

Support and Information



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Kleefstrasyndrome.org

A website and forum for anyone affected by Kleefstra syndrome

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. The guide was written jointly by Dr Miranda Coberman MB BS and Dr Karlijn Vermeulen, psychiatrist at Radboud University Medical Centre, Nijmegen, Netherlands.

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Kleefstra syndrome and mental health

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Kleefstra Syndrome and mental health

A guide for families

Notes

Introduction

As a parent of a child with Kleefstra syndrome, one of my greatest fears is the future, having read about the syndrome and the psychiatric issues that may accompany it. There is a large spectrum of Kleefstra syndrome, both physically, cognitively and with regards to medical/psychiatric complications. As it is so rare, information regarding mental health is scanty and difficult to access. I have compiled this leaflet with the help of Dr Karlijn Vermeulen, psychiatrist at the Radboud University Medical Centre in the Netherlands, who has studied the psychiatric aspects of Kleefstra syndrome, in order to help parents understand what may happen in the future and hopefully to feel more in control in accessing help from health care professionals. None of us can predict if our children will be affected by any of the conditions in this guide, but we can educate and empower ourselves by being prepared.

Dr Miranda Coberman

Kleefstra syndrome

Kleefstra syndrome is a rare genetic condition caused by chromosome 9q34.3 microdeletion or mutations of the EHMT1 gene. It is hypothesised that the enzyme which the EHMT1 gene encodes plays a vital role in neurodevelopment (development of the brain and nervous system), and that disorders in its function can result not only in neurological and physical issues, but also in behavioural problems and psychiatric disorders.

These appear to change over time and it appears that the onset of puberty can trigger not only emotional issues, but also psychiatric problems and regression in learnt skills which worsen with age (Reference 1).

There is a wide spectrum of functioning in children/adults with Kleefstra syndrome, from physical to mental health. Intellectual disability (ID) ranges from mild to severe, alongside a wide range of physical illnesses, some of which themselves are rare. The degree of ID is not directly related to the prevalence of co-occurring diseases, but may affect the way in which they present.

References are numbered. You can find them on page 6.

References

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Range of behaviour/psychiatric morbidity in Kleefstra syndrome

Children with Kleefstra syndrome are commonly reported to be of a happy and content character and temperament. Very often there are features of autistic spectrum disorder (ASD). Below are some of the behavioural/psychiatric conditions that have been seen in people with Kleefstra syndrome when they are patients. It is not an exhaustive list and has been compiled using a search of available medical literature and also from the Kleefstra Syndrome UK conference in 2015 (Reference 5).

Psychiatric conditions

In order of life-time prevalence, from the most common to the least :

- Autism spectrum disorders (ASD, including autism, up to 95%)
- Anxiety disorders (up to 45%) (including generalised anxiety, but also specific phobias)
- Major depression (up to 40%)
- Psychosis (reference 2) (up to 30%)
- Obsessive compulsive disorder (up to 30%)
- (Hypo)mania (up to 25%)
- Attention deficit/ Hyperactivity disorders (Reference 2)

Behavioural symptoms

- Sleep disturbances, including problems falling asleep and waking frequently in the nights (References 2, 3) (up to 80%)
- Self-injurious behaviour
- Apathy and catatonia (Reference 3)
- Impulsive behaviour (Reference 3)
- Aggressive/emotional outbursts
- Stereotypical movements. Up to 90% show stereotypy and very typical movements of the hands and fingers.
- Chaotic behaviours (Reference 3)

In all cases changes in behaviour should be investigated to ascertain if there is an underlying cause. A possible cause could range from physical complaints such as pain, reflux or constipation, to a psychiatric disorder such as those mentioned above. Other causes could be behavioural problems that correspond with the child's level of development, such as temper tantrums at a mental age of 2-3 years.

References are numbered. You can find them on page 6.

Treatment

This section includes general advice for Kleefstra syndrome, based on clinical experience in a cohort of 24 Dutch patients. No official study on treatment in Kleefstra syndrome has been performed yet.

Specialised neurological and psychiatric care as well as behavioural therapies are recommended for individuals with significant behaviour problems and/ motor disorders (Reference 4). It is important to access professional care early as this may help to reduce the extent of any regression. As yet there is no published research into this. It is also vital to treat sleep disturbance in adolescence /early adulthood as this seems to precede any regression (Reference 8). Regression can follow physical illness, severe depression or manic/psychotic illness.

“ Be alert to changes in sleep patterns ”

Treatment should be started as soon as symptoms of a psychotic illness or severe sleep disturbance emerge. This often goes along with a sudden decline in functioning, and this includes patients functioning at below their chronological age. A sudden change in sleep pattern (frequent awakening in the night or stopping sleeping at all) often precedes a physical or psychiatric illness. So, please be particularly watchful/ alert if your child's sleep pattern has changed for more than 72 hours, without any extra sleep during the daytime.

When a psychiatric disease is diagnosed by a professional, the normal treatment guidelines should be followed. Mild to moderate mood and anxiety disorders respond in general to non-pharmacological treatments, such as increased activity for depression and EMDR (eye movement desensitisation reaction) in the case of PTSD (post traumatic stress disorders).

Music therapy in particular can be of additional value for relaxation and increased activity in children with developmental delay, such as those functioning at under 2 years of mental age.

References are numbered. You can find them on page 6.

“ Music therapy can help as well ”

Sometimes a disease is severe and needs to be treated with medication as well. For manic and psychotic episodes, normal to high doses of atypical antipsychotics seem to be most effective in Caucasian patients with Kleefstra syndrome, while people with other ethnicities are well treated with normal dosages. The atypical drugs cause fewer side effects and are well tolerated in people with Kleefstra syndrome.

The best effect was given by olanzapine (especially in the case of severe sleep disturbance/ manic symptoms) and by aripiprazole, especially when there were psychotic symptoms, but no severe sleep problems or manic symptoms. This advice is based on an observational cohort study of 24 patients with Kleefstra syndrome in the Netherlands.

Professionals need to be alert to possible paradoxical responses to drug therapy commonly used for psychiatric illnesses. This means that the drug has the opposite effect to the desired effect. This commonly occurs in patients with vulnerable brains, such as those with intellectual disabilities, especially when benzodiazepines are prescribed to calm down a patient, although this is not always the case.

In one case, medication was not effective enough and was followed by deep brain stimulation, which was effective for extreme OCD symptoms (Reference 6).

Summary

This leaflet briefly summarises possible psychological/psychiatric features seen in Kleefstra syndrome in order to inform parents and involved caregivers. The take-home message is that psychiatric diseases occur frequently in patients with Kleefstra syndrome compared with other patients with intellectual disabilities (Reference 7). Please inform your child's doctor (general practitioner/neurologist/ paediatrician) about this! And try to plan in advance which services to contact in case of emergency. We hope this will lessen distress both for the patient and the wider family unit.

Miranda Coberman and Karlijn Vermeulen