History of Schizophrenia and Its Treatment

Fizah Zubair

1st Year BDS, Islamabad Medical and Dental College, Islamabad Pakistan

Key Points
➢ Schizophrenia is a developmental disorder having environmental and genetic roles. ➢ In the past supernatural origin was considered its cause. ➢ Drug therapy is used a treatment, clozapine is used due to least side effects, but counselling is preferred treatment option at early stages. ➢ Family support has great effects.

Genetic and environmental variables are thought to have a part in schizophrenia, which is classified as a neurodevelopmental illness. Animal studies demonstrate how developing hippocampal injuries result in prefrontal cortex dysconnectivity. Deficits in the temporoprefrontal neural circuit were found by magnetic resonance imaging and postmortem examinations. In the pathophysiology of the illness, abnormalities in microcircuitry may be caused by decreased oligodendrocyte numbers and expression of oligodendrocyte genes and synaptic proteins.[1] It has proven difficult to find biomarkers for schizophrenia. By using the functional connections of the superior temporal cortex and machine learning methods, at the individual level, first episode drug naive (FEDN) schizophrenia patients have been identified with an accuracy of 78.6 percent, and their reactions to antipsychotic therapy have been predicted with an accuracy of 82.5 percent. The information and correlation between blood oxygen level dependent signals of the superior temporal cortex and other cortical areas discovered by MRI were used to construct the functional linkages. This was discovered to be useful in distinguishing FEDN schizophrenia and forecasting treatment outcomes.

Schizophrenia has been defined in a variety of ways throughout time and places, with a trend to significantly limit the term in recent years. The majority of people with schizophrenia have a chronic, recurring illness that causes severe residual morbidity and worsens their behavior. It is unclear what influences the course of schizophrenia once it develops and whether treatments can change how the illness affects a patient. Premorbid adjustment, age and mode of illness onset, gender, duration of psychosis, schizophrenia subtype, primary negative symptoms, and extrapyramidal signs like tardive dyskinesia, plasma HVA, and brain path morphology are some of the specific clinical and biological factors that are related to treatment response and outcome and are both trait and state dependent. The persistent side effects of antipsychotic medication therapy may also have a positive or negative impact on the course of the disease and can change the neurological underpinnings that regulate how the illness manifests and how the patient responds to treatment. Finally, it has been argued if the disease' active phase involves a pathologic mechanism that fuels the development of the condition. We might assume based on this debate that while certain characteristics of the sickness, such as its intensity and course, may be somewhat predictable, a variety of events can have both positive and negative impacts on the course of the illness and its result.[2]

History:

Since ancient times, there have been records of schizophrenia-related symptoms. The devil possessing someone or the gods attacking someone for immoral behavior were common theories concerning the origin of odd behavior (a kind of divine punishment). According to ethnographic research, schizophrenia exists in every culture that exists now. There have been discovered skulls from the Stone Age with holes. According to studies, these holes were created while the person was still alive to serve as a conduit for evil spirits to go. Trepanning is the name given to this procedure. Despite being one of

the most prevalent mental disorders, schizophrenia is still a mystery. Emil Kraepelin, who coined the term dementia preacox to identify it, was the first to recognize it as a distinct mental disorder in 1887. The term "schizophrenia" was originally used in 1911 by Eugen Bleuler.[3] As far back as the second millennium before Christ, documented records of schizophrenia may be found in ancient Pharaonic Egypt. The Book of Hearts, a piece of the Eber papyrus, goes into great length about depression, dementia, as well as the thinking disorders observed in schizophrenia. Ancient Egypt seems to have equated heart with mind. The alleged causes of psychical ailments were purulence, faeces, a poison, or demons. They were also thought to be symptoms of the heart and uterus. Most of the time, it seems that the Egyptians regarded mental problems as physical ailments. The Atharva Veda, one of the four Vedas, the main books of Hinduism, contains accounts of Hinduism that date back to around 1400 BC. Ancient Indian hymns and incantations may be found in the Vedas. A balance between the five elements (Buthas) and the three humors (Dosas) has been said to be the key to good health, and an imbalance between these different elements has been linked to mental illness.

Around 1000 BC, a Chinese book named The Yellow Emperor's Classic of Internal Medicine documented the signs of madness, dementia, and convulsions. Psychotic behaviors were frequently attributed to demonic or supernatural possession. Although the general populace was certainly aware of psychotic diseases, a review of ancient Greek and Roman literature revealed that no condition existed in these countries that would match the current diagnostic criteria for schizophrenia.[4]

Symptoms:

It is well recognized that social cognitive deficiencies play a significant role in schizophrenia. Social cognitive deficiencies are thought to be a key factor in schizophrenia people's functional outcome. The negative symptoms of schizophrenia include a sociality as well as a lack of facial movement, face expression, eye contact, and verbal inflection. Social responsiveness is also compromised (prosody). The absence of expressive gestures, a lack of voice inflection, social inattention, and a general deficit in attention are the four most common so-called negative symptoms of schizophrenia. Deficits in theory of mind are also prevalent in schizophrenia patients, and these deficiencies are associated with a lack of expressiveness. Furthermore, internal emotional experiences and associated sensations (perhaps linked to insular function) do not appear to be as aberrant in schizophrenia as emotional response, which is also crucial to highlight.[3]

Causes:

Patients most likely inherit several risk genes that, if a crucial threshold is reached, interact with the environment and each other to develop schizophrenia. Premature delivery, low birth weight, and prenatal hypoxia are three common complications. These early environmental dangers seem to affect brain development subtly. A serious mental illness with an uncertain cause is schizophrenia. The development of this illness is thought to be influenced by both hereditary and environmental factors. Numerous risk genes for schizophrenia have been identified by genetic association and genome-wide association studies, including neuregulin1, DISC1, D-amino-acid oxidase activator (DAOA/G72), zinc finger protein 804A (ZNF804A), and transcription factor 4 (TCF4). Environmental variables may combine with genetic factors to affect the beginning and course of the disease. Examples include obstetric difficulties with hypoxia, prenatal infection, season of birth, drug misuse, and migration. These findings were not exclusive to schizophrenia, but this gene-environment interaction may include epigenetic changes such DNA methylation and histone acetylation.

Additionally, it is thought that these risk factors may have an impact on brain tissue during prenatal neurodevelopment and may trigger the emergence of psychotic symptoms in young adults during the prefrontal cortex's synaptic pruning process. By using TMS to examine changes in intracortical and

intercortical connectivity at sub second timescales in schizophrenia patients, it was shown that this defective connectivity were associated with aberrant brain lateralization and cerebral asymmetries. Patients with schizophrenia were shown to have a defective corpusculum-mediated inhibitory link between both main motor cortices (M1).[3] Another investigation that confirmed the existence of a different interhemispheric link found that the facilitatory connections between the left dorsal premotor cortex and the right M1 was selectively disrupted. The link between the right cerebellum and the left M1 was shown to be inadequate in schizophrenia patients as a third impaired interhemispheric route demonstrating a disturbed direct cerebellar-M1 connection.[1] The biggest risk factor for schizophrenia, which is a complex condition, is a favourable family history. While the lifetime risk is only around 1% in the general population, it is 6.5 % in first-degree relatives of patients and more than 40 % in monozygotic twins of those who are afflicted. This risk reflects the genetic closeness between the relative and the proband, according to research on extended families, adoption, and twins.[4]

Treatment:

Pharmacological An oral atypical antipsychotic, such as risperidone or olanzapine, is the first line treatment for a patient experiencing their first episode of psychosis. Drug firms have emphasized the improved side effect profile of these medications, but atypical antipsychotics can have side effects that are just as incapacitating as those associated with conventional antipsychotics. Therefore, individuals with a history of disease who are currently on a typical antipsychotic, are clinically healthy, and do not experience any negative side effects shouldn't switch to an atypical. Clinicians must think about switching patients on conventional antipsychotics who experience extrapyramidal adverse effects to an atypical medication. Clozapine is the best medication for 20–30% of individuals who are treatment-resistant, according to meta-analysis Treatment resistance is characterized by an inability to improve after receiving two or more antipsychotic medications, one of which should be atypical, at an appropriate dose for at least six to eight weeks after excluding confounding variables such concordance failure or drug abuse. A full blood count must be performed on a frequent basis to prevent agranulocytosis, which affects less than 1% of clozapine users. When treatment resistance is verified, clozapine—the only antipsychotic that can lessen both positive and negative symptoms in people with treatment resistance—should be administered.[5]

Common side effects of antipsychotic drugs:

First generation antipsychotics:
Extrapyramidal effects: Dystonia, Pseudo-parkinsonism, Akathisia, Tardive dyskinesia, Sedation, Hyperprolactinaemia, Reduced seizure threshold, Postural hypotension. Anticholinergic effects: Blurred vision, Dry mouth, Urinary retention, Neuroleptic malignant syndrome, Weight gain, Sexual dysfunction, Cardiotoxicity (including prolonged QTc)

Second generation antipsychotics:
Olanzapine: Weight gain, Sedation, Glucose intolerance and frank diabetes mellitus, Hypotension

Risperidone: Hyperprolactinemia, Hypotension, Extrapyramidal side effects at higher doses, Sexual dysfunction.

Amisulpiride: Hyperprolactinemia, Insomnia, Extrapyramidal effects.

Quetiapine: Hypotension, Dyspepsia, Drowsiness, Clozapine, Sedation, Hypersalivation, Constipation, Reduced seizure threshold, Hypotension and hypertension, Tachycardia, Pyrexia, Weight gain, Glucose intolerance and diabetes mellitus, Nocturnal enuresis Rare serious side effects: neutropenia (93%), agranulocytosis, (0.8%) thromboembolism, cardiomyopathy, myocarditis.

Conclusion:

In middle age, schizophrenia typically develops. Environmental risk factors combine with genetic risk to create the illness. Lack of understanding, auditory hallucinations, and delusions are the most typical signs. When a young adult has atypical symptoms and abnormal behavior, clinicians should be on the lookout for the disease. Treatments can enhance

functionality, lessen symptoms, and minimize suffering. Treatment delay makes the prognosis worse.[5] Families do have a significant role in how the illness progresses; patients with supportive parents do better than those with hostile or unsupportive ones.[5]

References:

1. Schmitt A, Hasan A, Gruber O, Falkai P. Schizophrenia as a disorder of disconnectivity. European archives of psychiatry and clinical neuroscience. 2011 Nov;261(2):150-4.
2. Cao B, Cho RY, Chen D, Xiu M, Wang L, Soares JC, Zhang XY. Treatment response prediction and individualized identification of first-episode drug-naive schizophrenia using brain functional connectivity. Molecular psychiatry. 2020 Apr;25(4):906-13.
3. Kyziridis TC. Notes on the history of schizophrenia. German Journal of Psychiatry. 2005;8(3):42-8.
4. Astorga, A. Alvarez, Alba Lubeiro Juárez, Eva Sotelo, Mercedes Llorent Vaquero and Vicente Molina Rodríguez. “F76. CHILDHOOD TRAUMA Related to abnormal social cognition in Schizophrenia.” Schizophrenia Bulletin 44 (2018): S249 - S249.
5. De Zwarte SM, Brouwer RM, Agartz I, Alda M, Aleman A, Alpert KI, Bearden CE, Bertolino A, Bois C, Bonvino A, Bramon E. The association between familial risk and brain abnormalities is disease specific: an ENIGMA-relatives study of schizophrenia and bipolar disorder. Biological psychiatry. 2019 Oct 1;86(7):545-56.