

CASE REPORT

Psychiatric Comorbidity in Prader-Willi Syndrome A Case Series

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Abstract

Prader-Willi syndrome is a genetic disorder. Psychiatric comorbidity can occur in persons with Prader-Willi syndrome varying from emotional and behavioural disorders characterised by impulsiveness, temper tantrums, with occurrence of other psychiatric disorders in the form of obsessive compulsive disorder, mood disorders and psychotic illnesses. We present 3 patients with Prader-Willi syndrome with psychiatric comorbidity (German J Psychiatry 2009; 12: 28-31).

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Introduction

Prader-Willi syndrome (PWS) is a genetic disorder. About 70 % of affected people have a deletion of 15q11-13, 30 % have maternal uniparental disomy and a very small proportion of people have an imprinting error affecting genes in the q 11-13 area of chromosome 15. The incidence ranges from 1:10,000 to 1:20,000 births, with equal distribution in both sexes and all ethnic groups (Whittington et al., 2001). This neurogenetic multisystemic disorder is characterised by infantile hypotonia, mental retardation, feeding difficulty in infancy that evolves to an extreme drive to eat in childhood, dysmorphic features, short stature, hypogonadism, sleep apnoea, diabetes and severe maladaptive behaviours, including obsessive compulsive and oppositional behaviours. Reports have described association between PWS and emotional and behavioural disorders including frequent and severe outbursts of temper, mood abnormalities, psychotic disorders and obsessive-compulsive disorder (Whitman et al., 1987).

In addition to the syndrome's characteristic hyperphagia and food seeking, individuals with PWS also have increased risks of non-food consumption and various compulsive behaviours. These include skin picking, hoarding, redoing and concerns with symmetry, exactness, cleanliness, ordering and arranging (Clarke et al., 2002). Relative to others with mental retardation, persons with PWS are at increased risk for developing full-blown, obsessive-compulsive disorder (Dykens et al., 2002). They may show increased rates of tantrums, oppositionality and aggression. They are at increased risk of developing psychotic disorder or affective illness with a psychotic component, especially young adult patients and those with the maternal uniparental disomy as opposed to paternal deletion (Clarke et al., 1998). Atypical antipsychotics have also proven helpful in persons with psychotic features or extreme aggression and impulsivity (Soni et al., 2007).

Patient 1

Mr A is a 27-year old, white single Caucasian male. He was living in a residential home. On September 2005, he became

highly irritable, developed sleep disturbance, was talking excessively, had increased motor activity with features of disinhibited behaviour such as stripping himself naked in front of others. These disruptive behaviours led to hospital admission after a Mental Health Act assessment. On admission his mental state examination revealed evidence of pressure of speech, tangentiality, religious grandiose ideas, persecutory delusions, with ideas of reference and mood congruent auditory hallucinations. He was diagnosed to have a manic episode with psychotic symptoms and was started on tablet risperidone 2mg initially. He had no features of obsessive-compulsive disorder. All baseline blood investigations were normal. There was no past history of psychiatric illness or family history of any mental illness. The dose of risperidone was gradually increased to 4 mg daily and he started showing considerable improvement and was subsequently discharged to the care of the community mental health services. He continued to take Risperidone for a year and the dose was reduced to 3 mg per day due to side effects such as weight gain. As it was the first episode of mania, it was decided by the treating psychiatrist and the patient that the Risperidone can be stopped completely in the end of December 2006. He remained symptom free and continued to live in the residential home for residents with PWS.

In January 2008, changes in his behaviour were noted. He started behaving bizzarely, became very agitated, was talking excessively, became verbally aggressive and started to break things in his room. He started expressing grandiose ideas of a religious nature. He was asking people around him to repeat religious statements and became suspicious that people were trying to poison him. He also had insomnia. There was no history of illicit drugs or alcohol use. A Mental Health act assessment was carried out followed by admission to hospital. A diagnosis of bipolar affective disorder, current episode mania with psychotic symptoms was made. Persecutory and referential delusions were secondary to the grandiose beliefs. Mood was irritable. He was restarted on oral risperidone with a plan to switch over long acting injection risperidone to improve long-term compliance. As his manic symptoms did not settle down even after 2 injections and 4 mg of oral risperidone, semisodium valproate was added as a mood stabilizer. After two weeks of this combination therapy, he became much more settled and his mood became euthymic with no evidence of psychotic symptoms. He was subsequently discharged from hospital to the community team. He is currently being investigated for narcolepsy in the sleep clinic, as there were symptoms suggestive of this disorder during his inpatient admission. EEG and MRI scans were done which were normal.

Patient 2

Miss S, is a 40-year old Caucasian woman who has PWS. Her records refer to "abnormal behaviour soon after birth" and she was treated for meningococcal encephalitis when she was 3-months old. At two years of age, some developmental problems were noted. She attended a mainstream school till she was 14 and lived with her parents up to 18, when she was placed in a specialist unit for people with learning difficulties. It was recorded that her 1Q was 77 and her perform-

ance IQ was 80. When she was 28 years of age, she began showing some bizarre behaviour at the unit where she was residing. She flooded the bathroom more than once and had begun to write obscene letters to people and obscene words on walls and cars. The letters began with insulting words and would be laden with sexually explicit suggestions. She then shaved her head and was observed to be making odd movements with her head. She became more withdrawn and started wetting her bed. She was prescribed fluoxetine 20 mg once a day and trifluoperazine 5 mg once a day, which was noted to have had some benefit.

She then started complaining of hearing voices and began rubbing and scratching her scalp. In a marked departure from her usual behaviour, she attacked a member of staff and was admitted to an acute psychiatric unit for individuals with learning disability. The dose of fluoxetine was increased to 40 mg and the voices apparently resolved. The next year she was hit by a car and suffered a fractured nose and shoulder injuries. She stopped her Fluoxetine and began stealing food from bins and the kitchen. She then started writing letters again and in one incident locked a fellow resident in a room. She spoke of hearing a voice in external space telling her to "eat herself to death". Risperidone was commenced and she showed a dramatic improvement. Risperidone was increased to 6 mg per day, which further improved her mental state. The obscene letter writing stopped and she no longer complained of hearing voices. Unfortunately she developed hyperprolactinemia on risperidone and the medication was changed to quetiapine, to which she responded extremely well. Symptoms such as polyphagia and picking and scratching at the skin also resolved considerably.

Patient 3

Mr A, a 34-year old Caucasian single male, was diagnosed to have diagnosed PWS at the age of about 18 years, with borderline learning disability (verbal IQ 73, performance IQ 78, full scale score 74 on WAIS III) presented with the second episode of depression in 2007. He was living in a care home and became very much discontented with the supervision in the home and strongly wanted to return to his home with his mother and sister. He expressed suicidal wishes and walked alone towards the motorway without telling anyone. Mental status examination revealed evidence of low and irritable mood, suspiciousness about others as if they are watching his every activity and repeatedly expressed his dissatisfaction about the care home and suicidal wishes to get away from his supervised accomodation. He complained of hearing a male voice asking him to flee away from this care home. He was put on mirtazapine 45 mg and risperidone 1 mg and responded well after eight weeks of treatment.

Prior to 2006, while living in the care home, he presented a host of challenging behaviours including setting fire in his trousers in front of carers, threatened to jump from the first floor window and had walked in front of the traffic and also made allegations of abuse. He showed persistently low mood with several self-harm attempts, one being of very serious nature- overdose with 50 paracetamol tablets in September 2006 that necessitated hospital admission, where he re-

sponded well to citalopram 20 mg and risperidone 5 mg daily.

He had exhibited disinhibited behaviours of inappropriate sexual touching of both male and female adults and children, both in social situations and in the ward. He showed extreme frustration and anger in the supervised atmosphere of the hospital, which he thought was imposing restrictions on his freedom and attempts to minimize his food seeking behaviours. His threat of self-harming behaviours and serious overeating necessitated short-term detention under Mental Health Act. He needed reminding, prompting in supervision of personal care and personal hygiene. He appeared to be stubborn, threatening, demanding, and experiencing suicidal ideas. His alleged 'hearing of voices' which directs him to "steal foods" is indicative of his maladaptive behaviours. He showed features of emotional instability, immaturity, very low self-esteem, unpredictable behaviour and tendency to steal and hoard food, which resembled compulsive behaviour.

Mr. A has longstanding difficulties in relation to both mood and behaviour which appeared to be primarily related with his diagnosis of PWS and consequent placement in supervised care homes. He has developed a behavioural repertoire that is adaptive for him in the context of his uncontrollable cravings for food that resulted in a pattern of compulsive behaviour. Constant confrontation and conflict with the set boundaries in the care homes made him prone to recurrent depressive episodes which were mainly of reactive in nature and which responded well with supportive psychotherapy and minimal medications.

Discussion

Varieties of psychopathology are quite common in PWS and are found to be higher among persons with PWS than among persons with intellectual disability of other origins (Reddy et al., 2007). It was interesting to note that all the three patients here had disturbances of mood. Sudden bursts of disturbed mood, as part of the behavioural pattern in PWS, are generally trigger-dependent and short lived. In about 15–17% of persons who have PWS, mood disorders are comorbid (Vogels et al., 2004). During late adolescence and adulthood, delusions, most often of paranoid type, may appear. Hallucinations are not common in individuals (Boer et al., 2002). Psychotic symptoms usually occur in the background of mood symptoms. Careful clinical analysis of hallucinations is warranted as in the third case it appeared to be a part of manipulative behaviour relating to food-seeking tendencies. Learning disability may be one potential cause of maladaptive behaviours in PWS.

In the first case the patient had a diagnosis of bipolar affective disorder, which responded well to sodium valproate and risperidone. The second patient had evidence of a psychotic illness and responded to risperidone as well as the third patient who did well on a combination of citalopram and risperidone. All of our 3 patients did well on risperidone except for the second patient who developed hyperprolacti-

nemia and was changed to quetiapine. Low doses of risperidone have been found to be useful in the treatment of maladaptive behaviours as well (Durst et al., 2000). Atypical antipsychotics are therefore useful in treating the psychotic symptoms of PWS.

To conclude, psychiatric comorbidity can occur in people with PWS and it is important to recognise and treat these illnesses along with the behavioural manifestations using a multidisciplinary approach with both medication and consistent behavioural strategies.

References

- Boer H, Holland A, Whittington, J. Psychotic illnesses in people with Prader-Willi syndrome due to chromosome 15 maternal uniparental disomy. *Lancet* 2002; 359: 135-136.
- Clarke DJ, Boer H., Webb T. Prader-Willi syndrome and psychotic symptoms, case descriptions and genetic studies. *Journal of Intellectual Disability Research* 1998; 42: 440-450.
- Clarke DJ, Boer H, Whittington J, Holland A, Butler J, Webb T. Prader-Willi syndrome, compulsive and ritualistic behaviours: the first population-based survey. *British Journal of Psychiatry* 2002; 180: 358-362.
- Durst R, Rubin-Jabotinsky K, Raskin S, Katz G, Zislis J. Risperidone in treating behavioural disturbances of Prader-Willi syndrome. *Acta Psychiatrica Scandinavia* 2000; 102: 461-465.
- Dykens EM, Leckman JF, Cassidy SB. Obsessions and compulsions in Prader-Willi syndrome. *Journal of Child Psychology and Psychiatry* 2002; 37: 995-1002.
- Reddy LA, Pfeiffer SI. Behavioral and emotional symptoms of children and adolescents with Prader-Willi syndrome. *Journal of Autism and Developmental Disorders*. *Journal of Autism and Developmental Disorders* 2007; 37: 830-839.
- Soni S, Whittington J, Holland, A, Webb T, Maina E, Boer H, Clarke D. The course and outcome of psychiatric illness in people with Prader-Willi syndrome: implications for management and treatment. *Journal of Intellectual Disability Research* 2007; 51: 32-42.
- Vogels A, De Hert M, Descheemaeker M, Govers V, Devreindt K, Leguis E, Prinzie P, Fryns J. Psychotic disorders in Prader-Willi Syndrome. *American Journal of Medical Genetics* 2004; 127: 238-243.

Whitman BY, Accardo P. Emotional symptoms in Prader-Willi syndrome in adolescents. *American Journal of Medical Genetics* 1987; 28: 897-905.

Whittington JE, Holland AJ, Webb T. Population prevalence and estimated birth incidence and mortality rate for

people with Prader-Willi syndrome in one UK health region. *Journal of Medical Genetics* 2001; 38: 792-798.