old boy, from a remote village in Balochistan, was brought to the emergency care of The Aga khan University Hospital, Karachi.

He had a 14-day history of abrupt onset of behavioral changes and disturbed sleep after complaining of gastrointestinal discomfort for a day. He had become withdrawn and stopped participating in household chores. His oral intake and self-care had also declined. He was reported to have been fearful that someone would attack his brother. He was hearing voices and was seen talking to himself. There was increased irritability with crying and shouting spells and was repetitively seeking forgiveness from family members. He was unable to offer prayers effectively. No history of fits, falls or head injury was reported. The family denied any stressful event or trauma preceding these symptoms. There was no substance use history nor previous psychiatric history. He was initially seen by doctors near his home and tried on multiple antipsychotics and ultimately brought to Karachi.

On mental state examination he was noted to be restless and smiling excessively while not participating in the interview. At moments he would stare off for a while. His speech was broken and incoherent. He was hemodynamically stable. The initial impression in the ER was of a brief psychotic episode. Blood work and a neurology consult were done.

After neurology clearance, he was transferred to the psychiatry ward and started on an atypical antipsychotic. Within a day he progressively developed catatonic symptoms: became mute, stopped eating, stayed in bed, had posturing and at times would have increased physical activity. Antipsychotic was stopped and benzodiazepine was started, and neurology was re-consulted. Lumbar puncture with autoimmune panel was sent. MRI brain was also done. As patient started becoming hemodynamically unstable, electroconvulsive therapy was scheduled. His appetite and movement improved slightly, and his vitals stabilized after ECT. Unfortunately, after two ECTs, the patient had a generalized tonic clonic seizure. Neurology was called again to discuss the likelihood of an autoimmune encephalitis (unfortunately panel results came after 10 days). Patient was shifted back to pediatric neurology, with plans to start pulse steroids. EEG showed intermittent temporal slow waves and anti-epileptics were started. Patient continued to have seizures and showed no improvement on pulse steroids.

Ultimately, CSF results returned and were positive for anti NMDA receptor antibodies. Intravenous immunoglobulin and then plasmapheresis was administered. Patient’s condition worsened and he developed poor cardiac function and had acute loss of consciousness. He was shifted to the pediatric ICU and intubated. COVID-19 serology was sent and revealed positive findings despite negative PCR. Patient was hypotensive and echocardiogram revealed depressed cardiac functions. Cardiac function did not improve despite ionotropic support and patient developed refractory wide-complex tachyarrhythmia which did not revert, and he developed bradycardia and passed away. This sequence of events occurred over a total of 19 days.

NMDA-receptor encephalitis, multiple organ dysfunction, post plasmapheresis cardiac dysfunction and COVID-19 Multisystem Inflammatory Syndrome in Children (MIS-C) were the hypothesized causes of death.

**DISCUSSION**

This case series highlights the varied presentations of catatonia and different etiologies behind it, as summarized in Table 1 below. This also shows the importance of history and a comprehensive workup and examination. Catatonia itself can be treated in a similar manner, despite various causes. Nonetheless, ultimately it is crucial to identify primary pathology and treat, as delay in treatment can increase mortality.
Table 1: Summary of the three cases

<table>
<thead>
<tr>
<th>Cases</th>
<th>Presentation</th>
<th>Etiology</th>
<th>Treatment</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Social withdrawal, fearfulness, decreased sleep, decreased appetite and poor self-hygiene. Later developed mutism, psychomotor retardation, staring and mutism.</td>
<td>Catatonia secondary to hyperthyroidism</td>
<td>Oral lorazepam</td>
<td>Catatonia resolved</td>
</tr>
<tr>
<td>Case 2</td>
<td>Mutism, decreased appetite, generalized rigidity, immobility, decreased responsiveness.</td>
<td>Catatonia secondary to Bipolar Affective Disorder</td>
<td>Benzodiazepines and subsequently Electroconvulsive Therapy (ECT)</td>
<td>Catatonia resolved</td>
</tr>
<tr>
<td>Case 3</td>
<td>Behavioral changes, disturbed sleep, social withdrawal, decreased oral intake, poor self-care, fearfulness, irritability, self-talking. Later developed mutism, immobility, posturing.</td>
<td>Catatonia due to autoimmune encephalitis</td>
<td>Benzodiazepines and subsequently Electroconvulsive Therapy (ECT)</td>
<td>Demise of the patient</td>
</tr>
</tbody>
</table>
The challenges in diagnosis & management of Catatonia are multifaceted:

1. Catatonia is a clinical syndrome characterized by a constellation of autonomic, behavioral & psychomotor disturbances & by virtue of its diverse presentation, range from bizarre postures, behaviors & movements, inactivity interspaced with bursts of activity, that can appear as disorders of volition & can lead to confusion, misdiagnosis & treatment failure for unsuspecting clinicians.  

2. Furthermore, the symptoms tend to fluctuate & therefore present an added challenge.

3. The cases discussed here reflected varied etiologies of Catatonia range from Psychiatric disorders to medical conditions.

4. The challenge is further aggravated with no single symptom being pathognomonic of the syndrome.

5. The exact percentage of catatonia in Pakistan is not known. Based on western literature, it is considered a rare syndrome, taught in specialist psychiatry training only. Catatonia as a syndrome in not taught in undergraduate & post graduate medical education in Pakistan. The problem of recognition of psychiatric morbidity is further compounded by the absence of mandatory psychiatric clerkship & Prof examination in all medical schools in country sparing two in Karachi.

6. The delay in detection is compounded by lack of use of standardized diagnostic criteria, e.g., the BFCRS. Seasoned clinicians fail to detect Catatonia when compared to standardized criteria.

7. Consultation Liaison Psychiatry is an established sub-specialty in the developed world. The presence of consultation liaison services in the country represents isolated pockets of care. There’s therefore significant disparity in access to high quality mental health care for the end user in Pakistan as compared to the Sustainable Development Goal of universal health coverage set out by the WHO.

Consultation-Liaison Psychiatry is an integral partner focusing on the psychiatric care of people who are medically ill. The CL psychiatrists see a diverse patient population as mental health issues cut across all specialties & throughout the lifespan. Historically, CL- Psychiatrists have shown improved patient outcomes in terms of access to care, morbidity, length of stay, patient engagement, satisfaction & outcomes. It is based on the integration of biopsychosocial model in the care of general hospital inpatients. Referral rates to consultation liaison Psychiatry services depend on physician knowledge & attitudes on mental health issues of patients under their care. As a start we need academic & research activity directed to yield an assessment of needs to guide future direction, with the aim of development of sustainable & contextualized Consultation Liaison Psychiatry services in public sector hospitals of Pakistan. We propose that Psychiatry needs to be integrated as an essential specialty to be taught & tested in professional exams in undergraduate medical education. The other possible directions may include a need for proactive outreach to physicians caring for patients in general hospitals.

8. The projected scope of this multipronged exercise will lead to clinical services development, training & research in Pakistan. The overarching goal is to address the gap in access to quality healthcare by the end user, which will serve & guide as a direct measure of impact.

CONCLUSION
Catatonia presents in varied clinical situations and prompt recognition and treatment are essential to prevent morbidity and mortality. Consultation-Liaison Psychiatry is an integral partner focusing on the psychiatric care of people who are medically ill.
REFERENCES

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Shireen Najam; concept, case management, data collection, data analysis, manuscript writing
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