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Case Report

An extremely rare case of 45X0/46Xi (Xq) Turner mosaic co-existing with schizophreniform disorder, a multidisciplinary management challenge: a case report and literature review

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ABSTRACT

Turner syndrome has various presentations such as short stature, webbed neck, amenorrhea, cubitus valgus, renal anomalies, cardiac defects, etc. Still, the concurrent psychiatric concerns with Turner syndrome are not well-established in the literature. Although most patients with Turner syndrome do not have any mental disorder, a significant proportion of patients with Turner mosaic develop schizophrenia and affective disorders. Very few sporadic cases have been reported in the literature that support the association of the Turner mosaic with schizophrenia and affective disorders worldwide. In this case report we will be discussing an 18-year-old who was identified as the 45X0 / 46Xi (Xq) Turner Mosaic by karyotyping. During her follow-up visits, she was diagnosed with a schizophreniform disorder. Individuals who have both these comorbid conditions are infrequent in this case. A multidisciplinary approach to management consisting of antipsychotics, supportive psychotherapy, and endocrine replacement therapy was initiated for our patient and she responded well on follow-up visits. Our case report adds a potential clue that emphasizes the association of Turner mosaic with the development of schizophrenia. It highlights the importance of early diagnosis of the syndrome and understanding its association with schizophreniform disorder, which should warrant the clinician's early psychotherapy specified toward the psychological as well as the emotional aspects which might play a major role in preventing severe psychiatric complications in these patients. A literature review on this topic is also presented.

Keywords: Case report, Turner mosaic, Schizophrenia

INTRODUCTION

The incidence of schizophrenia is about 1.5 per 10,000 people.[1] It is a psychotic illness that has a serious impact on the mental and social well-being of a person. The social stigma and discrimination experienced are significantly higher in women. Turner syndrome affects approximately 1 in 2000-2,500 live female births.[2] The prevalence of Turner mosaic is quite low. There are very few case reports in the literature that highlight the association of Turner mosaic with schizophrenia and affective disorders. Both Turner syndrome and schizophrenia are independently rare conditions, and their concurrent existence imposes a serious impact on the mental health and overall quality of life of these patients. The reported psychiatric conditions associated with Turner syndrome include schizophrenia, eating disorders, behavioral and emotional disturbances, autism spectrum disorders, and intellectual disability.[3] So, early diagnosis and follow-up with a multidisciplinary approach result in a better prognosis. The proposed hypothesis is that genes in the X chromosome play a role in the pathogenesis of schizophrenia. In normality, in a 46 XX karyotype, only one X chromosome is active per cell due to X inactivation. Women with Mosaic Turner syndrome and schizophrenia may have additional mutations in one or both of their X-chromosomes, which

thereby results in an abnormal expression of a particular gene product that in turn confers increased susceptibility to schizophrenia.[4] However, there are conflicting reports for the same.[5]

CASE REPORT

Our patient was an 18-year-old unmarried girl, belonging to an upper-middle-class family, who came to our OPD with complaints of primary amenorrhea. When she was 20 years old, family members reported irritability, decreased sleep, and muttering to herself. The patient reported hearing voices while in an awake state. No signs or symptoms of fear or suspicion suggesting delusions were found in the initial assessment. No signs of negative symptoms of schizophrenia, such as apathy, were found in the history and examination. Furthermore, there were no disturbances in speech and thought. There was no report of sad mood, suicidal ideation, over-talkativeness, a feeling of constant worry, or repetitive intrusive thoughts. There was no history of similar complaints and no family history of psychotic or affective disorders.

Table 1: Hormonal analysis.

Test parameters	Test value	Normal range
LH (IU/l)	23.8	5 to 25
FSH (IU/l)	114.9	3.4-12
TSH (mIU/l)	1.30	0.4-4.0
AMH (ng/ml)	0.1	2-6.8

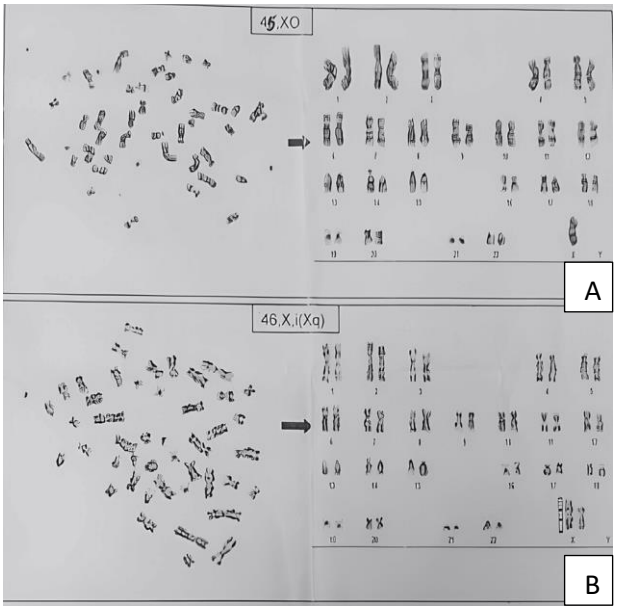

Figure 1 (A and B): Karyotype of the patient.

On general examination, she had a height of 142 cm, a weight of 65 kg and the calculated BMI was 32.23, an obese woman. She had a short neck, a broad chest, and dysmorphic features. The breast was Turner stage 3, and the axillary and pubic hair was absent. The femoral pulse was intact without any radio-femoral delay or radio-radial delay. On genital examination, she had underdeveloped genital organs with hypoplastic clitoris. A gentle one-finger examination of the vagina was about two centimeters deep. The rectal examination was normal. Routine blood tests were normal, such as hemogram, kidney function tests, liver function tests, and urine. Evaluation of peripheral leukocyte karyotyping identified 45X0/46Xi (X q) as shown in Figure 1. Hormonal analysis was performed and is depicted in Table 1. The luteinizing hormone level was normal, while the follicle stimulating hormone (FSH) was elevated, the thyroid-stimulating hormone value (TSH) was normal, anti-mullerian hormone (AMH) levels were significantly low, and random blood sugar was normal. The ECG had a normal sinus rhythm and the chest radiograph was normal as shown in Figure 2. Echocardiography was a normal study. The pelvic magnetic resonance revealed a hypoplastic uterus with poorly defined ovaries as shown in Figure 3 (transverse plane) and Figure 4 (sagittal plane). CECT brain was of normal study as depicted in Figure 5 (axial view).

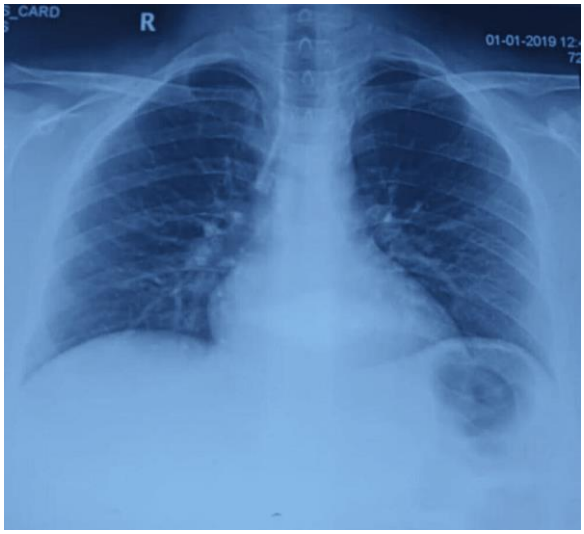

Figure 2: Chest X-ray of the patient.

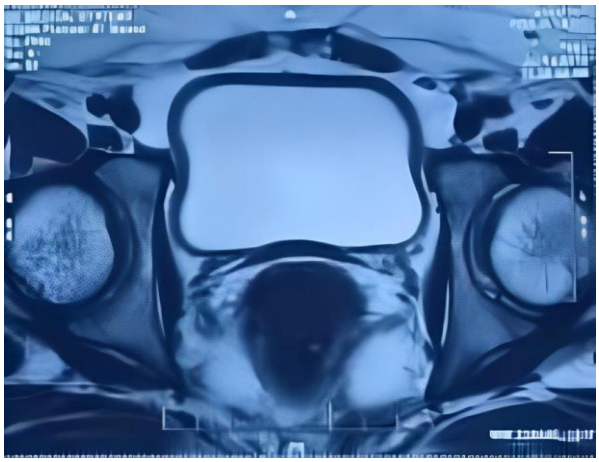

Figure 3: MRI pelvis of the patient taken in transverse plane.

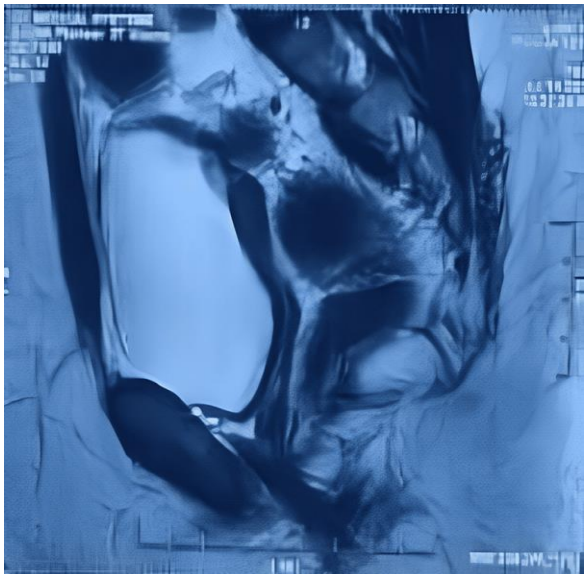

Figure 4: MRI pelvis of the patient taken in sagittal plane.

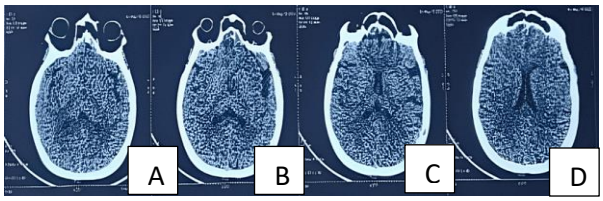

Figure 5 (A-D): CECT brain of the patient taken in axial view.

A multidisciplinary team consisting of gynecologists, psychiatrists, and endocrinologists was involved in managing the case. She was started on levonorgestrel and ethinyl estradiol for six months given her concerns regarding amenorrhoea, after which she started to have menstruation. Psychiatric consultation was sought and a diagnosis of paranoid schizophrenia was made based on clinical examination. Objective evaluation of intellectual disability was carried out using the revised Wechsler Adult Intelligence Scale (WAIS-R). Her intelligence quotient was found to be normal. Initially, the patient started with aripiprazole; after an adequate trial with a maximum dose, she was switched to a combination of olanzapine, zolpidem, and pregabalin. The latter two medications were added to manage insomnia. In our counselling sessions, we found that she had low self-esteem since she was disturbed by her short stature and amenorrhea. She compared herself with her cousins who had normal height and looks. Psychotherapy sessions were conducted to change her outlook.

Follow-up and result

She was on regular follow-ups every six months and responded well to low-dose combination therapy.

DISCUSSION

This case highlighted the difficulties and challenges faced in the management of Turner Mosaic 45X0/46Xi (X q) co-existing with schizophreniform disorder. This case highlighted the paradigm of the challenges faced in managing such a rare combination of presentations. Finally, our successful management of this case identified how early psychotherapy, pharmacotherapy, and regular follow-up were necessary to provide favourable prognosis in these patients and also how a multidisciplinary approach by gynecologists, psychiatrists, and endocrinologists serves as a crux in managing such complex conditions.

The study by Prior et al showed that 18 cases of the total 19 recruited cases had reported co-morbid schizophrenia and Turner syndrome, which was mosaic in variety and was very similar to our case. The incidence of Turner syndrome is three times more common in schizophrenic women compared to the general female population. Turner syndrome and schizophrenia are completely rare entities. furthermore, individuals who have both diseases are extremely rare.[4] In the study by Feng et al it was shown that patients with Turner syndrome and an associated mental disorder were classified as having a schizophreniform or manic-depressive type of illness, according to clinical characteristics. And also, the mental disorder in patients with Turner syndrome was similar to the psychiatric disorders seen in patients with mental retardation.[6]

A retrospective COHORT study conducted by Björlin et al that included 1392 patients had shown that women with Turner syndrome had an increased risk of neurodevelopmental or psychiatric disorder, an eight-fold increased risk of intellectual disability, and a four-fold increased risk of autism spectrum disorder. Furthermore, women with Turner syndrome had two twofold risk of developing schizophrenia and related disorders, eating disorders, behavioral and emotional disturbances with an early childhood onset.[3] A case of a possible association between Turner syndrome and bipolar disorder was also reported in the literature.[7]

Various studies explain the association of defective X chromosome which leads to several psychiatric issues in patients with Turner mosaic. It was also hypothesized that a locus on the X chromosome may be the trigger in the pathogenesis of psychotic and affective disorders.[4] There was also a reported case of Turner mosaic with schizo-affective disorder, which also concluded that gene products of the defective X chromosome could be the possible clue for the neuroanatomical changes and mental illness developing in these patients.[6] Similarly, we hypothesized that our case was a paradigm of the proposed mechanism of the X chromosome and its possible association with schizophreniform disorder.

The neuroimaging findings report that people with Turner syndrome have abnormalities in the anatomy, function,

metabolism, and connectivity in certain areas of the brain. Therefore, this explains the potential cause of the behavioural and cognitive variation typically found in these individuals. Genomic imprinting and exposure to hormones namely estrogen and growth hormone are also likely to have a significant impact on the maturation and functioning of the brain since estrogen tends to revert these defects when supplemented.[8] Murphy et al have studied magnetic resonance imaging in 18 cases of Turner syndrome and they observed decreased volumes of the hippocampus, basal ganglia, and parieto-occipital brain matter, Thereby opening a new way of thinking that X chromosome is essential for the development of cerebrum, grey matter and diencephalon.[9]

Further studies have shown that the polymorphism of the HOPA gene located in Xq13 is associated with schizophrenia, mental disorders, and also hypothyroidism. Moreover, Xq13 contains the center of X inactivation and a gene that escapes X inactivation, and peculiarly that particular gene product may be involved in the X inactivation, and also in the pathogenesis of sex chromosome abnormalities such as Turner syndrome. These genes that escape the X-inactivation may produce their gene products in excess, leading to schizophrenia.[10,11]

In most cases, the psychiatric symptoms that appear with Turner syndrome respond to low-dose psychotropic agents for a short duration (<6 months). Mental disorders subside with treatment and all patients return to their premorbid level and also remain well without relapse. Low-dose estrogen can be added, but should not be used for a long period and can be gradually discontinued after remission of psychiatric symptoms. It was also reinforced that by identifying patients with Turner syndrome in childhood, providing them with psychotherapy and early endocrine replacement therapy, and providing special education to patients with learning disabilities, the appearance of affective disorders such as depression and anxiety could be reduced in this group of patients.[6]

But strikingly Kawanishi et al clearly described that it is just an oversimplification to connect psychosis with Turner syndrome. It reported a case of a woman with Turner syndrome with schizophrenia, and her daughter was schizophrenic too but without any chromosomal defect of Turner syndrome.[5]

CONCLUSION

In conclusion, we present a unique case of Turner mosaic 45X0/46Xi (Xq) co-existing with schizophreniform disorder which was diagnosed early and managed appropriately by a multidisciplinary team. This case also substantiates the hypothesis of the Turner mosaic association with schizophrenia and highlights a possible association of the X chromosome with the development of schizophrenia and affective disorder. Early detection and intervention could help to reduce the duration of untreated psychosis and thereby improve the prognosis. Further, more detailed studies with a larger sample size are needed to confirm the proposed hypothesis. A combination of pharmacotherapy, psychotherapy, and early endocrine replacement therapy is of utmost importance in Turner mosaic patients.

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REFERENCES

1. McGrath J, Saha S, Chant D, Joy Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. Epidemiol Rev. 2008;30:67-76.
2. Atton G, Gordon K, Brice G, Keeley V, Riches K, Ostergaard P, et al. The lymphatic phenotype in Turner syndrome: an evaluation of nineteen patients and literature review. Eur J Hum Genet. 2015;23(12):1634-9.
3. Avdic H, Butwicka A, Nordenström A, Almqvist C, Nordenskjöld A, Engberg H, et al. Neurodevelopmental and psychiatric disorders in females with Turner syndrome: a population-based study. J Neurodev Disord. 2021;13(1):51.
4. Prior TL, Chue PS, Tibbo P. Investigation of Turner syndrome in schizophrenia. Am J Med Genet. 2000;96(3):373-8.
5. Kawanishi C, Kono M, Onishi H, Ishii N, Ishii K. A case of Turner syndrome with schizophrenia: genetic relationship between Turner syndrome and psychosis. Psychiatry Clin Neurosci. 1997;51(2):83-5.
6. Feng Z, Tian H, Liu J. Turner's syndrome with mental disorders resembling schizophrenia and affective disorder. Hong Kong J Psychiatry. 2001;11(3):2-6.
7. Rödström M, Johansson BA, Bäckström B. Acute mania and catatonia in a teenager successfully treated with electroconvulsive therapy and diagnosed with turner syndrome and bipolar disorder. Case Rep Psychiatry. 2021;17:2021.
8. Mullaney R, Murphy D. Turner syndrome: neuroimaging findings: structural and functional. Dev Disabil Res Rev. 2009;15:279-83.
9. Murphy DG, DeCarli C, Daly E. X-chromosome effects on female brain: a magnetic resonance imaging study of Turner's syndrome. Lancet. 1993;13:1197-200.
10. Jung SY, Park JW, Kim DH. Mosaic Turner syndrome associated with schizophrenia. Ann Pediatr Endocrinol Metab. 2014;19:42-4.
11. Roser P, Kawohl W. Turner syndrome and schizophrenia: a further hint for the role of the X-chromosome in the pathogenesis of schizophrenic disorders. World J Biol Psychiatry. 2010;11:239-42.

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