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Case Study

AYURVEDIC MANAGEMENT OF STXBP1 ENCEPHALOPATHY WITH WEST SYNDROME - A CASE REPORT

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ABSTRACT

Developmental delay, intellectual disability, and epilepsy are hallmark features of STXBP1 encephalopathy. This condition is often associated with West syndrome, characterized by intractable epilepsy, developmental regression, and hypsarrhythmia on EEG. Even though timely intervention is crucial, Conventional medical systems lag behind to tackle the developmental regression and to gain control over the intractable epilepsy even with multiple anti epileptic drugs (AEDs). This is a case of a 7-year-old girl with an STXBP1 mutation, clinically diagnosed with West syndrome. She presented to the Kaumarabhritya OPD with significant developmental issues, including inability to sit without support, difficulty rising from a lying position, tremors, poor coordination, truncal ataxia, impaired speech, cognitive deficits, socialization issues, and intractable epilepsy. Ayurvedic management strategy was designed incorporating treatment principles of *Apasmara* (seizures), *Unmada* (insanity), *Vatavyadhi* (*Vata* disorders), and *Sirakampa* (head tremors), as an adjunct to ongoing AED regimen. Remarkable improvements were observed in motor, social, and language domains in a period of 4 months. Treatment efficacy was assessed using the Hague seizure severity scale, (improved from 24 to 49) and Gross Motor Function Measure score (increased from 18% to 30%). Receptive language age advanced from 0-1 month to 7-8 months, and expressive language age improved from 0-1 month to 10-12 months. Vineland Social Maturity Scale score improved from 3.5 to 8, and Indian Scale for Assessment of Autism score decreased from 130 to 105. This case report highlights the efficacy of Ayurvedic interventions in curtailing intractable epilepsy, arresting the neuronal regression and triggering the brain growth velocity.

INTRODUCTION

STXBP1 is a member of the Munc18-1 protein family which plays a major role in the secretory and synaptic vesicle fusion machinery involved in the hormonal and neuronal transmission. STXBP1 variants impair neurotransmitter release, especially in GABAergic interneurons, leading to uncontrolled excitatory neuron firing. Developmental delay, cognitive dysfunction, intellectual disability, and epilepsy are usually associated. STXBP1 encephalopathy with epilepsy is a type of developmental epileptic encephalopathy (DEE)[1].

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Besides epilepsy, STXBP1 gene mutation causes neurological deficits, including severe early-onset forms of intellectual disability, autism, and movement disorders[2]. West syndrome mostly occurs in the first year of life and presents as spasms with characteristic EEG changes known as hypsarrhythmia and it is strongly associated with developmental delay or regression[3]. STXBP1 encephalopathy is a leading cause of West syndrome. Seizure types include epileptic spasms, focal seizures, and tonic patterns. In Ayurveda, genetic diseases fall under *Adhibalapravrutta vyadhi*[4] (diseases with genetic predisposition). This can be considered as *Beejabhaga avayavadushti* (diseases occurring in the level of genes)of *Garbha* (product of conception), which has a negative effect on the brain growth potential, leading to *Masthishkaapachaya* (brain atrophy) of the child, manifesting as *Apasmara*, altered muscle tone, development delay and social communication defects.

Any defect at this embryonic stage will alter the proper functioning of *Tridosha* (body humours) and hamper the development of all *Dhatus* (structural tissues) which inturn manifest as *Dhatukshayaja sarvangavata* (diminution of structural tissues due to *Vata*). *Sannipatika apasmara* (intractable seizures) is again worsening the underlying encephalopathy thereby causing developmental regression. This can be considered as the *Upadrava* (complication) of *Apasmara*.

CASE REPORT

Patient information

A 7-year-old girl presented to the outpatient department with several notable symptoms: inability to sit with balance, tremors, poor coordination of movements, truncal ataxia, myoclonus, developmental delay, impaired speech, reduced eye contact, poor response to name calls, and poor peer interaction. She was delivered full-term via vaginal delivery without perinatal or postnatal complications. Early developmental milestones included a social smile at 2 months, neck holding at 2.5 months, and rolling over at 3 months. At 3 months, the child received the DPT vaccine, followed by hyperpyrexia on the same day and a first seizure episode the next day. The seizure semiology included deviation of the head and eyes to the left, left eye twitching, and tonic posturing of all four limbs, lasting 30 seconds, with postictal drowsiness for about 5 minutes. Another seizure occurred the following day, leading to hospitalization and initiation of antiepileptic drugs (AEDs), Clonazepam and Phenobarbitones. Recurrent seizures persisted for one month, necessitating loading doses of AEDs. At 4.5 months, the child began experiencing flexor spasms lasting 2-3 seconds, with clusters of up to 20 episodes per day. She was put on ACTH, but no clinical responses were observed. So vigabatrin was started and she is continuing the same till date. There was a regression in milestones, including the loss of social smile, emotional reciprocity, and head control, along with the onset of titubation. Physiotherapy enabled partial recovery of milestones: neck holding by 1.5 years, rolling over by 2 years, unidextrous reach by 2.5 years, palmar grasp by 3 years, sitting with support by 3.5 years, and transfer of objects by 4.5 years. However, emotional attachment with parents remained deficient. Autistic features, such as self-play, repetitive hand movements, and poor peer group interaction, were also observed. A DNA test identified a mutation in the STXBP1 gene located on Exon 5. The patient continues to receive AEDs along with regular physiotherapy, speech therapy, and occupational therapy. Family history revealed childhood seizures in her paternal uncle. Parental genetic evaluation detected a heterozygous single nucleotide variant of Exon 9 of the GABRB1 gene.

Clinical findings

Head to foot examination revealed microcephaly and facial dysmorphism with low set ears. She was conscious but not oriented to time and place. 3rd, 5th and 6th cranial nerves were affected since she has convergent squint and nystagmus. Facial nerve is also affected which is evident from drooling. Motor system examination shown hypotonia with hyper reflexia. Truncal ataxia was also noted. Deep tendon reflexes such as Knee jerk and ankle jerk had a grade of 4+ with clonus. Muscle power of both upper and lower limbs were 2/5. Titubation of head and truncal ataxia shown the involvement of cerebellum

Diagnostic assessment

MRI Brain – Plain study on 18/08/2023

Mild diffuse cerebral atrophic changes

Therapeutic interventions

On the initial phase, *Hinguvachadi churnam* [5] in a dose of 2.5 grams twice daily with food and *Mahat Panchagavya ghritam* [6] in a dose of 5 ml twice daily before food were given for 1 month. Then dose of *ghrita* was increased to 10 ml twice daily before food. *Talam* with *Dhanwantaram* 101 *avarti* and *Rasnadi churnam* was done. This medication continued for 2 months. After admission as inpatient, internal medicines like *Dhanadanayanadi kashayam*[7] in a dose of 30 ml twice daily before food along with *Balarishtam*[8] 7.5 ml twice daily after food. External procedure started with *Kadikizhi* (potali made with medicated *Churna* dipped in *Amladravya*) with *Kolakulathadi churna*[9] and *Dhanyamla*. Then *Rasnadasamoola ghrita*[10] was introduced in the dose of 5 ml twice daily before food. Treatment procedure during that time was *Takradhara*[11] with *Panchathiktakam kashayam* and *Mahanarayana tailam.*[12] Continuing on the same internal medicines, next treatment planned was *Pradeham* with *kolakulathadi churna* and *Balaksheera* and *talam* with *Maharajaprasarani tailam* and *Kachooradi churna*. Then *Mahat panchagavya ghrita* was given in a dose of 5 ml twice daily before food. *Trivrutadi kashayam* (40 ml twice daily before food) was also given At that time, treatment ongoing were *Patrapotala sweda* and *Siropichu* with *Mahanarayana tailam*. Next, *Sirodhara* [13]with *Mahanarayana tailam* was administered. At the next stage, for *Rasayana* purpose *Siva gutika* in a dose of ½ tablet twice daily after food was started and procedure charted was *Mustadi rajayapana vasthi*.[14]

Table 1: Timeline of IP management

Date	Internal medicines	Treatment	Remarks
30/9/2023 – 30/10/2023	1.*Hinguvachadi churnam* 2.5 grams twice daily with food 2. *Mahat Panchagavya ghritam* 5 ml twice daily before food		*Agni deepthi* improved Seizure frequency reduced to 2-3 episodes per day
31/10/2023 – 30/11/2023	Rpt 1 2.*Mahat Panchagavya ghritam* 10 ml twice daily before food	*Talam* with *Dhanwantaram* 101 *avarti* and *Rasnadi churnam*	Seizure frequency reduced to 1-2 times a day
1/12/2023 – 31/12/2023	Rpt 1,2	Rpt *Talam*	Child became seizure free

Table 2: Follow up and outcome

Date	Internal medicines with dose	Treatment procedure	Remarks
3/1/2024 – 7/1/2024	1.*Dhanadanayanadi kashayam* 30 ml bd before food 2. *Balarishtam* 7.5 ml bd after food	*Kadikizhi* with *Kolakulathadi churna* and *Dhanyamla* for 5 days	Flaccidity reduced, *Agnideepthi* improved
8/1/2024 – 14/1/2024	Rpt 1 & 2 3. *Rasnadasamoola ghrita* 5 ml twice daily before food	*Takradhara* with *Pancha thiktakam kashayam* and *Mahanarayana tailam* for 7 days	Tremors reduced
15/1/24 – 21/1/2024	Rpt 1,2 & 3	*Pradeham* with *Kolakulathadi churna* and *Bala ksheera* and *Mahanarayana tailam* for 7 days. *Talam* with *Maharaja prasarani tailam* and *Kachooradi churna* for 7 days	Reduction of titubation & truncal ataxia
22/1/2024 – 28/1/2024	Rpt 1 & 2 3. *Mahat Panchagavya ghrita* 4.*Trivrutadi kashayam* 40ml bd before food	*Patrapotala swedam* *Siropichu* with *Mahanarayana tailam*	Sit without support attained, eye contact improved
29/1/2024 – 4/2/2024	Rpt 1,2 3, 4	*Sirodhara* with *Mahanarayana tailam*	Expressive language improved
5/2/2024 - 12 /2/2024	Rpt 1,2 3, 4, 5 6. *Siva gutika* ½ tablet twice daily after food	*Musthadi rajayapana vasthi*	Ataxia reduced, body balance improved

The patient underwent a comprehensive clinical evaluation, utilizing assessments such as the Gross Motor Function Measure (GMFM-88)[15], Vineland Social Maturity Scale (VSMS)[16], Indian Scale for Assessment of Autism (ISAA), and the Receptive-Expressive Emergent Language Scale (REELS). Seizure severity was measured using the Hague Seizure Severity Scale. Post-treatment, notable improvements were observed across multiple domains including gross motor skills, fine motor skills, social interaction, and language abilities. Specifically, the patient's receptive language skills showed significant progress, advancing to the point where she could speak 4-5 bisyllables. She also demonstrated the ability to sit unsupported for 2-3 minutes. Additionally, there was a marked reduction in tremors and titubation. Quantitatively, the GMFM scores increased from 18% to 30%. Social communication and perception improvements were reflected in the VSMS scores, which rose from 3.5 to 8. The ISAA score showed a substantial decrease from 130 to 105. In terms of language development, receptive language age advanced from 0-1 month to 7-8 months, and expressive language age improved from 0-1 month to 10-12 months. Finally, the Hague Seizure Severity Score improved significantly from 24 to 49

DISCUSSION

Patient visited the hospital with the diagnosis of STXBP1 encephalopathy associated with West syndrome. In Ayurvedic framework, this condition was identified as a *Sannipathika dosha dushti* (a complex imbalance of the three *Doshas*) which occurred due to

beejabhaga avayava dushti (diseases occurring in the level of genes), resulted in *Masthulunga majja kshaya* (encephalopathy) with *Vatakapha* predominance. Intractable seizures were found to worsen the *Samprapthi*, thereby causing developmental regression and developing encephalopathy. It was seen as a case of which lead to *Masthishka apachaya* (brain atrophy) of the *Garbha* (product of conception) resulted in *Dhatukshayaja sarvangavata* (diminution of structural tissues due to *Vata*). At 3 ½ months of age, seizure episodes started and its frequency and intensity worsened with time. So that the child was put on multiple AEDs. But child used to experience 2-5 episodes per day. Then developmental regression occurred. This can be viewed as *Sannipata apasmara*, worsening the *Samprapthi* causing functional damage of brain tissue. The main features manifested are *Kampa* (tremors), *Apasmara* (seizures), *Unmada* (insanity) and *Vatavyadhi* (diseases occurring due to *Vata*). So a treatment protocol was framed incorporating *Apasmara chikitsa* (treatment of epilepsy), *Unmada chikitsa* (treatment of insanity), *Vatavyadhi chikitsa* (treatment of *Vataroga*) and *Sirakampa chikitsa* (treatment of tremors of head). Management was focused on Srotosodhana (clearing of channels), *Vatakapha samana, Laghu brimhana* (light and nourishing) and Rasayana (rejuvenation). Initial OP management was planned to control intractable epilepsy by adopting *Sannipata apasmara chikitsa*. Treatment was started in an outpatient basis giving *Hinguvachadi churnam* in a dose of 2.5 grams twice daily after food intended for improving Agni and then *Mahat Panchagavya ghritam* in a dose of 5 ml twice daily before food which has *Srotosodhana* and *Apasmarahara* property. After 1 month, dose of *Ghrita* increased to 10 ml twice daily. Along with that, *Tailam* was started with *Dhanwantaram* 101 *Avarti* and *Rasnadi churna*. The same medication was continued for next 2 months. The child became seizure free. Inpatient treatment was started with internal medicines like *Dhanadanayanadi Kashaya* for addressing *Kapha avarana vata* and to pacify vitiated *Sirogata vata. Balarishta* possessing *Jataragni deepana* and *Vata samaka* property was given. Since *Srotorodha* is evident, *Kadikizhi* having *Rooksha ushna guna* was planned. Flaccidity of muscles reduced and *Agnideepthi* of the child improved. On the next stage, *Rasnadasamoola ghrita* was introduced which has the indication of *Sirakampa* (tremors of head), *Apasmara* (seizures) and *Unmada* (insanity). *Takradhara* (pouring medicated buttermilk over head and body) which is an exclusive *Keraleeya Ayurveda chiktsa* was employed for *Srotosodhana* (clearing the channels). *Panchathiktakam kashayam* having *Srotosodhana* and *Kleda samana properties* was the drug of choice. *Mahanarayana tailam* indicated for severe neurological deficits was used for *Abhyanga* (massage) after considering *Vatakapha vridhi*. Then a *Pradeha* which is *Vata kapha hara* in nature was done with *Kolakulathadi churna*. It was done in *Balaksheera* owing to its *Vata* pacifying and *Brimhana* nature. *Mahanarayana tailam* was also used here. Along with that*, Talam* with *Maharaja prasaranitailam* which has special indication in *Sirogata vata* mixed with *Kachooradi churna* having *Pitta hara* property was done. Titubations and Truncal ataxia reduced considerably after this. Then *Trivritadi kashayam* mentioned in *Sirakampa* context of Bhaishajya ratnavali was added owing to its *Sodhana* (elimination) as well as *Vyadhisamana* (pacifying the disease) property. Then switched on to *Mahatpancha gavya ghrita* which is highly recommended for *Srotosodhana* and for *Apasmara*. A *Patrapotalasweda* (sudation done with a *Potali* of leaves) to address *Vatakapha* was administered then. *Siropichu* (applying cotton dipped in *Taila* over head) with *Mahanarayana tailam* was done since *Siras* is the main *Vyadhi desha* and to check *Upasaya*. So treatment was switched on to *Sirodhara* (pouring medicated oil over head). It was done with *Mahanarayana tailam. Rasayana* therapy is mandatory while treating these types of diseases. *Kanmada rasayanam* indicated for *Vatakahaja vyadhis* was selected and *Sivagutika* was used here. *Mustadi rajayapana vasthi* was done next. Physiotherapy was going parellely with the treatment. The overall result of this treatment protocol was evident from the changes that occurred in the domains of gross motor, fine motor, speech and language domains. The attainment of milestones like sit without support, hand to hand transfer of objects, speaking of bisyllables, reduction of tremors, titubation, truncal ataxia substantiate the above fact.

CONCLUSION

A complete cure for West syndrome and STBPX1 syndrome cannot be claimed by any of the medical system. The framing and its timely application of a systematic and structured protocol in Ayurveda after analyzing *Dosha, Dushya, Bala* etc of a *Roga* and rogi can make improvements in reduction of frequency and intensity of seizures, improving muscle tone, reduction and tremors, gradual attainment of milestones and improvement in receptive and expressive language. So Ayurvedic treatment can make dramatic changes even in cases of genetic disorders.

DECLARATION AND PATIENT CONSENT

Authors certify that they have obtained a patient consent form, where the care giver has given consent for reporting the case in the journal. The caregiver understands that her name and initials will not be published and efforts will be made to cover the identity but anonymity cannot be guaranteed.

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