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Psychotic Manifestations Triggered by Severe Hyperglycemia in a Female with Type 1 Diabetes: A Clinical Case Insight

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Abstract

Metabolic disorders can lead to psychosis which is rarely reported as a neuropsychiatric complication of controlled diabetes. This case study presents a 23-year-old female with known Type 1 Diabetes Mellitus (T1DM) having developed acute psychotic symptoms on the background of severe hyperglycemia in the absence of diabetic ketoacidosis. She displayed persecutory delusions, visual hallucinations and disorganized behavior, which improved within few minutes of aggressive insulin therapy and fluid replacement. No previous mental history was mentioned. Laboratory and neuroimaging results excluded structural, infectious or toxic causes. It is also shown in this case how hyperglycemia may cause neuropsychiatric symptoms, and there needs to be additional consideration of metabolic causes to the differential diagnosis of acute psychosis. It is essential to early identify and correct metabolic imbalance to reverse the psychiatric symptoms and prevent the misdiagnosis and unnecessarily long-term antipsychotic therapy. Another issue brought to attention in the case is the necessity of intensive glycemic control and multidisciplinary approach to care in young patients with diabetes whose case is complicated by neuropsychiatric alterations.

Keywords: ***Type 1 Diabetes Mellitus, Hyperglycemia, Acute Psychosis, Metabolic Encephalopathy, Neuropsychiatric Symptoms, Insulin Therapy, Case Report, Endocrine-Psychiatric Interface, Glycemic Crisis, Delirium vs. Psychosis***

1.Introduction

Very complicated interconnection of metabolic diseases with psychiatric symptoms is one of the most difficult niches of modern clinical medicine which demands multidisciplinary knowledge and subtle insight to pathophysiological processes. Of the numerous metabolic imbalances that may induce neuropsychiatric symptoms, severe hyperglycemia is, in particular, a poorly identified but critical causal factor of acute psychotic attacks. The two-ways correlation between diabetes mellitus and psycho-pathological disorders is highly reflected in medical literature and multiple studies have proven that the rates of psycho-pathological disorders are higher in diabetic patients than in a general population. The given case is, however, rather unlikely and not well-known in terms of psychosis as the given phenomenon of hyperglycemia directly causing acute psychotic symptoms because this incident is rather uncommon and not properly explored in terms of academic and clinical interest. Type 1 diabetes mellitus or the absolute insulin deficiency that results due to the autoimmune destruction of pancreatic beta cells is a prevalence of about 1.6 million individuals amongst Americans, and is considered to be a lifelong disease that needs careful management to avoid acute as well as chronic complications(1). Pathophysiology well known to be complex of hyperglycemia-induced neuropsychiatric symptoms with osmotic, electrolytic disorder, dehydration, a possible direct neurotoxic effect of excessively high levels of glucose in the brain tissue. Based on recent progress on neuroscience studies, it has been seen that, with acute hyperglycemic episodes, the functioning of the normal neurotransmitters may be disrupted too especially the dopaminergic and glutamatergic pathways which play a major part in the maintenance of the normal perception and cognitive process. Hyperglycemia-induced psychosis clinical manifestations may differ between mild (perceptual disturbance only) and the severe (usually hallucinations and disorganized behavior) with a possibility to impersonate primary mental diseases such as schizophrenia or acute psychotic disorder. This diagnostic complexity is even worsened by the fact that the patients also may be present with autoimmune conditions since emerging studies have proposed on possible shared pathophysiological articulation between auto immune conditions and psychiatric findings. It finds an example of such complex relationships in the case offered below, a clinical case of a young Somali refugee woman with repeated psychotic experiences that were directly related to the severe hyperglycemic states and, therefore, the example will help shedding light on the management challenges and cultural considerations to be involved in in treating such presentations. The knowledge of these links is important to clinicians working in various fields since,

with a timely notice as well as proper treatment of psychosis caused by hyperglycemia, the period of a psychiatric hospital stay can be avoided, and the danger of being misdiagnosed with a primary mental disease can be eliminated.

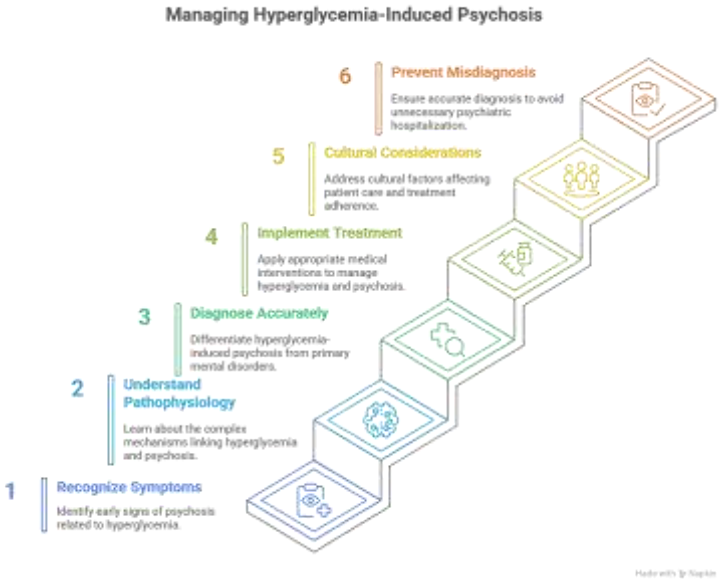

FIGURE 1 Managing Hyperglycemia-Induced Psychosis

2.Epidemiological Background and risk factors

Epidemiological profile of neuropsychiatric complications of diabetes discloses a mix of risk factors going beyond mere glycemic regulation to involve genetic heritage, environmental factors and socioeconomic determinants of health. Studies conducted on a population-based basis have shown that the rate of experiencing psychiatric disorder among those with diabetes mellitus is considerably high as opposed to controls (of the same age), with estimates varying between 15-30 percent depending on study design and type of psychiatric disorder in question. Whether an acute psychotic symptomatology may develop due to hyperglycemia seems to depend on a combination of related variables, such as the extent and duration of the hyperglycemic phases, the predisposition of a person due to his/her genetic polymorphisms with regard to the metabolism of neurotransmitters, and the occurrence of other underlying conditions that may stimulate the development of the metabolic disturbance(2). The young adults with type 1 diabetes constitute one of the most vulnerable groups because of the number of factors that can impair their adherence to medications as well as have increased rates of eating disorders, substance use and because of the psychological burden that the disease might force them to handle at a tender age. Gender specific considerations, in turn, are also relevant, with female patients with type 1 diabetes potentially experiencing other issues regarding hormonal changes, higher autoimmune comorbidity, and psychosocial pressure that may interfere with adherence and overall conduct of the illness. There are specific epidemiological factors to consider in the case of the refugee population that have considerable impact not only on diabetes management but also the mental health progress of such patients, such as providing limited access to the healthcare resources, the lack of cultural understanding and management of the chronic diseases, the distortion of the social support systems, and the trauma of displacement and acculturation stress. The studies that have been conducted on the prevalence of diabetes in Somali immigrants have shown alarming trends such as the prevalence of type 2 diabetes is higher in Somali immigrants than the general population, lack of diabetes health literacy, and imminent barriers to the receipt of culturally relevant healthcare. The combination of refugee status, autoimmune diabetes, and acute psychiatric symptoms forms a rather complicated clinical picture that should be approached carefully and take into account the cultural specifics and language difficulties, and consider the possibility to affect the acceptance and compliance to the treatment with the beliefs about traditional healing. Moreover, the restricted access to culturally competent mental care to groups of refugees may lead to the development of disadvantageous outcomes in terms of a late observation of mental symptoms, overutilization of emergency care services, and many difficulties associated with a withdrawal of treatment, which can lead to diminished overall health and the high costs of healthcare use.

3.Neurobiologic foundation and Pathophysiological Processes

The neurobiological pathways related to the development of hyperglycemic psychotic symptoms are known to ve through a complex chain of metabolic processes, along with the induction of inflammation and the activation of neurotransmitter pathways all of which lead to a loss of the normal functioning of the brain and misperception(3). On the cellular level, hyperglycemia generates an osmotic derangement causing cellular dehydration, most pertinent of all in neurons and glial cells within brain areas involved in perception, reality testing, and executive functioning.

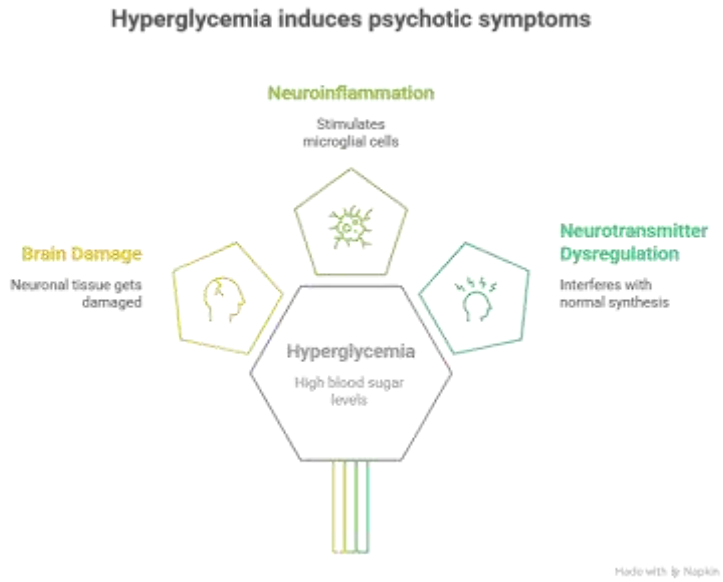

FIGURE 2 Hyperglycemia induces psychotic symptoms

The blood-brain barrier which is usually a protective process that keeps the chemistry of the brain in its finest state is also compromised in cases of severe hyperglycemia due to which it becomes permeable to inflammatory mediators, oxidative stress products, and toxins of metabolism that directly damage the neuronal tissue. Advanced glycation end products (AGEs) that are the products of non-enzymatic rate reaction between glucose and proteins when hyperglycemic conditions are prolonged occur in brain tissue, and AGEs are involved in neuroinflammation as they stimulate microglial cells and nearly free pro-inflammatory cytokines (interleukin-1beta, tumor necrosis factor-alpha, and interferon-gamma) production. Such inflammatory agents have been reported to interfere with normal neurotransmitter synthesis and metabolism especially of the dopaminergic system in the mesolimbic and mesocortical system that is essential in ensuring normal perception and the inhibition of psychotic symptoms. Glutamatergic system, involved in excitatory neurotransmission and the focus of the pathophysiology of schizophrenia and other psychosis, is dysregulated in acute hyperglycemic episodes by a multitude of actions such as modified NMDA transmitter receptor performance, disturbed glutamate-glutamine brain-astroglia exchange, and augmented oxidative stress that smashes glutamatergic synapses. Ketosis, commonly concomitant to devastating hyperglycemia in type 1 diabetes, adds further neurobiologic complications, by generating the ketone bodies, which might be capable of crossing the blood-brain barrier, and changing regular brain metabolism, including the neurotransmitter manufacture and synaptic performance. The cholinergic system, which helps in attention, memory, and cognitive processing also gets dysfunctional in the cases of hyperglycemic events, which further contributes to cognitive disorders and behavioral anomalies that are a typical complaint in the cases of affected patients(4). The recent studies revealed a set of genetic polymorphisms that can predispose some people to the emergence of neuropsychiatric symptoms during metabolic stress, such as alterations in genes that code glucose transporters, neurotransmitter receptors, and inflammatory mediators. The autoimmune aspect of type 1 diabetes further complicates the situation since continuous inflammation leading to destruction of pancreatic beta cells might react with neural antigens, which can cause the autoimmune encephalitis or any other neuroinflammatory disorder that may present itself with psychiatric symptoms.

4.Diagnostic Problems and Clinical Presentation

The psychosis secondary to hyperglycemia is usually comprehensive with a wide definite array of neuropsychiatric signs whose manifestation can closely resemble chief psychiatric disorders thus presenting tremendous nosologic challenges to clinicians on various fields of specialization. The acute course of positive psychotic symptoms (auditory and visual hallucinations, paranoid delusions, disorganized speech and behavior, and alteration of reality) usually present in patients as well as evidence of a serious metabolic decompensation (polyuria, polydipsia, dehydration, and altered mental status)(5). The timeline between hyperglycemic crises and psychotic symptoms is also a key sign in the diagnosis, since the onset of the symptoms almost always occurs when the glucose is in sharp elevation and its manifestation is reversed with proper metabolic management, which is not the case with primary psychiatric condition, where the symptoms are prone to be chronic and persistent.

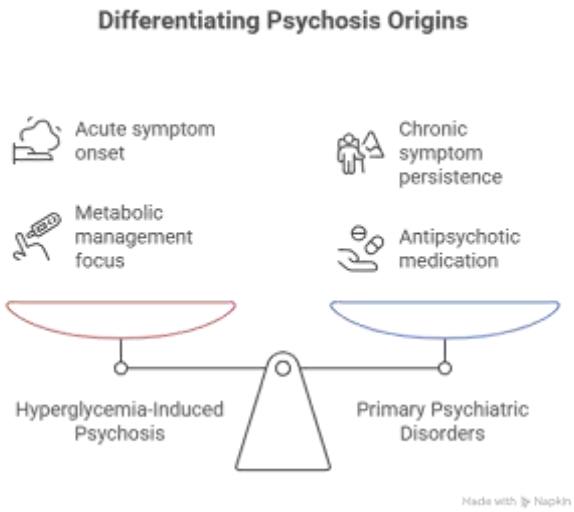

FIGURE 3 Differentiating Psychosis Origins

The clinical specificity of this diagnosis, however, may be confounded by a number of factors such as the inability of the patient to give credible historical information due to altered mental status, the late presentation of patients to health care after critical illness and excessive work up, the presence of other medical complications that may distort clinical presentation until this is sought, and possible persistence of psychotic symptoms even after glucose levels are corrected by extinguishing residual neuroinflammation or altered brain anatomy(6). In severe cases of hyperglycemia, specific distinctions should be made between the sensations of delirium, with altering levels of consciousness and decremented attention, and psychosis that in cases of clear consciousness does not violate reactions to orientation and attention. This differentiation is vital to planning the right treatment because delirium should be treated with most considerable administrative attention directed to the core metabolic imbalance, whereas psychosis can prompt the short-term prescription of antipsychotics and controlling the level of glucose along with it. The cultural dimension plays an important factor in changing clinical presentations and evaluation of psychiatric symptoms, especially amongst patients with non-western backgrounds who describe distress or show it in a somatic symptom, or religious or spiritual terms or culturally adopted symptom pattern that may not be understood in other cultures and can lead clinicians to misjudge. The presence of language barriers also adds to the difficulty in carrying out the diagnostic work because it is critical to properly assess the level of thought content, perceptual disturbances, and cognitive functioning, which is not always possible without the ability to communicate effectively between the patient and the clinician and, in many cases, such communication may require interpreters who must be professionally trained in terms of mental health terminology. Additional diagnostic complexity is associated with the presence of concomitant autoimmune illnesses, since these patients would be at a higher risk of experiencing autoimmune encephalitis, neuroinflammatory diseases, or other organic brain syndromes which may display psychiatric symptoms. Laboratory testing should thus be done that involves extensive metabolic laboratory tests, inflammation markers, autoimmune antibodies, and neuroimaging in cases where necessary to eliminate possible likelihood of other excuses of acute psychiatric manifestation(7). The difficulty of getting reliable collateral information pertaining to the family members is especially pertinent in refugee populations where family member may lack health literate, resist in talking about specific mental health

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symptoms and/ or fear being labeled as infected with psychiatric conditions that may lead to under-reporting and/or downplaying of the levels of symptomatology.

5.Management Options and Therapeutic Strategies

Treatment of hyperglycemic psychosis is multidisciplinary requiring an integrated approach to minimize the acute metabolic crisis and the neuropsychiatric manifestations along with cultural, social and patient factors that would affect approval and response to treatment. The first step in the treatment of diabetic ketoacidosis is stabilization and involves treatment of severe hyperglycemia with proper administration of insulin, fluid replacement to correct dehydration and electrolyte disorders, and close observation to anticipate any complications of diabetic ketoacidosis such as cerebral edema that may worsen neurological problems. The rate of glucose lowering should be deliberately monitored to avoid the rapid change in osmolality that may enhance the neurological symptoms or trigger cerebral oedema, usually aiming at a 50-75 mg/dL an hour glucose decrease until the level gets to 200-250 mg/dL, and then at a slower normalisation(8). The co-management of psychotic symptoms, presents particular challenges, because antipsychotic medication, especially in patients with diabetes is fraught with numerous metabolic side effects, drug interactions among the antipsychotics and the diabetes medications, and the ability of the antipsychotics to aggravate glucose control by influencing insulin sensitivity and glucose metabolism. The risk of metabolic complications with first-generation antipsychotics (e.g. haloperidol) is less than that with second-generation agents, which allows consideration of the former in cases of acute management of the symptoms, however, close monitoring of the extrapyramidal adverse effects, as well as QT prolongation, is crucial, especially when electrolyte imbalances are present. Decisions to start antipsychotic treatment should be made primarily on a symptom severity, safety and the extent of psychotic symptoms hindering medical care with an understanding that most patients will improve significantly on psychiatric symptoms simply with restoration of metabolic stability. The long-term management plans should deal with aspects underlying the presence of the problem of poor glycemic control, such as measurement of diabetes information and self-management abilities, social support infrastructure and availability of diabetes management resources, and barriers to medication adherence (finances, cultural beliefs, other life priorities). The education programs specifically on the refugee population, should take into account the culture that the population belongs to, should be at corresponding language and literacy levels, and should aim at discussing the traditional belief of what it means to have diabetes on the one hand and how to treat it on the other hand, which are sometimes not prepared with the Western medical practices. Community health workers, cultural liaisons or peer support programs can also be useful to boost treatment engagement and long-term outcomes in these groups. Repeat Psychiatric The second visit of a psychiatric doctor is of essence to check on recurrence of psychotic symptoms, continuation of treatment with antipsychotic medicines and provision of psychosocial support of those patients who might develop anxiety or depression due to their medical condition or the traumatic exposure to psychotic episodes(9). Education and support of the family form a vital part of the management plan especially among cultures whose family members are critical in deciding the course of medical treatment and management of medicines necessitating a cultural friendly practice that does not interfere with the normal family process but does facilitate maximum medical care.

6.Conclusion and Future work

The distinctive clinical manifestation mentioned through this case report poses some significant openings to the possibility of future research with great potential to inform us concerning the relationship between metabolic and psychiatric conditions and beneficial to the health improvements of those populations that are affected by such complications. Prospective cohort SFs that investigate the incidence and risk factors and outcomes of hyperglycemia induced psychosis in various group of people is long overdue so that evidence based guidelines are established in preventing and recognizing and treating this condition and especially the need to find genetic, environmental, and cultural influences that predisposes some individuals to neuropsychiatric subsidies during metabolic crises. Further studies by neuroimaging using more sophisticated methods like functional magnetic, resonance, imaging, positron emission tomography, and diffusion tensor imaging may be of help in gaining knowledge regarding structural and functional alterations in the brain during hyperglycemic states that may help find biomarkers that can be used as predictors of patients at the greatest risk of developing psychotic symptoms and thus allow preventive efforts to be focussed on those patients. A genetic research on polymorphism in the genes involved in the efficacy of glucose metabolism, neurotransmittor functioning, and immune system

regulation might reveal the biologic processes underlying the fact that some people are more susceptible to being poisoned by a psychosis induced by hyperglycemia and might also offer the therapeutic targets on preparing the personalized treatment strategy. Intervention studies focusing on the efficacy of diversion rates of diabetes education programs culturally adapted to the refugee population, peer support interventions, and integration care models of refugee population diabetes management could offer evidence-based methods of improving diabetes management and the risk of acute complications to these disadvantaged segments of populations. Pharmacological studies aimed at determining the best practice in using antipsychotics medication with diabetic patients with the acute symptom of psychosis should be conducted to determine how to select a specific medication, doses and the extent of treatment and reducing the metabolic side effects and drug interaction. Patient longitudinal studies after having psychosis caused by hyperglycemia may offer a good source of data in the long term psychiatric morbidity, diabetes morbidity progression, and quality of life assessments and therefore provide recommendations in the prognosis and long term care interventions. The research on the cost-effectiveness of various care delivery models on refugee populations with diabetes could be beneficial to providing information to healthcare policy related to refugees with diabetes and healthcare resources priorities. An examination of the experience of illness, care preferences and barriers to care based on patient and family-focused qualitative research may be used in the creation of more effective and culturally specific interventions. Translational studies of the molecular pathways related to neuroinflammation and mediated by glucose and its association with psychiatric symptoms may discover new treatment targets and markers to be used to identify treatment response. International cooperative studies to compare the results and methods of care provision within various healthcare systems and in different cultural settings might be of help to get an idea of the best practice that could be taken after in management of complex medical-psychiatric disorders within different communities. It is possible that the development and validation of screening tools to screen patients at risk of hyperglycemia-related psychotic events will allow earlier intervention that will prevent the occurrence of complex episodes.

The above thorough clinical study demonstrates the importance of the special note that hyperglycemia induced psychosis should be approached as a specific clinical condition that may not be managed by general knowledge, cultural awareness and multi disciplinary care to bring out optimal results of the patient. The case described demonstrates how autoimmune diabetes combined with refugee status and acute psychiatric symptoms forms a complicated clinical picture that violates the principle of the traditional healthcare provision and proves the necessity of more integrated and systemic as well as culturally responsive forms of medical care. Treatment of such patients is successfully managed only when healthcare providers stop focusing on a definite, specialty-based schema and look at it instead with a holistic view of the interplay between biological, psychological, social, and cultural factors, which contribute to health outcomes and response to the treatment. The neurobiological processes behind hyperglycemia-psycchosis are a promising field of scientific research which may provide knowledge to not only diabetes treatment but also our overall knowledge on a relation between metabolism and psychological disorders and whether or not inflammation is related to this. As health care systems are facing a greater challenge to provide care to culturally diverse populations with multi-layered cultural heritage and social realities, the cultural competency development is not only an ethical prerequisite but a clinical step towards facilitating effective care provision and producing valuable health outcomes. The moral obligation and practical necessity to invest in culturally responsive care derive not only on the impact of unmet needs of refugee populations with chronic diseases on the outcomes of patients and individuals but rather on the entire community and the health system. The approaches to future healthcare delivery should learn lessons through cases like the one discussed, it is important to stress that prevention in the form of extensive diabetes education, the identification of patients at-risk, as well as an active control over social factors that define health outcomes should be taken into consideration in the efforts to provide society with high-quality healthcare in the future. Technological potential to make the treatment of diabetes more effective and prevent the development of acute complications is also only going to grow, but only with respect to thoughtful consideration of digital health literacy, cultural feasibility, and equal access to the resources of technology. Curriculum reconstruction in medical education and training programs needs to change and anticipate the realities of future providers in health care to develop the delivery of medical, psychiatric, and social needs of progressively diverse patients with interdisciplinary collaborations and system-based procedures of care. Development of evidence-based recommendations of managing hyperglycemia-induced psychosis will necessitate further research, clinical practice, and convergence of various medical specialties, patient advocacy groups, and community organizations. In the end the objective of health care must be not only to treat acute medical crises but to lead the patients and families to the knowledge, resources, support that will help

them gain the long term health and well being in a manner that also respects cultural values as well as the individual taste with the context of an effective medical care.

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Conflicts of interest

The authors have no conflicts of interest to declare

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