WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 16, 1322-1329. Cash Study ISSN 2277– 7105

CEREBROTENDINOUS XANTHOMATOSIS-ANUKTA VYADHI - A CASE STUDY

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Article Received on
10 July 2018,
Revised on 30 July 2018,
Accepted on 20 August 2018
DOI: 10.20959/wjpr201816-13243

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ABSTRACT

Cerebrotendineous Xanthomatosis (CTX) which is one of the genetic disorder under the condition of leukodystrophies. Mutations in the CYP27A1 gene, located on chromosome 2q33-qter.[1] Pal P.K.(2012)[2] stated that it is the lipid storage disorder with predominant accumulation of cholestenol and cholesterol in almost every tissue of the body. Where extra neurological and neurological symptoms develop. Such disease is not explained in Ayurveda, therefore CTX can be correlated with *Anukta Vyadhi* explained by Charak (C.C.30/291-292).[3] Management of such disease depend on factors involved such as *Dosha*, *Dushya* (*Vikar Prakriti*), *Adhishtan* (place of lesion) and *Nidan* (*Samutthan Vishesh*). Being a chronic disease, it is also responsible for depression. So management for depression is also important part in treatment of CTX. A case recorded and was treated in our institute. Results obtained were encouraging which are presented in full paper.

INTRODUCTION

Cerebrotendineous xanthomatosis (CTX), also called as cerebral cholesterosis,[4] is an autosomal recessive form of xanthomatosis.[5][6] It falls within a group of genetic disorders called the leukodystrophies.

Symptoms of CTX, as described by Pal P.K. (2012)[2] is lipid storage disorder with predominant accumulation of cholestenol and cholesterol in almost every tissue of the body. Extra neurological manifestation begins in childhood and include bilateral cataracts, chronic diarrhoea and tendon xanthomas found in Achilles tendon and over the extensor tendons of fingers, toes, on tibial tuberosity and in the triceps. Neurological manifestations generally start around 20 years of age. It may include progressive mental retardation, presenile dementia, pyramidal and extra pyramidal signs, behavioural changes, convulsions, cerebellar signs specially ataxia and dysarthria, sensorial motor neuropathy, bulbar palsy and bulbar palsy with dysphagia. Diagnostic test includes serum cholestenol, elevated cholestenol or cholesterol in the tissues. Neuro imaging study shows cerebral cerebellar and cervical chord atrophy, hypodensity in cerebral and cerebellar white matter.

Cerebrotendineous xanthomatosis is associated with mutations in the CYP27A1 gene, located on chromosome 2q33-qter.[7] The disorder is inherited in an autosomal recessive manner. This means the defective gene responsible for the disorder, is located on an autosome (chromosome 2 is an autosome), and two copies of the defective gene (one inherited from each parent) are required in order to be born with the disorder. The parents of an individual with an autosomal recessive disorder both carry one copy of the defective gene, but usually do not experience any signs or symptoms of the disorder.

Elevated levels of serum cholestanol are diagnostic of Cerebrotendineous xanthomatosis. Alternatively, analysis of 27-hydroxycholesterol and 7 alpha hydroxycholesterols can be used. Genetic testing of the CYP27A1 gene is confirmatory and is increasingly being used as a first line test as part of symptom specific gene panels (genetic eye disease, ataxia and dementia).

The standard treatment is chenodeoxycholic acid (CDCA) replacement therapy. Serum cholesterol levels are also followed. If hypercholesterolemia is not controlled with CDCA, an HMG-CoA reductase inhibitor ("statins" such as simvastatin) can also be used.[8][9] It is also known as "Van Bogaert–Scherer–Epstein syndrome".[10]

Cerebrotendinous Xanthomatosis is not described in Ayurveda. Therefore, it can be termed as *Anukta Vyadhi* in Ayurveda. It can be correlated with Ayurvedic concept of *Avrit Vata*. *Vata Prakopa* results mainly because of two factors. They are as follows.

1. Due to diminution of tissue elements i.e *Dhatukshayajanya*. Chakrapani stated that there is *Sara Kshaya* (Chk.Com.C.C.28/60).[11]
2. Due to occlusion of its channel of circulation i.e *Marg Aavrodha*. Obstruction in Strotas is produced with the help of *Pitta* and or *Kapha Dosha*. Being *Sukshma* and *Prerak* in *Guna* obstruction to *Gati* of *Vayu* is there. It is called as *Margavarodha of Vayu* (*C.C/28/59*).[12]

Charak has described different *Avarana* such as *Kaphavritta Vayu*, *Pittavrita Vayu*, *Raktavritta Vayu*, *Mansavritta Vayu*, *Medavritta Vayu*, *Asthivritta Vayu*, *Majjavritta Vayu*, etc (*C.C/28/60- 71*).[13] *Charak* also mentioned that vitiated *Vayu* lodges in to place and manifest different symptoms with respect to that place such as *Koshthashrit Vayu*, *Pakvashayashrit Vayu* etc. Vitiated *Vayu* lodges in particular *Dhatu* and their respective symptoms are also narrated by Charak. They are *Raktagata Vayu*, *Mansagata Vayu*, *Asthimajjagata Vayu* (*C.C.28/24- 34*).[14]

As such disease was not explained in ayurvedic texts or classic management of such disease mainly depends on concept of *Anukta Vyadhi* as explained by Charak. When disease was not explained, management is contemplated mainly depending on Dosh, Dushya and Nidan (C.C.30/291- 292).[15]

A Case Profile

35 years old, male patient B/B relative and admitted in GACH, Nagpur in Kayachikitsa department had:

Chief Complaint

Patient had *Chankraman Asamarthata, Kati-Ubhaypad Shula Evum Shithilta, Asan Uthhapan Asamarthata, Aspasth Vakpravritti, Ubhay Gulf Shoth Evum Shula, Alpanidra, Daurbalyanubhuti* and *Ubhaypad Pradeshi Vakrata* for 15 years.

Past H/O

H/O Fall from bicycle15 years ago, Convulsion 6 years ago, Typhoid 5 years ago and chronic diarrhoea in childhood. H/O Operation for bilateral juvenile cataract at the age of 20 years.

Family History: Non-specific. No H/O consanguineous marriages.

Vaiyaktik Vrittant

***Aahar*:** Patient taken mixed type of food (Non-veg once/week), *Katu Rasa Pradhan* with dominant *Ushna, Tikshna, Ruksha* and had habbit of *Vishamashan, Paryushit Aahar*.

***Vihara*:** Sedentary life Style.

***Vyasan*:** No history of any addiction.

***Asthavidh Parikshana*:** *Jivha* was *Sama, Aspasta Shabda, Akruti* was *Krish*(BMI-15), Nadi-90/min and rest all *Parikshana* was normal.

***Urah Parikshana*:** NAD

***Udar Parikshana*:** *Adhaman* without Organomegaly.

Investigations

CBC with ESR: Hb%: 12.8 gm/dl, TLC: 7500/cumm, Platlets: 2.38 lac/cumm, ESR: 28 mm/hr. BSL Fasting: 83 mg/dl, Post-prandial: 101 mg/dl.

LFT and KFT: WNL, CRP: 5 mg/dl,

Lipid profile: Triglycerides: 104 mg/dl, HDL: 71.4 mg/dl

Urine Routine and Microscopic: No Abnormality Detected,

Serum vitamin B12: 1102 pg/ml

MRI Brain: Impression: MRI study of brain reveals symmetrical T2/ FLAIR hyperintense signal involving B/L cortical spinal tract along. Symmetrical areas of blooming on GRE images involving. B/L Dentate nuclei. Diffuse cerebral and cerebellar atrophy. These imaging features are s/o "Cerebrotendinous Xanthomatosis".

Peripheral nerve conduction: Present Peripheral Nerve Conduction study is suggestive of Predominantly Axonal Neuropathy motor more than sensory.

MANAGEMENT

Initially *Rasa Pachak vati* 2 BID, *Mansa Pachak Vati* 2 BID, *Medo Pachak Vati* 2 BID, and *Ajmodadi Churna* 5gm BID for 8 Days was given to alleviate *Sama Avastha*. *Shirodhara* with *Bhrami* and *Til tail* once a day for 21 days for *Tarpana*. *Balapushti Yog* 5 gm BID with milk to alleviate *Vayu* vitiated because of *Dhatu Kshaya*, *Vacha Churna Jivha Pratisarana* 5 gm BID with *Madhu* for slurred speech, *Dashang Lepa* once a day in morning at the sight of

Xanthoma, *Ubhay Padpradeshi Shastishali Pinda Svedha* for 30 min once a day, *Guduchi Siddha Majja Basti* 60 ml daily was administered in morning for 30 days *Syrup.Vatantak* 10ml BID and *Ajamansarasa* 100 ml OD was advised.

OBSERVATIONS AND RESULT

Table-1: Table Showing the Effect of Therapy on Dimensions of Xanthoma.

S. N.	Muscle Bulk Of Lower Limb	LEFT B.T. [17/01/2018]	LEFT A.T. [23/02/2018]	RIGHT B.T. [17/01/2018]	RIGHT B.T. [23/01/2018]
1.	16 Cm above Patella	36 cm	36 cm	36 cm	36 cm
2.	10 cm below tibial tuberosity	26 cm	**27 cm**	26 cm	**27 cm**
3.	Xanthoma Upper border Mid of border Lower border	 21cm 24cm 26cm	 21cm 24cm **24cm**	 22cm 24cm 26cm	 22cm 24cm 26cm

Table-2: Table Showing the Effect of Therapy on Pain by Visual Anoulougs Scale.

S. N	Parameter	B.T. Score (17/01/2018)	A.T. Score (23/01/2018)
1	VAS	08	04

Table-3: Table Showing the Effect of Therapy on Sign and Test for Ataxia in CTX.

S.N.	SIGN/TEST	B.T. [17/01/2018]	A.T. [23/02/2018]
1.	**Romberg sign**	Unable to perform	Able to perform but Positive
2.	**Finger nose Test**	Positive	Negative
3.	**Knee Heal Test**	Positive	Negative

Table-4: Table Showing the Effect of Therapy on Muscle Power Grade.

S. N.	Muscle Power	LEFT B.T. [17/01/2018]	LEFT A.T. [23/02/2018]	RIGHT B.T. [17/01/2018]	RIGHT B.T. [23/01/2018]
1.	Upper Limb	5/5	5/5	5/5	5/5
2.	Lower Limb	3/5	**4/5**	3/5	**4/5**

Table-5: Table Showing the Effect of Therapy on Muscle Tone.

S. N.	Limbs	LEFT B.T. [17/01/2018]	LEFT A.T. [23/02/2018]	RIGHT B.T. [17/01/2018]	RIGHT B.T. [23/01/2018]
1.	Upper Limb	Normal	Normal	Normal	Normal
2.	Lower Limb	Flaccid	Flaccid	Flaccid	Flaccid

Table no-6: Table Showing the Effect of Therapy on time required for Buttoning of shirt.

S.N.	Buttoning of shirt	Time Required in Seconds B.T. [17/01/2018]	Time Required in Seconds A.T. [23/02/2018]
1.	Opening Button of Shirt	22 secs	11 secs
2.	Closing Button of Shirt	29 secs	22 secs

Table no-7: Table Showing the Effect of Therapy on Deep Tendon Reflex.

S. N	Reflex	LEFT B.T. [17/01/2018]	LEFT A.T. [23/02/2018]	RIGHT B.T. [17/01/2018]	RIGHT B.T. [23/01/2018]
1.	Biceps	+++	+++	+++	+++
2.	Triceps	+++	+++	+++	+++
3.	Brachioradalis	+++	+++	+++	+++
4.	Supinator	+++	+++	+++	+++
5.	Knee	+++	+++	+++	+++
6.	Ankle	+	+	+	+

Table-1 shows that there is reduction in of left xanthoma in its lower border by 2 cms and increased muscle bulk 10 cms below tibial tuberosity by 1 cm. **Table-2** shows markedly reduction in VAS from 8 to 4. **Table-3** highlighted that there were improved signs of ataxia **Table-4** that Vas Scale also reduced from 8 to 4 score. Muscle power Grade presented in **Table-5** enhance in lower limb from 3/5 to 4/5 in this case. **Table-6** shows revamp in opening and closing time of buttons of shirt by 11sec and 7sec respectively. **Table-7** manifest deep reflexes which remains exaggerated except ankle reflex which remains diminished.

DISCUSSION

According to Ayurveda, CTX can be corelated with *Anukta Vyadhi*. The treatment of such diseases can be done by considering the vitiated status of *Dosha*, *Dushya*, *Adhishtan* and *Nidan*. Keeping this concept of management, the said patient was treated. *Atiprvrutti* of *Abadhatu* was found in consequence *Vata Dosha* was dominantly vitiated. *Atiprvrutti of Abadhatu* was also responsible for *Kshaya* of *Rasa* leading to *Dhatukshsya* in other *Dhatu* with respect to *Kedarkulya Nyaye* (*S.S 7/3*).[16] There was *Asarta* in *Saptadhatu* (*Chk.Com.C.C.28/60*)[11] and hence *Dhatu Kshayajanya Vyadhi* might have been resulted in this patient. At same time *Vimarggamana* (*C.V/5/24*)[17] of *Aba Dhatu* (Chronic childhood diarrohea), might had been taken place to *Bhaya Twacha* with the help of *Prakopit* and *Vikutt Vayu* which was accountable for development of *Shotha* (Xanthoma)(*C.C/12/8*).[18] According to *Samprapti* of *Vyadhi*, *Dhatukshaya* specially *Majja Dhatu Kshaya* was responsible for all neurological symptoms and signs. During management, *Samprapti*

Ghatakas was kept in mind and patient was managed accordingly. So, for proper formation of *Uttarotardhatu* enhancement of *Dhatuagni* of respective place was done by *Dipana* and *Pachana Chikitsa* initially. For improvement of *Majjakshaya* (Cerebral atrophy) *Shirodhara* was advice to achieve *Tarpana Karma* which help by increasing blood perfusion to brain. *Vatashaman Chikitsa* was advised by using some drugs. As it was dominant factor in complete *Samprapti*. *Majjakshaya* was treated according to *Ayurvedic Maulik Siddhant* i.e *Samanya Vishesh Siddhant* (*C.S. 1/44*)[19], hence *Gudduchi Siddha Majjabasti* was administered. *Shothara Lepa* for local application was used for *Shotha*. As we know *Sharirik Vyadhi* is responsiple for *Manas Vyadhi* and vice versa (*C.Sh. 4/36*) [20]. In chronic diseases like this case, patients gradually land in depression i.e *Manoavasad*; to reduce this *Ashwasan, Harshan, Shirodhara* and physiotherapies were advice to patient which boost patient moral to fight against disease.

CONCLUSION

The combination of this Ayurvedic treatment can be helpful in treating the cases of CTX. Prolonged duration of treatment might have been given in such cases, however the trial was on only one patient and multiple such cases can be taken for study by similar line of management.

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