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Pediatric Schizophrenia

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Introduction

Pediatric Schizophrenia can have its onset before 18 years. It can be during childhood (<13 years) or adolescence (13-18 years).[1] It has also been defined as Early Onset Schizophrenia (EOS- <18 years) or Very Early Onset Schizophrenia (VEOS- <13 years).[2] One study suggests an onset cut-off at age 14.7 years below which schizophrenia has significantly more positive symptoms and poorer psychosocial functioning as compared to schizophrenia with better outcomes above the cut-off.[3] It is agreed that onset of schizophrenia before age 12 is very rare.[4] Reliable population-based incidence figures for EOS are still lacking, while males predominate in clinical samples of EOS.[1]

Understanding Early Onset Schizophrenia Through A Case Vignette

Y is male (born 5/12/2015), a student of Prep, the only child living with his parents and paternal grandparents. The pregnancy was uneventful, birth was normal vaginal, and he had normal typical development. He was fully vaccinated. There was no family history of psychiatric disorder. He was normal until 5 years of age when, for no apparent reason, he started running from one room to another, crying and shouting for a long time. He seemed very frightened. He was inconsolable and unstoppable. He stopped responding when addressed and asked questions. His eye contact became very less. He seemed to be looking at the void. He lost his sleep. Y then started laughing for no reason and for long time. There was no emotional connection with the family members. He was found laughing in the toilet. From his utterances, the family inferred that Y was afraid of imaginary things like a millipede, a witch, and a 'Brahmarakshas' (a demon). Y was afraid of going out of his home in the open. He avoided meeting people visiting his home, saying that they were demons and should be killed. He said strange things like, 'break it, kill it, knife him' without any reason. He would repeatedly say such phrases or sentences. He was very anxious and restless. His play, studies, and interaction with family all stopped. His daily routine was disrupted. Y became fearful of stray dogs and even of his own pet rabbit. He

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started smelling his toys and clothes. He wetted and soiled his clothes. His appetite suddenly increased, and he started shoving large amounts of food into his mouth. Y seemed unaware of his surroundings. He seemed not to recognize his parents and home. He would say, "I belong to Lucknow, Please take me home, please take me to my mother, please take me to my father," although he was in his own home and his parents were close by. Y was taken to a 'mazaar' for faith healing and to a shopping mall and seeing people there, he said that they were demons and God would punish them. Y would cry and weep and say, "Don't beat me, don't burn me, they have killed me, I am dead, they have made my mother a kitten, don't kill my mother, I am lost." He would not watch TV and be fearful of it, saying that he is trapped inside it and that please he should be rescued and let out. At another time, "I have fallen into a pit and stuck there and should be helped out." Y would be afraid of the flames of the kitchen stove, but at another time he said he himself is a big fire. When Y's mother tried to hold and soothe him, he would scratch and bite her. Once, he tried to strangle his mother and grandfather. Y spoke of a dark woman who would kill all of them. In his lucid periods, Y was his usual affectionate self, and interacted and behaved normally with the family. But these lucid periods were short, an hour at the most, and then the psychotic symptoms returned. Y was seen by a physician and a psychiatrist. His physical examination, EEG, and CT brain scan were normal. Later, a brain MRI showed bilateral peritrigonal hyperintensities in the cerebral hemispheres, suggesting either delayed myelination or demyelination. Neurological examination was normal and the peritrigonal hyperintensities were thought of unclear significance. Y and his mother were seen by me through online video consultations initially. The mother was requested to make detailed videos of Y in different activities and contexts. Since Y's speech was often unclear, the mother transcribed what he said in Hindi. The mother and Y were serially fortnightly examined online through unstructured psychiatric interviews. No special psychiatric tools were used. The initial diagnosis was non-organic psychosis and as the clinical picture became clearer, it was changed to VEOS. The mother has explained this diagnosis and is encouraged to gather information from the specified websites and on their own. The diagnosis was devastating for the parents, and they required a lot of support and reassurance. Y was already on Risperidone 1-mg daily for ten days before PS (Dr. Prabhat Sitholey) saw him and then dose was titrated upwards in increments of 0.5 mg every 15 to 21 days till 4 mg daily and then to 5 mg daily for a month, and then to 6 mg daily and held constant. Trihexyphenidyl was required to manage extrapyramidal side effects at risperidone 4 mg daily dose and above. Risperidone doses were like adult doses, although these were started low and built up slowly. Little improvement was seen before the risperidone 4 mg daily dose and 3.5 months of risperidone use. Improvement was very gradual and not steady or consistent. A symptom would improve to some extent for a few days to return. This was very disappointing and frustrating for the parents. The mother was encouraged to take up the role of a play – an occupational therapist and a teacher. First, her role was to calm and reassure Y, look after his nutritional needs, sleep, and safety. She was then to engage him in play and other activities of daily living and get Y to regain control over his bladder and bowel and to retrain him in proper use of toilet and ablutions. As Y slowly started improving after about 3.5 months, he was gradually made to study at Prep level without any pressure and with a lot of encouragement. Y had difficulty in doing even those academic tasks in language and arithmetic he could do well before his illness started. He could not pay attention. He was distracted not by anything external but by what was happening in his mind. He seemed lost. Socialization was attempted by taking him to the playground and introducing him to the children there. He was made to face and meet the visitors. At first, Y was reluctant to socialize being fearful and avoidant but gradually, he became better in this regard. Y was not able adjust and cope with his school. About a year after his treatment started, Y joined another school that was tolerant of him and accepted him as he was. As Y got better, his normal behavior started returning. He was a lot more calm. His sleep improved. His running, shouting and crying reduced. His control over his bladder and bowel improved. He started communicating better. His

talks started making sense. His mood became better and more appropriate. He was not so fearful and anxious. He started smiling and laughing meaningfully. Eye contact greatly improved. He started listening to his mother and obeying her. He started paying attention to the stories his mother told him. His attention and concentration became better. He would demand that he be told a story at bedtime. He would dance and recite poems. He played with his father and mother and with his peers cooperatively and enjoyed it. Over the next few months, according to the mother, Y was about 65% improved and soon improved to about 80%. However, it did not mean that all his psychotic symptoms had been remitted. He still became anxious and fearful without any reason but for a short time and could easily be soothed and comforted. Y still said that there was a ghost under his bed but when made to check for it and not finding anything there, he was reassured. The parents were given a diagnosis of very early onset schizophrenia (VEOS). Hallucinations and non-systematized brief delusions with themes of violence, and of losing home and parents, of being precariously trapped, torture, and death were present. Disorganized behavior was present. The duration of the illness till the diagnosis of non-organic psychosis was 4 months. The diagnosis could not have been a bipolar disorder with psychotic symptoms as there was no affective polarity. It could not be autism, which typically starts before age three and the symptoms have a continuous, unremitting course. On the other hand, Y in his lucid moments, behaved normally as before he fell ill. Y's psychosis was not transient. The parents were encouraged to read about Y's diagnosis on specified websites and gather information in their own way. Their questions were answered. PS told them about his experience of handling such cases before and that a good outcome can be expected with patience and regular long-term treatment.

Clinical Presentation: Selective Aspects

The core clinical features of EOS include Hallucinations, delusions, passivity phenomena, thought and speech disorder, reduced or inappropriate emotional reactivity, lack of volition, motor abnormalities like posturing, mannerisms, stereotypies, and catatonic immobility or excitement are present in schizophrenia across various age groups. It is associated with poor premorbid functioning and early developmental delays, which are more frequent and severe (20%, in comparison to 10% in AOS). Impaired sociability occurs in 33% of EOS. Premorbid IQ in EOS is, on average, 80 to 85 as compared to 90 to 100 in AOS. About 33% have mental retardation.[5]

There is a link between self-reported isolated psychotic symptoms in childhood and later schizophrenia. Of those who self-report strong psychotic symptoms, 70% develop schizophrenia and 26% develop schizophreniform disorders. None of these children developed schizophrenia during adolescence. Therefore, it seems that isolated or attenuated psychotic symptoms in combination with developmental impairment constitute a high-risk premorbid phenotype. A prodrome characterized by gradual social withdrawal, declining school performance, uncharacteristic, odd behavior and ideas, eccentric interests, change in affect and unusual and bizarre experiences is more common in schizophrenia than in other disorders.[6] Capacity to form friendships and love relationships is very impaired. Poor outcome is predicted by premorbid social and cognitive impairments, a long first episode, long duration of untreated psychosis, and negative symptoms. Impaired social functioning and negative symptoms are strong predictors.

Neurobiology

It may be that obstetric complications are a consequence rather than a cause of abnormal neurodevelopment.[7] Smaller head size at the time of birth in persons with schizophrenia may be due to defect in genetic control of neurodevelopment or else due to an earlier environmental factor such as viral exposure. Influenza and Toxoplasmosis have been implicated but the evidence is not conclusive. The mechanism in these conditions may be cytokines-mediated disruption of neurodevelopment that expresses as post-pubertal disruption of neurotransmitter functions. Childhood viral infections show an association with schizophrenia (RR = 2.1), though it is not clear whether this is a cause or consequence of schizophrenia-related deficits.[8] It

is hypothesized that abnormal brain development, however, caused and set in motion, whether at the micro synaptic level or at the macro level of neural networks, is expressed as neurocognitive deficits that interact with environmental risk factors to produce psychotic symptoms.[9] Cross–sectional structural brain changes like reduction of total grey matter (GM), especially bilateral insula, anterior cingulate cortex, thalamus, and superior temporal cortex, irrespective of the stage of illness, are present in schizophrenia. Front insular and superior temporal changes are consistently noted and appear to be related to clinical symptoms such as hallucinations.[10,11]

These findings along with ventricular enlargement, are the most robust findings. These brain changes are similarly present in EOS and AOS, supporting the continuity between them. EOS patients have a higher rate of developmental brain abnormalities than controls. Volumetric changes are associated with a number of surface anatomical properties, such as thickness, surface area, and gyrification. Increased gyral curvature along with sulcal thinning affecting frontal, temporal and parietal lobes are noted in EOS. In adolescent-onset schizophrenia, both thickness and surface area reductions are seen in the prefrontal and superior temporal cortex. White matter (WM) changes in EOS are more widespread but less consistent than in AOS. WM changes strongly suggest structural dysconnectivity and are present in left frontal and temporal areas and in their connections to frontal, temporal, insular, hippocampal, amygdala and occipital areas. Progressive ventricular enlargement and volume reduction occur after the onset of schizophrenia, affecting the whole brain. In EOS there is greater progressive reduction in frontal areas. But its not clear whether these changes are due to schizophrenia or antipsychotic medication.[5]

Brain changes precede the onset of schizophrenia. Present evidence suggests that a disruption of developmental trajectories during critical periods preceding and immediately after the onset of illness contributes to the diverse changes in the GM structure that characterize schizophrenia. fMRI studies suggest that schizophrenia patients show inefficiency in recruiting brain regions when engaging in specific cognitive tasks. This is most apparent in the tasks that require prefrontal recruitment, where increased recruitment of areas non-relevant to the task occurs.[12] In the resting state, EOS patients show abnormal time-based correlations among regions that form large brain networks. Cortical neuronal coordination, as shown by oscillatory activity, is abnormal in prefrontal GABAergic interneurons. Almost all major neurotransmitter systems are involved in schizophrenia. The most well-understood are dopaminergic and serotonergic systems.[13]

Glutamatergic/GABAergic systems are strongly suspected of mediating cognitive dysfunction. Cognitive deficits are linked to recovery and functional outcomes. Cognitive performance deficits are wide. In EOS there is a notable reduction in IQ. The biggest cognitive deficit is in executive functions, along with processing speed deficits. Verbal memory deficits are pronounced in EOS. The deficits appear early and remain static before and after the development of schizophrenia. In adolescent-onset schizophrenia, there is a decline in verbal memory along with a lesser age-related progress in learning and processing speed.[14]

Conclusion

Hence, In Y's case the premorbid development was normal, onset acute and psychosis persistent. An adult dose of risperidone of 4 mg per day was required for initiation of response.

Only partial remission in 1.3 years of treatment but a significant return of normal behavior could be obtained. It cannot be said that Y's psychological maturity has increased since the onset of his schizophrenia. It remains to be seen whether Y will progress to full sustained recovery and catch up in his psychological development as judged by his progress in education and behavior. Whether side effects of risperidone, if any, necessitate change in medication will need to be determined. The family will need to be motivated for long-term treatment and follow-up. EOS is continuous with AOS not only in clinical picture and course but also in having similar neuropsychological deficits and neurobiological abnormalities. Western literature has shown a worse course and outcome for EOS as compared to AOS. Whether this is so in India remains to be seen.

In view of its rarity, multicentric research should help increase knowledge about EOS.

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