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Case Report

Kleefstra syndrome and sleep disorders: An Italian case report

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Abstract

Kleefstra Syndrome (KS)is a rare genetic syndrome affecting approximately 1 in 200,000 individuals and is caused by either a deletion of the subtelomeric region of chromosome 9q (50%) or by a loss of function mutation in the Euchromatin Histone Methyl Transferase 1 (EHMT1) gene (50%). In this case report we analyze the case of an 8-year-old boy affected by KS from the parent's point of view. The focus of the report is the detailed narrative analysis of the parent's experience written directly by the mother and the complex intervention to reduce a severe sleep disturbance associated with the syndrome. A clinical assessment was carried out, focused on understanding the extent and frequency of the awakenings with a specific assessment questionnaire.

The association of therapy with melatonine and trazodone was highly decisive and improved the well-being of the child and the family. The Author is carrying out further studies for the drafting of guidelines for sleep disorders in KS.

Introduction

The relationship between parenting and Neurodevelopmental Disorders (ND) is still to be considered a central element of the profession of the clinician who approaches complex neuro disabilities.

Within the ND macro group, ASDs (Autism Spectrum Disorders) are a series of hetero phenotypic conditions, associated with a symptomatic dyad consisting of communication and relationship deficits and restricted and stereotyped interests and/or sensory processing disorders. ASD prevalence is widely scientifically recognized as increasing [1] and it is established to be around 1/79.

The cases considered more serious and more demanding for family management are those associated with conditions of low IQ, low level of adaptation [2], and ID (Intellectual disability) conditions associated with comorbidities [3]; among the comorbidities, in particular, sleep disorders associated with dysgenetic conditions and autism are markedly destructive for parents and involve fatigue, difficulty in keeping a job, and a high incidence of factors related to personal, physical and psychological stress [4].

Both parents of children with ASD and Kleefstra Syndrome (KS) perceive in most cases a high level of stress [3,5] which, however, in many cases, they are able to manage through a profound change in their lifestyle habits and by resorting to the network of supports and formal and informal services. Kleefstra syndrome (KS) [6] is a rare genetic syndrome affecting approximately 1 in 200,000 individuals and is caused by either a deletion of the subtelomeric region of chromosome 9q (50%) or by a loss of function mutation in the Euchromatin Histone Methyl Transferase 1 (EHMT1) gene (50%) [7-11]. Common features associated with KS are developmental delay,

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intellectual disability, childhood hypotonia, and distinct facial features. In adolescence or adulthood, patients with KS may also experience developmental regression and psychosis. Much of the literature has focused on the genes contributing to KS and the phenotype, but no study has evaluated the impact of the diagnosis on parents. Therefore, the purpose of this mixed-method study was to assess how having a child with KS impacts parental well-being.

The aims were to evaluate the well-being of parents of children with KS, identify factors of their parental experience that may predict their well-being, and explore their experience of having a child with KS.

As a child neuropsychiatrist and father of a 20-year-old boy with KS, I have been in contact with the Italian KS Association for about three years. My medical role associated with my experience as a father led me to become a point of reference for many families and a real collaboration was born during the first pandemic period starting in March 2020.

We started a series of videoconferencing meetings which led me to consider the main times and difficulties of families, in particular the associated psychopathology and sleep disorders. Subsequently, thanks to the promotion of the Association, I was called to participate in the drafting of the international guidelines on KS which are being structured for 2024.

My experience on the forms of KS in the Italian casuistry has led to highlighting how in about 50% of cases there are forms of sleep disturbance, most of which require an accurate and sensitive pharmacological approach.

In this case report we analyze from the parent's point of view a case of an 8-year-old boy affected by Kleefstra syndrome, a rare condition due to deletion/microdeletion of the long arm of Cr9 or intragenic mutation of the EHMT1 gene.

The focus of the report is the detailed narrative analysis of the parent's experience written directly by the mother and the complex intervention given by me as a neuropsychiatrist.

Methodology

Clinical analysis of the case, interviews with the parents, and assessment

SCQ (Social Communication Questionnaire, Rutter M, Bailey A & Lord C (2003) [12] CBCL 6-18 (Achenbach, T. M. & Rescorla, L. A. (2001): Achenbach's CBCL is undoubtedly the one most widely used in epidemiological studies at an international level (Bird, et al. 1987; Bird and Gould, 1995 [13]; Rescorla, 2005 [13-15]). This checklist represents an economic tool to administer which has shown excellent psychometric properties: reliability between repeated administrations, stability over time, validity or ability to discriminate between the general population and the clinical population

(Tancredi, et al. 2000; 2002 [15] KS Sleep Disorder Questionnaire (Caterino E., 2020): the Questionnaire was developed by the Author to understand the phenomenology, and characteristics and to quantify sleep disorders in KS in Italy; it consists of a first anamnestic part, qualitative and quantitative detection of the disorder, a detection of interventions (educational, environmental, dietary and pharmacological).

Parent support and psychopharmacological approach

The intervention consisted of weekly video call sessions with the parents to improve the psychoeducational style and exclude any medical comorbidities (e.g. physical pain, dental or gastroenterological disorders).

I prescribed "slow release" melatonin at a dosage of 2 mg and "slow release" Trazodone at a dosage of 25 mg at 9 PM at 21 and Trazodone at a dosage of 25 mg.

Mother's narrative report

We asked the mother to write a personal report on her son, with particular attention to parenting, stress factors, and the management of the sleep disorder

Case report

Anamnesis and clinical description of the case

Eldest son of healthy and non-consanguineous parents, negative family history for the pathology of a neuropsychiatric and genetic nature. Full-term birth from a normal-running pregnancy (PN 3750 gr, apgar 9-10). At birth, finding of congenital clubfoot for which he wore plaster for 1 month and then a brace for up to 12 months. He did osteopathy for occipital plagiocephaly. Breastfeeding and weaning are complicated by food intolerances. Sleep characterized by frequent awakenings takes melatonin 2 mg. Diurnal sphincter control was achieved at 4 and a half years, and nocturnal control was not yet acquired. Motor development is characterized by an upright position reached at 14 - 15 months, and walking at 18 months. Language characterized by delay currently produces about 20 words with obvious articulatory difficulties. At 4 years old there is excellent communicative intentionality, he uses mimicry and gestures. Their parents report restricted interests and some fears that paralyze them (eg fear of dogs).

He attended kindergarten with an educator and a host teacher. He is currently attending Primary School with support from E. He is in charge at the UONPIA of B. (Italy) where periodic NPI follow-ups are carried out. In April 2019 appearance of episodes of "absence" of dubious interpretation, for this reason, an EEG was performed in poly sleep which showed sharp anomalies in the right hemisphere. He carried out psychomotricity privately twice a week from the age of 30 months until September 2020, now once a week. In November 2020 he also started a speech therapy course twice a week. Parents are trained in Augmentative Communication (CAA). Furthermore, it was suggested they should start therapy with the PROMPT method.

The results obtained in the Griffiths' III developmental tests at 4 years are as follows (chronological age of 55 months): Basis of Learning Scale: age equivalent 32 months, SQ <50 Language

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and Communication Scale: age equivalent 33 months, SQ <50 Eye-hand Coordination Scale: age equivalent 31 months, SQ <50 Personal-Social-Emotional Scale: age equivalent 33 months, SQ <50 Gross Motor Scale: age equivalent 41 months, SQ 69 General Development Score: age equivalent 36 months, SQ <50.

Therefore, there is evidence of an overall developmental delay of a moderate degree (developmental age of 36 months compared to the chronological age of 55 months). There is evidence of strength in gross motor skills, although it is an area that also presents a delay.

Evaluation with PSI at 4 years (Parenting Stress Index) shows high levels of total stress in both parents, which reach clinical levels. For both, this burden is linked to E.'s specific difficulties and to the relationship with him, which have repercussions on the possibility of fulfilling one's parental role in a serene way and feeling like a good parent, and consequently on the possibility of experiencing pleasure inside and outside family life

At the 5 evaluations, a slight/moderate degree of delay and a global delay of the expressive/receptive language is confirmed.

Parents report the onset of sleep disturbance (up to 16 nocturnal awakenings starting from 18 months after the cessation of breastfeeding), with increasing evidence of the child's irritability and strong parental stress.

The child's current clinical picture is characterized by DI of moderate degree (ICD 10: F71), a moderate hyperactive component (ICD 10:F90), obsessive-compulsive disorders, and serious sleep disturbance (ICD 10:G47.9).

Assessment

SCQ (12): Score 6<cut off for risk of communication relationship disturbance;

At CBCL 6-18 [13,14]: elevation in the clinical range of scores in the Attention Deficit Hyperactivity area and in Thought Disorders (obsessions-compulsions)

DSM-SCALES	Score	Internalizing	Soc-Thou-Att	Externalizing	Min	Max
Anxious/Depressed	5	59			64,5	69,5
Withdrawn/ Depressed	0	50			64,5	69,5
Somatic Complaints	0	50			64,5	69,5
Social Problems	4		58		64,5	69,5
Thought Problems	8		71		64,5	69,5
Attention Problems	10		66		64,5	69,5
Rule-Breaking Behavior	3			57	64,5	69,5
Aggressive Behavior	6			55	64,5	69,5
Other Problems	4	No T transformation			64,5	69,5

The Sleep Disorders Questionnaire sent to the mother shows multiple nocturnal awakenings (up to 10 per night, starting at 1 am with a maximum peak after 4 am) and dysfunctional behaviors (requesting water to drink, kicking, disturbing attitudes against the mother).

Below is a weekly report made by the mother with the use of 1 mg slow release melatonin:

The current assessment of the child is characterized by a moderate degree of ID (ICD 10: F71), a moderate hyperactive component (ICD 10: F90) and obsessive-compulsive disorders (F42), and severe Sleep Disorder (ICD 10: G47 .9).

	PApa	PApa	MAMMA	PApa	NONNA	PApa	MAMMA
	Lunedi	Martedi	Mercoledi	Giovedi	Venerdi	Sabato	Domenica
21	9.00 inizio	9.30	9.30	9.00	9.30	21.00	21.15
22	X	X	X	X	X	X	X
23	X	X	23.58 R	23.30 R	X	X	23.58 R
24	X	X	X	X	X	X	24.58 R
01	X	X	1.49 R	1.10 R	X	X	X
02	2.57 R	X	X	2.17 R	X	X	2.44 R
03	X	3.35 R	3.07 R	3.40 R	X	3.19 R	X
04	X	4.44 R	X	4.38 R	4.10 R	4.20 R	4.02 R
05	5.46 R	5.49 R	5.43 R	X	X	X	X
06	6.41 R	6.22 R	X	6.29 R	6.00 R	6.42 R	6.02 R
07	7.00 SVEGLIO	7.40 SVEGLIO	7	7.00 SVEGLIO	X	7.30 SVEGLIO	7.30 SVEGLIO
08			8 SVEGLIO		8 SVEGLIO		

Mother's narrative report: «BEING ENEA'S MOTHER: Either we will find a way or we will build one

Being a mother: I've always wanted to become a mother... since I was a child I imagined myself married at a young age, with 2 or 3 children, however, life has wanted something else for me and, sincerely, the more I think about it the more I am convinced that everything happened for a precise reason and that being Enea's mother is teaching me how to live in a way I never could have done.

I have always wanted to become a mother and so, when Enea was born, I was very happy, very happy to start this new life as a threesome.

Eneas weighed 3,750 kg, not exactly a feather, but the "easiest" thing and which I would do again immediately was giving birth. The day after the right deadline, at about 3.30 in the night my water broke, lots of water, a river I would say and when I got to the hospital the pain started around 6.00 in the morning when they took me to the delivery room. The entire labor took place in water as I strongly desired since during my pregnancy I was able to do a pregnancy course in the pool and it gave me a feeling of relief. So I did not suffer too much during those 3 hours of contractions even without having an epidural, thanks to the water, an element that helped me a lot. However, the birth took place outside, and at 10.00 precisely Enea was born.

Enea was immediately placed in my arms and began to suck my breasts.

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I've always wanted to become a mother and I've always wanted to be able to breastfeed my child for as long as possible and that's why Enea drank my breast milk until about 18 months, but breastfeeding was much more difficult for me than giving birth. The breastfeeding mother must live in symbiosis with her child and whenever he is hungry you must be ready for him, there is no more day and no more night, there are no more hours, and your needs as a Mother become secondary.

I've always wanted to become a mother but no prenatal course prepares you physically and above all mentally for what will happen and so the tsunami overwhelms you, full of emotions from the first days and the adrenaline that keeps you awake even for 3 days in a row, with panda-like dark circles that will never go away completely, at least for me, Elena.

The first problems

At birth Enea had something wrong in his right foot, it was a clubfoot or "turned inward" to help you understand, but apart from that everything else seemed normal, therefore we were discharged from the hospital after the usual 3 days of hospitalization and we returned home, nevertheless with the prescription of the orthopedic visit a few days later. Enea ate and grew quite a lot apart from the usual drop in the first few days and I was dead tired but happy, very happy indeed and I remember as if it were yesterday, that the day after giving birth, my partner told me he had "heart pain" from the happiness.

At the checkup for the foot, the orthopedist informed us that they would have to put a cast that they would remove and put back on every week for 5 weeks in order to try to rotate the foot and then, if this weren't successful, there would be an operation and, to avoid further relapse, Enea would have to wear a brace (tutore Ponseti) for at least 3 or 4 years.

This piece of news took me by surprise and it seemed to me the worst thing that could have happened to him, so little with that huge cast that couldn't be washed and that got in the way of our breastfeeding positions, dressing, etc. I began to search for news on clubfoot, operations, etc. on the internet and we were very worried that Enea would never walk well. Looking back on it now, I really wish that had been the worst thing that could have happened to us.

So we put the cast on for 5 weeks and luckily the foot didn't need the operation, but we had to start wearing the damn brace. For the first few months, he had to wear it day and night, as much as possible and this was quite annoying because the brace was made up of two little shoes tied together by a steel bar which therefore prevented various movements. I remember that this demoralized me a lot, even leaving the house and hearing everyone ask us what had happened and why he had that brace. In the meantime the months went by and Enea, apart from his brace, was doing well, growing, eating, and sleeping little. He slept, or rather he didn't sleep, like a child of his age because the awakenings were frequent but all related to breastfeeding as Enea woke up about every 2/3 hours during the day and night to eat.

Another annoying side of those months was dermatitis. Enea has suffered a lot since he was 3 months old, we have seen several dermatologists but a thousand creams we tried never solved the problem, I think I could get a degree in dermatology with all the research I have done on the matter and I understand that no cream cures you, unfortunately, a person is subject to ups and downs that come and go based on various factors (climate, washing, food, etc..) and this too seemed to me as one of the worst problems in life because I lived it with anxiety, anxiety because Enea was constantly scratching and moving his legs, with the brace among other things, and when he reached about 10 months, desperate for the lack of sleep (thinking it was only connected to the annoyance of dermatitis and the brace), we decided to remove the brace and see how it went.

If the problem with the clubfoot had returned (and it should have happened quite soon) then we would have had the operation, but that brace was a real torture! Luck was on our side that time because to date (almost 7 years of life) Enea's foot hasn't had any more problems and actually Enea runs, jumps, and walks beautifully!

That obstacle was overcome.. a pity that it was probably the minor one to overcome.

Nocturnal awakenings

Even though we had removed the brace, Enea still didn't sleep well, in the sense that even after he was one year of age, the nocturnal awakenings were continuous, but according to the pediatrician they were normal for his age since he was still being breastfed and also very often.

For this reason, when he was around 18 months I decided to stop breastfeeding him, following various advice, but this didn't improve his awakenings either.

I even got to count up to 15/18 awakenings per night and, since once I finished breastfeeding Enea used to sleep with me or with his dad (every other night) in our double bed, the nights were quite tiring anyways. We tried to put him in his room alone but unfortunately, I was never able to leave him crying (actually Enea didn't cry, but when you wake up he calls you, looks for you and, if you're not there, he wants you and won't go back to sleep).

Strange behavior and diagnosis

When, around the age of 2, Enea started attending the spring section of the nursery school, a few weeks after being introduced, we were called by the manager who immediately expressed her concern about some aspects of Enea's "strange" behavior.

It is true that, when he was two years old, Enea only said: "Pappa" "Mamma" G. (his uncle...), and very few other words with the same 2 syllables. It is true that Enea started walking at around 20 months (but there it was also the story of his foot and the brace which had not helped). It is also true that, after a few months of life, the pediatrician had identified a plagiocephaly which however, having been treated with

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osteopathy, had possibly healed (though we were not sure). But I had no other terms of comparison because he was my first (and only) child and I have to be honest: when I hear mothers say "I realized something was wrong" I have to admit that, as far as I'm concerned, I didn't realize it or maybe, who knows, I didn't want to notice it, but not even the pediatrician had ever highlighted any problems for us. On the other hand, the kindergarten, by comparing him to other children of the same age, immediately noticed. In fact, I must also admit that later, when I had the opportunity to stay in the classroom and see Enea with the other children, I immediately understood too that something was wrong.

That day when they told me at the nursery door, with Enea in my arms, that "something was wrong" and that we had to do neuropsychiatric tests, I shut myself in the car crying desperately. Since then, the endless bureaucratic process began, and we had to wait for the neuropsychiatric visit by the competent local health authority, but during the almost 10 months of waiting, we, as his family, immediately decided to take action privately, Enea started with psychomotricity therapy at 2 and a half years old and with speech therapy at 4 (unfortunately the latter was also quite late because according to Neuropsychiatry Enea did not need speech therapy as the possibilities of success with such therapy were statistically very low, luckily I followed my instinct) and he is still doing these therapies several times a week. Since then also the path that led us to Enea's diagnosis began, which lasted for 2 years. Two years of genetic tests, two years of specialists of all kinds in Bergamo, in Milan, wherever someone could give us any explanations. We arrived at the Sant'Anna hospital in Como to see Dr. AS, an internationally known geneticist, who from the very first minutes of the visit (Enea was then about 3 years old) told us: "Enea has a genetic syndrome: it can be seen from his facial features, from the sleep disturbance, from his psychomotor retardation, but be aware that it is not certain whether it will be possible to identify with genetic tests which syndrome it is. Most people with a rare syndrome are never diagnosed" These words were a sharp knife to the stomach, but I thought: until they find anything from genetic tests, there is still hope.

As a matter of fact, the first genetic tests carried out at the Bergamo's Hospital did not lead to any results - and I was still hoping. Furthermore, a few months later, Covid arrived and blocked everything. Three never-ending months at home with little, hyperactive Enea who woke up a lot at night and with my mother hospitalized at the end of her life in Bergamo: they were the longest and worst days of my life (until the day of the diagnosis, unfortunately). I still wonder how we managed to face them: because all through this story obviously there is also Enea's father, Cristiano, a wonderful father that Enea adores and who helped me to face those days of seclusion awaiting, among other things, our genetic tests.

And just at the end of 2020, we were called by Dr. X, a genetist in B. from whom we were sent to our reference neuropsychiatry, to read the diagnosis.

"THE HETEROZIGOUS DELETION OF EXOMES 13-17 OF THE EHMT1 GENE HAS BEEN IDENTIFIED" Obviously for us these words were Arabic and even when they told us that Enea's syndrome is called KLEEFSTRA SYNDROME (it took me a long time even to learn how to spell it correctly) name was given after the Dutch doctor who had discovered it about ten years before. Nothing was clear to us, so obviously, as soon as we got home we decided to investigate, to research, and this is when the blade cut off our heads. Yes, because in fact if we had really been stabbed, I think it would have hurt less, and the wound would have healed sooner or later.

Because hope, at that moment, had vanished. Because until you see it officially written down you still have hope. But then you have to give up, unfortunately, you have to feel all the pain, right down to your bones, because a child's illness is the worst thing you can wish upon someone, I wouldn't even wish it upon my worst enemy. Moreover, a child's lifelong illness makes you wonder every day what tomorrow will be like, his tomorrow because I'm not afraid to suffer again but I can't accept seeing him suffer. I remember that Cri. said to me that day: I will never be happy again in my life, which actually now, after 2 years, I don't think is true because Enea has made us and makes us happy every day. Of course, we have completely reconsidered our way of being happy, but Enea is now a cheerful, affectionate, sociable child who has made a lot of progress in the last year, progress that fills our hearts with joy.

The sleep disorder

His genetic syndrome is very rare, there are about 40 cases in Italy (estimated in 2020, now there are many more), and involves severe language delay (in fact, at 4 and a half years old, Enea was saying about fifty words or maybe less) cognitive delay, sleep disturbances and so on. It is precisely because of these sleep disturbances that the doctors carried out these analyses, focusing on this gene.

Because when he was 4 and a half years old, the sleep situation hadn't improved at all. We had tried melatonin of all kinds and other than that no doctor ever gave us any other advice about it.

Those were hard days, months, after the written diagnosis, and even though two years have passed there are hard days even now and there always will be.

But the worst pain for us, physical and mental pain was not sleeping for almost 5 years. We also put a night camera in his bedroom to count Enea's awakenings and, apart from the first 2/3 hours straight after he has fallen asleep without problems and even quickly around 8.30 pm in the evening, then, from midnight until 7 am, every hour or even every half hour he wakes up. His awakenings are similar to sleepwalking, because in my opinion he is not really conscious, he's like in a trance and makes a noise to call you. In recent years, billions of people have told us that we had to put Enea in his bedroom but our strength was exhausted and the thought of having to go back and forth from his bedroom to ours all night would have literally killed me.

At least, having him next to me in bed, I could calm him

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down with my hand and make him lie down again. My problem is that I suffer from traumatic sleep myself (I haven't told you that I often thought that Enea's sleep problems were my fault because I have always suffered from sleep disturbances too and I often happen to talk or scream at night, but without noticing anything. Having said that, Enea's syndrome was totally unrelated to us, this means that it did not depend on Cri. or me. (It was an incredible stroke of bad luck, as they told us: "You could have won the lottery or you could have had a child with a rare syndrome, the chances are practically the same.")

In addition, Enea moves like a tarantula in his sleep, he moves and kicks a lot, he doesn't do it voluntarily of course, he doesn't even notice but I lost count of the times I thought he had broken my back or my leg with a kick.

The Italian KS association and the intervention of the "father-doctor"

Despite the initial shock, however, the diagnosis of the syndrome brought us to the discovery of the "Italian association of the Kleefstra syndrome" with several registered members, led and founded by M.

Knowing that in Italy there were about 40 families in the same situation as us gave us a sigh of relief because being able to talk to them knowing that they understand exactly what we are talking about, sharing and supporting each other in the most difficult moments means a lot.

Among these families of the association, we learned about Dr. Ettore Caterino, a Neuropsychiatrist from the province of Grosseto with, among other things, a son affected by Kleefstra, Federico. I call him our "savior" because Ettore immediately made himself available to help us and the other Kleefstra families with sleep disorders. Being a neuropsychiatrist with a son affected by Kleefstra syndrome who hasn't slept for many, many years, who better than him could help us? We immediately got in touch via video calls and phone calls, so that Ettore was able to collect all the necessary data to study Enea's case.

Our first attempts to change medications were not successful: we first tried Slenyto, a 5 mg retarded melatonin which, however, had the opposite effect, that is to agitate Enea even more, then we tried a Circadin tablet which is always a 2 mg retarded melatonin but that was probably not enough for Enea.

Finally, about a year and a half ago, when Enea was 5 years old and a few months, we tried 1/3 of Trazodone tablet and 1 Circadin tablet that we give to Enea when he first wakes up around midnight because from 20.30 to 12.00 he falls asleep well and does not wake up.

In doing so we noticed a significant improvement after a few weeks: from midnight to 7.30 in the morning Enea currently wakes up 2 to 3 times, but it also happens that he only wakes up once per night. Another reason for Enea to wake up is that he is still using a diaper at night and unfortunately, we have to change it since one just doesn't last until the morning. We are trying to get him used to sleeping without a diaper, but it is not easy. Enea drinks a lot and pees a lot!

Thanks to Dr. Caterino's advice, we also realized how important it is what Enea eats before going to sleep, if he watches too much TV or if he doesn't exercise much during the day so that he isn't tired enough at night.

Now Enea is almost 7 years old and since she started sleeping we have seen the turning point. He started talking, and now he makes sentences and makes himself understood very well, an achievement that was unthinkable two years ago. We were told that there was a 90% of possibility that Enea would never speak, whereas now I sometimes have to ask him to play the game of silence.

It used to happen that he was very nervous during the day because, despite not sleeping at night, at kindergarten, Enea was unable to take an afternoon nap, consequently, he was unmanageable, with mood swings and crises, now this rarely happens, only if he has a night when he sleeps less or because he's not well and this is the way he shows it. The turning point has also helped us parents who are finally able to sleep better because there is no worse pain than not sleeping my biggest fear now is that it could regress but at the same time, we are lucky because we know that we can trust and rely on Ettore who will surely try to help us again. I've always wanted to become a mom and now I'm the mom of a wonderful child who has changed my life and I wouldn't be without even for a day.

I know that hearing him say: "Mum I love you" in his voice is a fortune that many parents of rare children don't have and I'm grateful for it. These are the little things that still make us happy, immensely happy indeed.

Being a mother is beautiful even if it is very tiring and for us parents of rare children, it is definitely more so.

Discussion

The case, due to its peculiarities and what was narrated by the mother, shows a high ability of the parent to describe his parental experience not only in emotional terms but also with a wealth of details that are very useful for the clinic.

Patients with KS often show a sleep disorder characterized by multiple nocturnal awakenings, irritability, and compulsive behaviors (e.g. pinching, kicking, drink requests); these aspects can reinforce in the parent's educational methods and behavioral responses reinforcing the behavior. Many parents describe that they are forced to allow their children to sleep with them even when they have grown up, to get up several times, to undergo continuous awakenings due to requests for cuddles or initially sweet physical contact (which is therefore well received by the caregiver), but which often becomes repetitive, obsessive (e.g. pulling hair in sleep) until it is no longer bearable. Many of the parents are forced to separate, and the father goes to sleep in another room, with inevitable repercussions on the couple's health and feelings. The central elements of good sleep management in syndromic forms associated with intellectual disability consist of aspects

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relating to physical health (daytime physical exercise), a decrease in visual and auditory stimuli that can increase the level of arousal in the evening (e.g. avoiding TV, Smartphones, tablets, cartoons, loud music), decrease the intake of glycides or stimulating foods (e.g. chocolate, coffee, bread, sugar, etc.). The habit of falling asleep rituals in the bed of the child or young person is a good practice (e.g. showering, use of the phone to relax, low lights, light head or foot massages, allowing newspapers or books to browse, etc.).

In my experience, analyzing 21 cases with KS, about 1/3 of children/teenagers/adults with KS manage to find more regular sleep with environmental and educational measures, another 1/3 need to take slow-release melatonin in addition to educational measures, 1/3 need to associate Melatonin with the use of psychoactive drugs. Trazodone, a 5-HT2A/C antagonist and one of the most sedating antidepressants, also used in other forms of ASD [4,16,17], is very useful precisely in the forms associated with KS (it resolved 4 cases of persistent disorder including Enea's). Enea's case is striking from this point of view because it shows a reduction in nocturnal awakenings (even 8 - 9 per night in 2020) down to only 1 max 2, due to the presence of nocturnal incontinence which disturbs the child.

This determined an improvement in Enea's cognitive performance (greater vigilance and attention during the day), a decrease in mood swings, and daytime irritability; in the parents, there was an important improvement in personal and couple health with a decrease in the subjective stress load.

Conclusion

KS requires specific interventions and a specific background on the part of the clinician. The constant relationship with the parents generates a strong experience given the specificity of the syndrome; availability by videoconference or telephone must be ensured. Pharmacological adjustments and the reassurance of the parent in the face of any moments of crisis (in which the drug does not seem to be effective) are one of the founding elements of the doctor-parent relationship.

Four steps are recommended with reference to the Sleep Disorder (SD)

1. General and specific assessment (medical history, physical examination, interview, questionnaire for sleep disorders);
2. Differential diagnosis with other medical conditions: e.g. dental pain, gastroesophageal reflux, bloating, bowel movements, urination disorders, etc.);
3. Psychoeducational intervention aimed at the parent;
4. Pharmacological intervention: first with slow release of Melatonin (dosage between 2 and 4 mg) and possible use of Trazodone (25 - 50 mg in the evening).

The use of other drugs in combination with Trazodone (e.g. Quetiapine) is indicated when serious comorbidities of a psychopathological type are evident.

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