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Marfan Syndrome and Schizophrenia: A Case Report and Literature Review

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Abstract

Introduction—Marfan Syndrome (MFS), a disease of microfibril dysfunction, has been associated with schizophrenia in multiple case reports.

Case Report—We present one case and review the literature that suggests these conditions may share a common etiologic pathway.

Discussion—A possible underlying mechanism of both schizophrenia and MFS is the abnormal expression of growth factors and signaling cascades.

Conclusion—MFS patients should be monitored for psychiatric symptoms and patients with signs of MFS should be referred for appropriate medical care. Also, by understanding shared mechanisms we may develop better understanding and treatments.

Keywords

Schizophrenia; Marfan Syndrome; MFS; Growth Factor; Signaling cascade; Genetic; Development

1. Introduction

Marfan Syndrome (MFS) is a variable, autosomal dominant disorder characterized by connective tissue defects in multiple organ systems [1]. A mutation of fibrillin 1 on chromosome 15 has been identified as a cause in many cases [2,3]. However, genetic testing is not very sensitive as fibrillin-1 mutations are found in other Marfan-like diseases, and up to a third of patients with MFS have mutations at related sites, though all lead to aberrant TGF-β signaling [1, 2]. Therefore, it is typically a clinical diagnosis utilizing a detailed history, physical exam, and imaging studies. The patient must have involvement of two major criteria in two organ systems, or one major criteria plus two minor criteria according to the Ghent criteria. Major criteria include lens dislocation, aorta pathology, skeletal features, a first degree relative with MFS, and the fibrillin-1 mutation [4].

The lifetime prevalence of MFS is two to three per 10,000 [5]. The lifetime prevalence of schizophrenia is about 1%, or 100 per 10,000 [6]. Interestingly, cases of patients with MFS and schizophrenia have been reported [7–9] and these two conditions occur together at a rate greater than expected by chance [10]. This association raises intriguing questions: 1) Does the underlying cause of MFS put one at risk for psychiatric illnesses? 2) How might microfibril dysfunction lead to the development of a psychotic illness? The following case illustrates the co-occurrence of schizophrenia in a woman with Marfan Syndrome.

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2. Case Report

The patient is a single, 47-year-old tall, thin female, previously a successful professional. She was physically well until age 46 when she was found to have aortic root dilatation and aneurysm requiring surgical repair. She was diagnosed with Marfan Syndrome at that time based on her arm span to height ratio, cardiovascular abnormalities, high arched palate, and positive family history.

The patient's first psychiatric hospitalization occurred about one year later. The patient felt she was being poisoned and reported abnormalities in her circulatory system, sexual organs, and eyes due to "gases" and warfarin. Her primary care physician referred her for voluntary psychiatric hospitalization. Collateral history revealed an untreated psychotic episode followed by the loss of her job after surgery though she had declined in functioning over the preceding three years. Her family history was positive for anxiety and episodic depression in one sister. She denied drug or alcohol use and her medications included only warfarin.

On exam, she was thought disordered, profoundly anxious, and denied mood symptoms. During her initial hospitalization, she was diagnosed with a non-specific psychotic disorder and had modest improvement on risperidone 0.5mg BID. She reported many inconsistent side-effects from the risperidone, including heart pounding, vaginal burning and paresthesias, though these improved and were felt to be somatic delusions. Unfortunately, she did not continue the risperidone as an outpatient, and required involuntary hospitalization four months later.

She presented the second time unable to perform her ADLs with latent and perseverative speech, thought blocking, disorganized thought processes and behavior, delusions of being poisoned, and was preoccupied with bizarre physical symptoms. An MRI was unremarkable and lab studies were within normal limits including a normal homocysteine level and thyroid studies. Risperidone was titrated to 3mg daily, which she tolerated well after 2 weeks of symptomatic improvement. Her paranoia decreased with improved goal directed conversations and behavior, linear thought processes, and insight, though with mild residual paranoia and anxiety. Schizophrenia was the discharge diagnosis. A friend lived with her for support after discharge, and she was unable to return to work, but did comply with outpatient care.

3. Discussion

The preceding case is a description of a woman with MFS who developed schizophrenia. Her diagnosis was schizophrenia, although other differential diagnoses included anoxic brain injury, bipolar illness, unreported substance use, and early dementia. Psychotic illnesses occur in patients with MFS at a rate greater than chance. Among other diseases with connective tissue defects, mitral valve prolapse from a chromosome 13q mutation may be associated with anxiety disorders [11]. Lujan-Fryns syndrome, a rare X-linked syndrome with Marfanoid and schizophreniform features, is associated with a connective tissue defect arising from the MED12 gene [12, 13]. Within schizophrenia research, evidence is accumulating for individual genetic mutations at a number of sites integral to cellular signaling cascades in the nervous system. [14,15]. It is possible MFS results from a defective fibrillin or other microfibril protein component with pleiotropic developmental effects on target tissue including the brain with associated TGF-β alterations that ultimately lead to schizophrenia [2,14]. Investigating the potential connection between MFS and schizophrenia may offer potential future disease models and therapy.

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4. Conclusion

Most of the information regarding the comorbidity of schizophrenia and MFS is in the form of case studies, but enough has been published to regard them as likely associated in a subset of patients. We believe carefully monitoring patients with MFS for development of psychiatric symptoms is warranted and referring patients who we suspect may have MFS for appropriate medical screening and treatment. By understanding if both diseases share a common etiology via a shared genetic defect in the fibrillin protein, we may further clarify the roles of growth factors and connective tissue proteins in neurodevelopment and pathogenesis of schizophrenia.

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