CASE REPORT

Brief psychotic episode in a patient with chromosome 2q37 microdeletion syndrome

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SUMMARY

A 21-year-old woman with moderate learning disability secondary to chromosome 2 microdeletion at q37 was admitted to a general adult psychiatric ward following a period of agitation with incessant pressure of speech, nihilistic delusions and worsening of sleep and eating patterns. Her presentation was preceded for a number of weeks by social stressors of an ill family member and another family member moving away. She had also been diagnosed and treated for a respiratory infection several weeks prior to presentation. Her presentation improved with low-dose antipsychotic medication and parallel input from the general adult mental health team and the psychiatry of intellectual disability team.

BACKGROUND

Ch2q37 deletion syndrome is a rare condition with approximately 130 reported cases in 2017. It has a higher frequency in women compared with men. Behavioural problems such as hyperactivity and attention deficits are common. There are some reports of genetic association with schizophrenia,^{1–3} but so far there has been only one other case of psychosis found in medical literature.⁴ Other than developmental delays, mild to moderate learning disability and autism spectrum disorder (ASD), there has been no other psychiatric association with this genotype. This case report documents a positive clinical outcome using 1:1 supportive nursing and low-dose antipsychotics in a non-specialist inpatient psychiatric setting.

CASE PRESENTATION

A 21-year-old woman with known moderate intellectual disability was referred to the psychiatry of intellectual disability team on an emergency basis following 2–3 weeks of changes in her behaviour. She had become labile in mood, with poor sleep and appetite, with significant weight loss (family reporting 6 kg weight loss over previous month). She spoke almost non-stop of people around her being dead and reporting animals biting and attacking her. She sustained several bruises on her limbs from clutching or pressing them too tightly. There was a significant increase in reassurance-seeking behaviour towards her family members. She was reported to arrange and rearrange items for no obvious reason, and carried with her a bag of items with strange explanations for each item.

The change in behaviour was sudden. There had been no recent change in living arrangements.

There was no significant change to structure or personnel at her training centre, and there was no known interpersonal conflict or difficulty. There was some psychosocial stress in the household as a family member was ill and receiving treatment for period prior to her presentation, and another family member had moved out some months prior to presentation. While it was common for the patient to engage in imaginative play, for example, talking to her stuffed animal toys and assigning them elaborate back stories, it was out of character to be agitated or upset by such thinking.

She was admitted to a general adult psychiatric ward due to the severity of her and her family's distress, as well as her psychotic symptoms and deterioration in her biological functioning. On admission she was presented as elated with pressure of speech and flight of ideas, continuously describing persecutory delusions of being bitten by dogs and bats and that people around her were dead or dying. It was difficult to obtain a precise history; it was never clear whether she actually saw or felt these animals. She was not observed to be responding to external stimuli, but she had been reported to be talking to herself excessively. Beliefs persisted despite evidence to the contrary.

Physical examination revealed bilateral brachymetaphalangy of digit 4, brachydactyly of the digit 4 bilaterally, short stature (height 159 cm), obesity (82.8 kg, body mass index (BMI) 32.8), frontal bossing, upslanted palpebral fissures, prominent columella, hypoplastic alae nasi and deep-set eyes. She had no signs of an active lower respiratory tract infection, central nervous system infection or urinary tract infection.

The patient was the proband of a chromosome 2q37 microdeletion syndrome, also known as Phelan syndrome. Genetic testing took place when the patient was aged 15 in the National Centre for Medical Genetics in Ireland. G-band chromosomal analysis reported an abnormal chromosome 2 that contained a small amount of unidentified material attached at band 2q36 resulting in a terminal 2q deletion, resulting in monosomy for the region 2q36-2qter. FISH (fluorescence in situ hybridization) analysis using an Abbott 2q subtelomeric probe which maps to 2q37.3 showed a deleted signal pattern consistent with the G-band findings. Array-CGH (comparative genomic hybridization) was not available in this laboratory at the time (May 2010) and was not performed. This abnormality was a de novo deletion as later testing of parental chromosome 2 was normal for both parents.

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The patient is the first of five siblings. She was born at full term by ventouse-assisted delivery. At 18 months old she was referred to the local paediatric team for assessment of global developmental delay. A CT brain showed arrested hydrocephalus and frontal lobe atrophy. A diagnosis of global developmental delay was made using standardised development scales and the family was referred for early intervention family support (Portage programme). At 3 years of age the family reports language delay, which was attributed in part to growing up in an international community in Saudi Arabia and inconsistent exposure to the English language. A diagnosis of moderate learning disability and Albright's hereditary osteodystrophy was made based on clinical and imaging information without genetic testing.

In school the patient required educational assistance due to moderate learning disability in the form of extra resource teaching and allocation of a full-time special needs assistant. Educational and social care assessments would report that her social abilities were relatively good with average adaptive skills, superior self-sufficiency, average community self-sufficiency, average social and personal adjustment scores, and an above-average personal-social responsibility score. Other issues the family reported throughout childhood were some difficulties in fine and gross motor skills that required physiotherapy support and occasionally attention-seeking and reassurance-seeking behaviour.

The patient was referred to the local paediatric team at aged 14 years due to features of obesity with a query of an underlying metabolic disorder. On assessment she was found to have macrocephaly with a head circumference of 58 cm, with a weight of 61.8 kg in the 75th growth centile and a height of 159.1 cm in the 25th–50th centile. Dysmorphic features as noted previously were found as was the presence of left-sided pes planus, for which she was referred to orthopaedics for correction. The patient was also referred for genetic testing to clarify the diagnosis, leading to the correct diagnosis of chromosome 2q37 microdeletion syndrome.

At age 19 the patient was formally assessed for ASD at the request of her father due to the association of this condition and ASD. The patient was assessed by a speech and language therapist, who diagnosed severe receptive language delay and moderate expressive language delay, and the patient was provided with speech and language programme. Assessment by a clinical psychologist found high-moderate learning disability with overall high adaptive and social skills. The team did not diagnose ASD as they felt she did not meet the diagnosis criteria and her presentation was more consistent with combined learning disability and language delay.

After leaving school the patient attended the vocational training centre in the local disability service up to the point of admission. Prior to the episode leading up to admission, she was participating in the training centre in a wide variety of activities, including social skills, leisure skills, independent living and work skills. She lived at home with her father and four siblings. Her mother lived abroad.

The patient had no history of mental health illness or prior residential or inpatient admission.

Her father had a diagnosis of depression. Her paternal grandmother had attended psychiatric services. It is unknown for certain what her psychiatric diagnosis was but was postulated to be mixed depression and anxiety. There was no other known family history of mental illness.

INVESTIGATIONS

On admission to the unit, routine bloods were unremarkable with only a slight rise in leucocytes and monocytes. Non-specific markers of inflammation such as C reactive protein and erythrocyte sedimentation rates were normal. Thyroid, liver and renal

profiles were normal. CT brain was unremarkable, negative for any ischaemic event or new hydrocephalus. Renal ultrasound was unremarkable, negative for Wilms' tumour (occasionally found in 2q37 microdeletion syndrome).

DIFFERENTIAL DIAGNOSIS

The key working diagnosis was that of a brief psychotic episode (International Classification of Diseases 10 F.23) due to the onset and duration of psychotic features.

A severe depressive episode with psychotic symptoms was considered but ruled out as her mood improved spontaneously following admission. The possibility of a bipolar affective disorder would need to be considered over time should there be significant affective disturbance in the future.

Investigations including tests of attention in addition to the temporal description of events ruled out a delirium-like state.

Acute stress disorders did not appear relevant as the stressors had been ongoing for several months to years, and the patient had been functioning as usual in the weeks preceding presentation.

A diagnosis of ASD was considered as it can present as a comorbid condition in patients with learning disabilities and is described in 2q37 microdeletion syndrome. However, in this case it did not seem to be contributory given the lack of a history of repetitive stereotyped patterns of behaviour or lack of deficits in social interaction. The patient was very sociable and interested in social interaction and has many friends in the day service.

Albright's hereditary osteodystrophy should be considered in patients with similar phenotype but was not considered here due to the distinct genotype.⁵

TREATMENT

The patient was admitted to an acute adult psychiatric unit as an involuntary patient under the Mental Health Act and was started on low-dose risperidone, an atypical antipsychotic medication due to the presence of psychotic symptoms. This dose was increased gradually in response to toleration and clinical presentation over a period of 1 week (1 mg twice daily). Her presentation had significantly improved on day 6 of admission. The patient had initially been disturbed by an ongoing building construction nearby but benefited from transfer to a quiet area of the unit. She was engaged by a 1:1 nurse who had dual training in mental health and learning disability providing special observations and interaction. She also was encouraged to attend the ward multisensory room. She was regularly reviewed by the consultant psychiatrist in the learning disability, and learning disability team and the adult psychiatric team with a shared care plan. The frequency and duration of her abnormal ritualistic behaviour were recorded, and behavioural management methods were employed to address them. By day 16 her presentation had improved to the point of her baseline and she was described as cheerful in demeanour. She was made a voluntary patient on day 21 and deemed fit for discharge pending the arrangement of respite and follow-up in learning disability residential care services.

OUTCOME AND FOLLOW-UP

The patient's clinical presentation improved with supportive nursing and careful titration of her antipsychotic medication. On day 34 of her admission she was discharged to the learning disability service and received 2 weeks of respite residential care. Her medication continued at risperidone 1 mg twice daily. The fixity and intensity of the persecutory delusions lessened with time and her behaviour gradually returned to her premorbid

state within about 2 months of onset. She reported benefit from time in the ward's multisensory room. She was reviewed regularly in the community by the psychiatrist in learning disability and the learning disability multidisciplinary team. Her medication was gradually reduced over a period of 12 months to risperidone 1 mg twice daily. Low-dose aripiprazole 2.5 mg was added at this point to counteract some increased weight gain and perceived risk of developing metabolic syndrome on risperidone (BMI 33). Her most recent metabolic and prolactin screen was within normal limits and her weight gain has stabilised.

DISCUSSION

Ch2q37 deletion syndrome is a rare condition with approximately 130 reported cases in 2017. Behavioural problems such as a hyperactivity and attention deficits are common, but case reports of psychotic episodes are rare.^{4–8} However, genetic

linkage studies on Micronesian populations have identified this genetic region as a possible susceptibility locus for psychotic disorders.^{1–3} Future genetic studies on the aetiology of schizophrenia may confirm this association. In this case it is unclear how relevant the microdeletion was in the development of a psychotic disorder. This is partially due to the fact array-CGH was not performed and more precise information on break points and size of the deletion is not available for comparison with existing genetic studies, for example candidate genes RLH, PER2, TWIST2, CAPN10 and KIF1A.⁶

Contributors KAL is first author. GG and MK made substantial contributions to the design and conception of the case report. KAL and NI both contributed to the data acquisition. KAL drafted the manuscript and NI provided critical appraisal. GG and MK provided revisions. All authors provided final approval on the finished version.

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Learning points

- ▶ The management of patients with a significant intellectual disability on general psychiatric wards may be unavoidable in acute situations,⁹ especially in jurisdictions where acute inpatient units that specialise in the psychiatry of intellectual disability are yet to be developed.
- ▶ The risks arising from vulnerability in these situations may be mitigated by 1:1 special nursing observations, but these need to be balanced with privacy-related and dignity-related considerations.
- ▶ Shared management by admitting psychiatrists and specialists in the psychiatry of learning disabilities ensured a comprehensive evaluation and smooth transition across the admission and discharge interfaces.
- ▶ The availability of dual-trained nursing staff with experience in general adult psychiatry and the psychiatry of intellectual disability was beneficial as was the use of a quiet room with lower levels of stimulation.
- ▶ Antipsychotics, where prescribed, should be used at lower doses given a higher propensity to cause side effects in people with an intellectual disability,¹⁰ and careful monitoring undertaken for the emergence of these side effects.
- ▶ There seems to be evidence of vulnerability to psychosis associated with deletions on Ch2q37^{1–3} but very few case reports. Nevertheless, it may be prudent to consider psychosis as a potential differential diagnosis in patients with Ch2q37 deletion syndrome who undergo significant behavioural change.

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