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BYLER'S DISEASE – A CASE REPORT

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ABSTRACT

Byler's disease or Progressive familial intrahepatic cholestasis is a rare genetic liver disorder of childhood that disrupt bile formation and presents with cholestasis of hepatocellular origin. It is characterized by a mutation in genes encoding proteins involved in the hepatocellular transport system. Main clinical manifestations include cholestasis, pruritus and jaundice. The exact prevalence remains unknown, but the estimated incidence varies between 1/50000 and 1/100000 births. In *Ayurveda*, this disease has similar features to *Shakhashrita* or *Ruddhapatha Kamala.* A 2-year-old female child diagnosed with Progressive familial intrahepatic cholestasis approached Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Kuthpady, Udupi, Karnataka, India with the complaints of yellowish discolouration of skin and sclera, dark coloured urine, pale-coloured faeces, severe itching with rashes all over the body, distension of abdomen etc. A detailed history was taken, and clinical findings were recorded. The patient was assessed based on liver function tests and also by the symptoms of the disease. The treatment history of the patient was recorded and the progress of the disease, as well as the effect of treatment, was assessed. Medicines given were *Pippali Rasayana*, Syrup Nirocil, and *Kumaryasava.* Considering that the disease PFIC has a poor prognosis with a chance of liver failure and with rapid progression, the treatment given is proved to be effective in improving the parameters thereby reversing the pathology of the disease. Hence it can be concluded that the treatment protocol was effective in the management of Byler's disease.

Keywords: Byler's disease, case report, *Kamala*, Progressive familial intrahepatic cholestasis, *Rasayana*

INTRODUCTION

Byler's disease[1] or Progressive familial intrahepatic cholestasis (PFIC) refers to a heterogeneous group of autosomal recessive liver disorders of childhood in which cholestasis of hepatocellular origin often presents in the neonatal period or first year of life and leads to death from liver failure at ages usually ranging from infancy to adolescence[2]. People with this condition generally develop signs and symptoms during infancy which may include severe pruritus, jaundice, hepatosplenomegaly, hyperbilirubinemia, elevated alkaline phosphatase[3] etc. Mutation in genes ATP8B1, ABCB11, ABCB4 causes PFIC[1]. Treatments in contemporary science may include Ursodeoxycholic acid therapy to prevent liver damage, partial biliary diversion, surgery and or liver transplantation[4]. *Acharya Kashyapa* described *Kamala* related to *Balaka* in *Vedhanadhyaya* of *Kashyapa samhitha*[5]. But *nidana, samprapthi* and *chikitsa* are not mentioned in *Kashyapa samhitha*. This disease has similar features to *Sakhasrita*[6] or *Ruddhapatha Kamala* with *Jatodaka Udara lakshana*s. In *Sakhasrita Kamala* the vitiated *Doshas* obstructs biliary canaliculi. By this, *Pitta* does not enter *koshta* and gets accumulated in the liver. The excessively accumulated *Pitta* in the liver spreads all over the body except *koshta*, hence causing *Tilapishta nibha pureesha, Haridratva of Nakha, netra, twak and mutra.*

CASE REPORT

A 2-year-old female child visited the outpatient department of Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Udupi, with the complaints of *Haridratva* of *twak, netra, mutra* (yellowish discolouration of skin, sclera, urine), *Swetavarna pureesha* (pale-coloured faeces), *Kandu (*severe itching with rashes all over the body), *Adhmana* (distension of abdomen) with associated complaints of *Krishata*(malnourishment) and *Kshut alpatha* (reduced appetite) for 2 years.

The child was born to consanguineous parents, normally delivered with a birth weight of 2.45 kg, cried soon after birth, sucking was initiated. Meconium was passed after 24 hrs. Later from day 3, the child was noticed with pale-coloured faeces which was neglected by parents. After that, the parents noted gradual distension of the abdomen in the child. On the 26th day of birth, parents noted gross distension of abdomen, pale-coloured faeces and dark coloured urine along with yellowish discolouration of skin and sclera. On consultation in hospital, the child was diagnosed with jaundice and was admitted to NICU, was subjected to investigations which revealed hepatosplenomegaly and cholelithiasis, which was treated symptomatically. Child gradually developed severe pruritus with rashes all over the body, bleeding from gums, fatigue, fever with Malena, which was also treated symptomatically, and the child got mild symptomatic relief from all complaints. But the symptoms of jaundice persisted. At 1 year of age child developed regurgitation and endoscopic findings showed esophagitis. Child was subjected to liver biopsy, and it showed predominantly canalicular cholestasis with moderate fibrosis, histologic features compatible with Progressive familial intrahepatic cholestasis. The child was on conservative management for 1 year. At 2 years of age (2019), they consulted in SDM Ayurveda Hospital, Udupi and is on ayurvedic treatment since then. In the past 2.5 years, they found good improvement in child's condition. The symptoms of severe pruritus have decreased to very mild and occasional, yellowish discolouration of skin and sclera has come down to very mild, and the colour of faeces has changed from pale to yellow. Negative history - no delay in milestones

Family history: the consanguineous marriage of parents. No other family member has a similar condition.

Prenatal maternal history: Mother has a history of the first trimester per vaginal bleeding.

CLINICAL FINDINGS

The Child was pale, afebrile and emaciated with short stature. There was Icterus and clubbing of fingers. The heart rate was 102/min, respiratory rate of 18/min, pulse rate was 102/min, and bodyweight of

11.2 kg. The abdomen was distended with the umbilicus inverted. There were no dilated blood vessels over the abdomen and no visible peristalsis. Bowel sounds were present. On palpation, the abdomen was soft and non-tender with moderate hepatomegaly and splenomegaly. The abdominal girth was 51 cm. Ultrasonography report on 9/8/2018 showed hepatomegaly with coarse echo pattern, cholelithiasis without sonological evidence of cholecystitis, and splenomegaly. The impression of liver biopsy dated 25/08/2018 showed predominantly canalicular cholestasis with moderate fibrosis (Ishak score 5-6/6). The histological features are compatible with progressive familial intrahepatic cholestasis. Based on the clinical presentation of *Tilapishtanibha pureesha, Haridratva* of *twak, netra, mutra, Alpagni* the condition was diagnosed as *Shakhashrita Kamala* with *Jatodaka Udara lakshana*.

The following medicines were administered

1. *Pippali Rasayana* 500 mg capsule thrice daily with honey before food
2. Syrup Nirocil 10 ml thrice daily after food
3. *Kumaryasava* 5 drops thrice daily after food

Pippali Rasayana and Syrup Nirocil was given on the first visit and was continued throughout the treatment with regular follow up. After 3 months there was an improvement in the levels of liver function test. Mild reduction in itching was observed. During this visit, *Kumaryasava* was added. After 7 months of treatment, more improvement was found in liver function tests and the symptoms, such as itching, and rashes were reduced to a great extent. Appetite was improved, weight increased to 11.95kg and abdominal girth reduced to 47 cm. The bilirubin levels returned to normal, and a marked improvement was seen in AST and ALT levels also. Same medicines were advised to continue with a follow up once in every 15 days. The patient was on follow up for the last 2.5 years.

ASSESSMENT OF LIVER FUNCTION TESTS

INVESTIGATION	1ST VISIT (12/03/2019)	4TH VISIT (15/6/2019)	5TH VISIT (12/10/2019)
Hb (gm%)	9.75	3	7.9
Total bilirubin (mg/dl)	6.1	0.6	0.4
Direct bilirubin(mg/dl)	3.1	0.3	0.2
Indirect bilirubin(mg/dl)	3.0	0.3	0.2
SGOT (U/L)	358	96	67
SGPT (U/L)	220	200	53
Serum Alkaline phosphatase (U/L)	219	293	450
Serum Total Protein	6.7	4.6	5.9

ASSESSMENT OF SYMPTOMS

SYMPTOM	1ST VISIT (12/03/2019)	5TH VISIT (12/10/2019)
Yellowish discolouration of skin and sclera	Prominent	Mild
Colour of faeces	Pale	Yellow
Colour of urine	Dark yellow	Dark yellow
Pruritus and rashes	Severe	Mild and occasional
Appetite	Reduced	Good
Abdominal girth	51 cm	47 cm
Weight	11.2 kg	11.95 kg

DISCUSSION

The patient was diagnosed as a case of *Sakhasrita Kamala* with the involvement of *Tridosha* associated with *Ambuvaha srotodushti*. The clinical presentation is characterised by *Tilapishta nibha pureesha* (Pale coloured faeces), *Haridratva* of *Nakha, netra, twak, mutra* (yellowish discolouration of skin, sclera, urine, nails), *Alpagni* (reduced appetite), *Kandu* (severe itching), *Adhmana* (distension of abdomen). The line of treatment explained for *Shakhashrita Kamala* in classics are initially *Vata Sleshmahara chikitsa* and after bringing *Pitta* to *koshta*, *Pitta samana chikitsa* is adopted[6].

Effect of *Pippali Rasayana*

Pippali is having properties like *Katurasa, Anushna veerya, Madhura vipaka, Deepana, Vrishya, Rasayana, Vatasleshmahara, Rechaka*. It is indicated in diseases like *Swasa, Kasa, Udara, Jwara, Kushta, Prameha, Arsha, Pleeha*[7]. *Acharya Susruta* states that *Pippali* is *Pitta avirodhi*[8].*Vagbhata* explains *Pippali* as *Sara guna yukta* and explained *Pippali* as *Agrya Oushada* in *Pleehamaya*[9]. *Pippali* has the action of *Samana* and also *Sodhana* by its *Rechaka* property. *Pippali* acts as *Hetu viparita* (against cause-*Dipana*), *Vyadhiviparita* (against disease-*Yakrit Plihamayakrit*), *Dosha viparita* (*Kaphavata hara, Tridoshahara, Pitta avirodhi*) and as *Rasayana*[10]. *Pippali* given with honey as *anupana* is *Kaphamedohara*[7]. Studies show that Piperine which is an active ingredient in *Pippali* is having hepatoprotective[11] effect and also has a role in the reduction of fibrosis[12].

Role of *Rasayana* in *Yakrit roga*

By having action on the level of *Agni*, *Rasayana dravyas* corrects the *Dhatwagni* which leads to proper *Rasa Raktha samvahana* and thereby attaining *Dosha-Dhatu saamyata*. *Rasayana chikitsa* in *Yakrit roga* can be inferred to have hepatoprotective activity by protecting the hepatic parenchyma and promoting hepatocellular regeneration thereby restoring the functional efficiency of the liver. Syrup Nirocil[13] is a patent medicine having ingredients *Bhumyamalaki*, *Eranda*, *Guduchi* and *Yashada bhasma*. It is having hepatoprotective properties, useful in liver and spleen disorders, anaemia etc. *Kumaryasava*[14] is having properties like *Kaphahara, Shulahara*, Shothahara and is indicated in *Yakritvridhi, Pleehavridhi, Adhmana, Gulma, Mandagni, Krimi, Panduroga, Shotha. etc*, it helps in balancing the *Dhatwagni*. Studies show that *Kumaryasava* is having the potential to reduce hepatic damage by interference with lipid peroxidation and oxidative stress[15]. It was observed that subjective and objective parameters of the patient have been improved significantly.

CONCLUSION

Byler's disease or Progressive familial intrahepatic cholestasis is a rare genetic disorder of the liver. This disease has similar features to *Sakhasrita Kamala* or *Rudhapatha Kamala* explained in *Ayurveda* classics. *Pippali Rasayana* has a significant effect on *Yakrit* and *Pleeha rogas*. Hence it can be concluded that the principles of treatment explained in *Ayurveda* can be used in the management of rare genetic disorders like Byler's disease.

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