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Case Report

Acute Onset of Psychosis Post-Operatively in an Adolescent with Prader Willi Syndrome

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Abstract

Psychiatric illness occurs with increased frequency in Prader-Willi Syndrome (PWS). Increasing age and the Maternal UniParental Disomy (UPD) subtype are risk factors. We report a 14 year old boy who developed an acute confusional state post operatively following slipped capital femoral epiphysis with an initial suspected diagnosis of delirium. His subsequent presentation was consistent with a mood-related psychosis. Management with atypical anti-psychotic medication and careful environmental regulation were effective in the acute period. Clinicians managing PWS in young people need to be aware of the potential for major environmental change and psychosocial stressors to precipitate psychosis.

Keywords: Behavioural; Psychiatric; Confusion; Antipsychotic treatment

Introduction

The behavioural phenotype in Prader Willi Syndrome (PWS) is characterized by insatiable appetite; food seeking, friendly disposition yet can be prone to temper tantrums, stubbornness and outbursts of rage. Perseveration, self-injurious behaviours, compulsive behaviours and skin picking also commonly occur [1].

A variety of psychiatric disorders have also been described in PWS, including affective disorders, psychosis, sleep dysregulation, autism spectrum disorders, anxiety and obsessive-compulsive disorders [2,3]. Data show that PWS patients with Maternal UniParental Disomy (UPD) of chromosome 15 are at a greatest risk for psychotic disorders [4,5].

Here we report a case in which a florid psychiatric disorder developed in a 14 year old boy post-operatively.

Case Report

A 14.7 year old boy with PWS (UPDmat) was admitted for surgery for a slipped femoral capital epiphysis. Previous assessment had indicated mild/borderline developmental delay. He lived at home with his parents, two siblings and attended a special school. He was mostly independent in his activities of daily living, although he required strict dietary supervision which is common for children with PWS. He was reported to be sociable and enjoyed peer relations. He had no other significant medical history and had been treated with recombinant growth hormone injections since the age of 6 years in a standard dose range of 4.5 to 7.5 mg/m^2/week with good efficacy for growth and body composition. He had no history of specific psychiatric disorders, although displayed a number of the neuro-behavioral characteristics typical of PWS, including food-seeking, skin-picking and a tendency for obsessive-compulsive behaviours. There was no family history of psychiatric disorders.

Surgery with a left Ganz procedure (peri-acetabular osteotomy with capital realignment and fixation) and prophylactic fixation of the right femoral head was undertaken. General anaesthetic agents used were Propofol and Ramifentanil. Growth hormone therapy was discontinued prior to the surgery. Lincomycin was administered pre-operatively and intraoperatively because of fever on initial presentation, although subsequently no infection was confirmed. Dexamethasone, paracetamol, morphine and metaraminol were also administered intra-operatively. Post operatively he had intravenous morphine infusion totalling 47 mg IV on day 1 and 25 mg on day 2. He was then transitioned to oral opioids, receiving 20 mg of oxycodone on post-operative day 3 and 15 mg on day 4. Lincomycin and Enoxaprin were continued post-operatively.

During the first three days after the operation, he was clear in his thinking and appropriate in his behaviour. On the fourth post-operative day he became more irritable and oxycodone was considered a possible contributor and discontinued as he was no longer in pain. On post-operative day five, he was confused, had sleep-wake disturbances and reported "seeing muffins and cakes" upon waking. This was initially suspected to be a hypnopompic phenomenon. Soon he started to talk irrelevantly and misidentify people, including visitors well known to him. Symptoms fluctuated and he was often drowsy during the day.

As the clinical presentation was suggestive of delirium, neurological consultation was obtained and extensive evaluation for an organic cause was undertaken, including Magnetic Resonance Imaging (MRI) brain under general anaesthesia (Sevoflurane) and EEG, both of which were normal. Serum electrolytes, urea, creatinine, liver function tests, arterial blood gas, blood glucose, ammonia, lactate, thyroid stimulating hormone, vitamin D, cortisol, serum B 12, anti-histone antibody, anti-cardiolipin Ig M titre, ANA screen, anti DNA antibodies, complements C3,C4,CH50 and blood and urine cultures were all normal. Haemoglobin level was mildly low at 110 g/L (RR 115-150) while haematocrit 0.32 (RR 0.35-0.48), ESR 129 mm/hr (RR 0-20) and C-reactive protein 40.1 mg/L (RR 0-10) were all thought to be consistent with recent surgery. No organic neurological problem

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was identified and Psychiatry and Sleep consultations were obtained.

Sleep patterns were dysregulated and confirmed with a sleep diary and actigraph monitoring. Melatonin was commenced in a dose of 3 mg at night. Sleep at night improved, but daytime drowsiness continued and modafanil was added which improved day-time alertness. No clear sleep disorder could be diagnosed and both these medications were discontinued after 8 weeks.

Symptoms of confusion, disorientation, drowsiness and uncharacteristic behaviour continued and worsened. He required one on one nursing to stop him attempting to ambulate on his operated hip. Risperidone 0.5 mg daily was commenced on post-operative day 11. Symptoms suggestive of mood disturbance and psychosis were increasingly observed. Mood was noticed to be more labile in the evenings and he was often unco-operative to staff. Specific psychotic symptoms emerged periodically. There was social and sexual disinhibition. During one interview he expressed delusional beliefs that he received a message from his father that his mother was dead. Hallucinatory behaviour was observed during wakeful periods. Confusion remained prominent but fluctuated and formal cognitive assessment was not possible. Short-term memory was poor with very short attention span. Deterioration ensued and by post operative day 14 he became doubly incontinent and handled faeces. Skin picking increased and he became more obsessive and irritable. The functional decline was striking compared to the independent, sociable boy who previously loved to walk his dog, chat with people and play games.

The dose of risperidone was gradually increased to 3 mg/day and strict behavioural management and supervision continued. Over a period of 8 weeks he gradually became more co-operative, his mood stabilized and inappropriate behaviours started to improve. Growth hormone was recommenced 6 weeks after admission and within 2 days, a further significant improvement in symptoms was noted. He became alert, was no longer confused and spoke appropriately for the first time in 8 weeks. However there was some persistence of mood symptoms, speech was mildly pressured and he had flights of ideas and felt that his head was "crowded with thoughts". These residual symptoms improved further over the next 2 weeks, coinciding with the dose of risperidone being increased to 4 mg/day. Soon after, he developed tremors and drowsiness and was successfully cross tapered to aripiprazole 7.5 mg/day.

Discharge occurred on post operative day 78 when he was stable and could be safely cared for (orthopaedic and behaviourally) outside the acute hospital environment. He successfully integrated into a group home and was doing well. Three months after discharge, he complained of excessive tiredness and wanted to discontinue the medications. After discussion with the parents on the risk of relapse and education of the early warning signs, aripiprazole was discontinued. After 3 months he relapsed with an acute onset psychotic disorder with prominent mood symptoms, auditory hallucinations and sleep disturbance. Risperidone was recommenced and his symptoms resolved quickly.

Discussion

One of the main challenges in this case was to differentiate whether the patient was suffering from delirium or acute psychosis. Delirium in children and adolescents is reported to be similar in presentation to adults [6] and is characterised by altered level of consciousness, change in cognition or perceptual disturbance, has an acute-onset fluctuating course and is due to a pathophysiological cause [7]. Our patient presented with features suggestive of delirium but no pathophysiological cause could be established and the presentation was protracted. There are reports of delirium occurring in children following recovery from volatile anaesthetics such as sevoflurane [8], however these rarely last for more than two days [9]; our patient had propofol which is less likely to cause delirium. Opioid medication and infection were considered as possible causes of the apparent delirium, but no infection was proven and there was no improvement after withdrawal of opioids. MRI and EEG findings did not support a diagnosis of delirium. EEG slowing is reported to be a sensitive and reliable indicator of cerebral insufficiency which characterizes delirium [10] and serial EEGs can be useful in ruling out delirium [11].

People with PWS, particularly with maternal UPD subtype are at risk of psychosis [5] and this can occur in adolescents [12]. Vogels [13] reported 6 adult PWS patients who developed psychosis with all having significant psychosocial stressors prior to onset of psychosis. Our patient showed signs of lability of affect, pressured speech and sexualised behaviour. Whilst these are in favour of psychosis, confusion as a primary symptom is uncommon in schizophrenia.

In the case series of patients with PWS and psychosis by Verhovenet, et al. [14] 90% had confusion and fluctuating mental state. Seventy-eight percent presented with acute, transient, episodic recurring psychoses of polymorphic phenomenology fulfilling Perris criteria of cycloid psychosis [15]. In our case, the relapse of psychosis after discontinuation of anti-psychotic medication is strongly suggestive that the post-operative episode was a form of acute psychosis rather than delirium.

The literature is unclear on what medication group is most useful in treating patients with PWS and mood-related psychotic disorders. Verhovenet, et al. [14] reported that mood stabilisers were helpful in their sample. However, Soni, et al. [12] reported that antipsychotics were more useful and found that those treated with mood stabilizers had a greater chance of relapse [12]. It has been suggested that the GABA system may be involved in the pathogenesis of psychiatric disorders in PWS as GABA-A receptor subunit genes are located at 15q13 [16-18]. Soni, et al. [12] found that medications such as Carbamazepine and Valproate which act on GABAergic systems to varying degrees were not effective in those with PWS. Also against this, the GABA-A receptor is not imprinted [1].

Fortunately our patient responded to risperidone and tolerated a successful cross taper to aripiprazole. It is known that PWS patients with maternal UPD with psychosis have a higher risk of extrapyramidal symptoms and weight gain [12] when treated with atypical antipsychotics. Our patient developed extra pyramidal symptoms but not weight gain because of strict environmental and behavioural management. We feel that it is likely that weight neutral antipsychotics such as aripiprazole may be better tolerated for long term treatment in this population.

Conclusion

In summary, we present a case of acute onset mood-related

psychotic disorder in an adolescent boy in the post-operative period. He initially presented with a confusional state with features of delirium. Major environmental stressors are believed to be the precipitating factor. Atypical antipsychotic medications and careful environmental regulation were efficacious in management. Clinicians who manage adolescents and adults with PWS should be aware of this possible post-operative complication.

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