Turner Mosaicism and Schizoaffective Disorder: The First Reported Case

Katherine Backes [1], Tiffany Christian [2], Gaurava Agarwal [1]

Key Words: Schizoaffective Disorder, Schizophrenia, Women, Turner Syndrome

Background

Current literature suggests that sex chromosomes may be involved in the pathogenesis of some mental disorders (1). Abnormalities in the X chromosome have been implicated in the association between Turner Syndrome (TS) and both schizophrenia and bipolar disorder (BD). TS is a genetic disorder that involves either a 45XO karyotype or a mosaic genotype with both 45XO and normal 46XX cells (2). Phenotypic characteristics associated with the syndrome include short stature, neck webbing, hair loss, gonadal dysgenesis and decreased secondary sex characteristics (2). Cardiac abnormalities, most commonly aortic coarctation, as well as skeletal abnormalities including shortened fourth metacarpals, shield chest, and cubitus valgus are also often associated (3). Neuropsychologically, patients typically have normal intelligence but may have specific difficulties with spatial reasoning (1). Many reports indicate that TS mosaicisms moderate physical, neuropsychological, and neuroanatomical outcomes that fall between females with 45X karyotypes and normal controls (4).

[1]*Northwestern University, Department of Psychiatry, Chicago, IL*
[2]*The Mount Sinai Hospital, New York, NY*

Address for correspondence: Tiffany Christian, MD, The Mount Sinai Hospital, One Gustave L. Levy Place, Box 1228, New York, NY 10029-6574
Phone: 212-659-9133; E-mail: tiffany.christian@mountsinai.org

Submitted: October 20, 2013; Revised: February 3, 2014; Accepted: May 30, 2014

While multiple genetic loci have been investigated in the search for schizophrenia genes, the HOPA (12bp) gene within the Xq13 as well as deletion within Xp22.3 have been implicated (2, 4, 5). Furthermore, since the study by Ebaugh et al. in 1968, which investigated chromosomal abnormalities in patients with affective disorders, numerous papers have also explored X linked inheritance in BD without consistent findings (6-10).

TS occurs approximately threefold more frequently in females with schizophrenia (1:600) compared to the general female population (1:2,000) (2). While approximately 50% of TS patients have the 45XO karyotype, females with both schizophrenia and TS are much more likely to have a mosaic karyotype (4, 6). The Prior et al. study showed that 18/19 of the reported cases of comorbid schizophrenia and TS were of the mosaic variety (4). No clear explanation for this statistically significant difference is currently available, but it may provide a more accessible starting point in exploring any unique aspects that the mosaic genotype might confer in the risk of developing schizophrenia.

While both bipolar disorder and schizophrenia have been linked individually to TS, we present the first report of an individual with both TS and schizoaffective disorder.

Case Presentation

"Molly" is a 28-year-old African-American female with schizoaffective disorder, bipolar type who was admitted to the inpatient psychiatric unit with vague homicidal ideations. She expressed that her boyfriend was "intentionally"

making her want to kill him, and that she might harm the "sexy high class woman" who was coming between them. At the time of her admission, she had been missing from her grandmother's house for several days and a police report had been filed. "Molly" was an unreliable historian but described her thoughts as "racing, beautiful," and endorsed a "high energy level" with an increased "sexual appetite."

Current literature suggests that sex chromosomes may be involved in the pathogenesis of some mental disorders …

The paternal grandmother with whom the patient lived was contacted for collateral. She described "Molly" as having several past manic episodes with worsening of psychotic symptoms over the last several years. She was first hospitalized at the age of 18 for grandiose delusions and bizarre behavior. Over the next ten years, she had multiple hospitalizations for the same. Between episodes, "Molly" was described as euthymic but with persistent auditory hallucinations and a disorganized thought process. She was poorly compliant with medications.

The paternal grandmother admitted that "Molly" was currently unemployed and had never been pregnant. Over the last ten years, she was unable to keep a job or stay in college for more than a few months. She hinted that "Molly" was born with some "chromosomal thing." Past medical history was significant for Grave's thyroiditis. She underwent an ablation complicated by hypothyroidism and ceasing of menses.

"Molly" has been living with her grandmother since birth and was adopted by her at the age of two. Her mother "refused" to take care of her due to an unnamed psychiatric illness. She reportedly had a normal childhood development and no problems in school. In addition to the patient's mother, her maternal grandmother and great grandmother were all reportedly hospitalized for unspecified psychiatric illnesses. Neither the patient nor her caregivers had been in contact with any maternal relatives since "Molly's" birth.

The mental status exam was remarkable for a short, overweight African-American female who was psychomotor activated, hyperverbal, thought disordered, and responding to internal stimuli. She had several delusions including being a Hollywood actress, the music manager for Kanye West, and having had multiple pregnancies. We had already suspected a possible chromosomal abnormality due to the patient's physical habitus.

Physical exam revealed short, stocky stature (65 in.) and shortening of the fourth digit bilaterally. Basic lab work including complete blood count, comprehensive blood panel, urinalysis, lipid panel, and thyroid studies were within normal ranges. Urinary drug screen, blood alcohol level, and pregnancy test were negative. Cytogenetic analysis revealed one normal X chromosome and an isochromosome for the long arm of the X chromosome. The abnormal isochromosome X (i [X] [q10]) showed two copies of the long arm of the X chromosome and deletion of the short arm consistent with TS (see Figure 1).

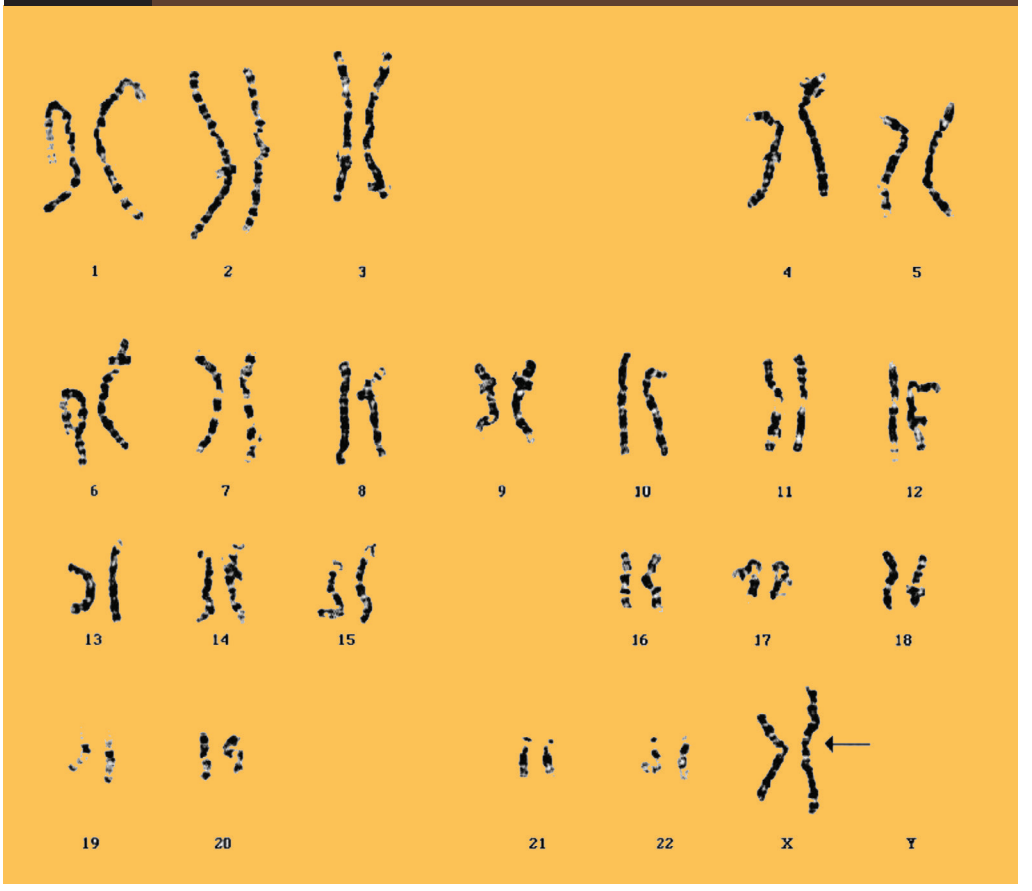
"Molly" had been trialed on multiple medications in the past and refused to be restarted on a mood stabilizer. Due to longstanding history of medication noncompliance, we aimed for stabilization using long-acting monotherapy. This was achieved with Haldol Decanoate. During the two-week hospital course, "Molly" participated in group and individual therapy and took part in her discharge planning. At the time of discharge, she no longer appeared manic or overtly psychotic, though she continued to have thought disorganization. Prior homicidal ideations had abated. She planned to return to living with her grandmother. Several months after discharge from the hospital, paternal grandmother reported that "Molly" was still living with her, complying with medications, and attending outpatient appointments. Her symptoms continued to be stable but she had not yet felt ready to find employment.

The psychiatry community must continue to discuss this potential link, as psychotic and affective disorders are likely to have genetically heterogeneous etiologies with the X chromosome possibly involved in the pathogenesis in a significant subgroup of patients suffering from mental illness.

Discussion

Although there are higher rates of TS in females with schizophrenia compared to the general population, overall, both TS and primary psychotic illnesses are relatively uncommon. Therefore, the probability of finding individuals with both disorders is small (4). We present the first report to our knowledge of the co-occurrence of schizoaffective disorder and TS. The phenotypic features described are consistent with that of the mosaic genotype. Past literature sug-

Figure 1



gests that a locus on the X chromosome may be involved in the pathogenesis of both psychotic and affective disorders (1, 4). Though there are currently multiple hypotheses regarding this phenomenon, the studies have been nonconclusive. The psychiatry community must continue to discuss this potential link, as psychotic and affective disorders are likely to have genetically heterogeneous etiologies with the X chromosome possibly involved in the pathogenesis in a significant subgroup of patients suffering from mental illness. In addition, gene products and neuroanatomical changes that might be linked to defective X chromosome induced mental illness could provide further insight into the underlying biology of mental illness which could lead to future treatment targets.

Patient Consent

Written informed consent for publication of this case report was obtained from the patient shortly after discharge from the hospital once her symptoms were stabilized and she was competent to provide consent. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

References

1. Catinari S, Vass A, Heresco-Levy U. Psychiatric manifestations in Turner Syndrome: a brief survey. Isr J Psychiatry Relat Sci 2006;43(4):293-295.
2. 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(2 Pt 2):239-242.
3. Rebar RW, Erickson GF. Reproductive endocrinology and infertility. In: Goldman L, Schafer AI, editors. Goldman's Cecil Medicine. Maryland Heights, MO: WB Saunders; 2011. p.116.
4. Prior TL, Chue PS, Tibbo P. Investigation of Turner Syndrome in schizophrenia. Am J Med Genet 2000;96(3):373-378.
5. Milunsky J, Huang XL, Wyandt HE, Milunsky A. Schizophrenia susceptibility gene locus on Xp22.3. Clin Genet 1999;55(6)455-460.
6. Fishbain DA, Vilasuso A. Manic-depressive illness associated with Turner's Syndrome mosaicism. J Nerv Ment Dis 1981;169(7):459-461.
7. Ebaugh IA Jr, Freiman M, Woolf RB, Sherman AL, Wnokur G. Chromosome studies in patients with affective disorders (manic-depressive illness). Arch Gen Psychiatry 1968;19(6):751-752.
8. Reich T, Clayton PJ, Winokur G. Family history studies: V. The genetics of mania. Am J Psychiatry 1969;125(10):1358-1369.
9. Pranzer MJ, Tandon R. Bipolar disorder associated with Turner's syndrome. J Nerv Ment Dis 1991;179(11):702.
10. Hebbar S, Payee H, Chandrasekaran R. Turner's syndrome with mania. Indian J Psychiatry 1999;41(1):73-74.