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A Case Report of Beals Syndrome with Hydrocephalus

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Beals syndrome, also known as Beals-Hecht syndrome or congenital contractural arachnodactyly, is a rare, autosomal dominant connective tissue disorder. It is characterized by crumpled ears, arachnodactyly, congenital contractures and scoliosis. A male infant of 37+5 weeks of gestation, and with birth weight of 3170 grams, had features of a long and narrow face, bilateral crumpled inferior helix, prominent antihelix of the ears, bilateral arachnodactyly, clenched position of the hands and flexion contractures of the elbows and knees. The infant had tachypnea and chest retractions shortly after birth, and was diagnosed with transient tachypnea of newborn with pneumothorax. He was subsequently treated with positive pressure ventilation and chest tube insertion. Chromosomal karyotype analysis was normal and screening for Marfan syndrome was negative. Echocardiographic findings were unremarkable. Cranial ultrasonography showed a left lateral ventricle dilatation of 0.5 cm and increase up to 1.2 cm on follow up. Brain MRI showed a progression of dilatation of the left ventricle, and a ventriculo-peritoneal shunt was done at 3 months of age. We present a case of a newborn male with Beals syndrome, accompanied with ventricular dilatation and progression to hydrocephalus that has not been previously reported.

Key Words : Beals syndrome, Congenital contractural arachnodactyly, FBN2 protein, Hydrocephalus

Beals syndrome is a rare autosomal dominant disorder, first named by Beals and Hecht in 1971.[1] Its major features are arachnodactyly, congenital contractures and ear deformities with absence of eye and heart anomalies. There have been two case reports of Beals syndrome in Korea.[2,3] We present a case of a newborn male with Beals syndrome, accompanied with ventricular dilatation and progression to hydrocephalus, which has not been reported before.

Case report

A male infant of 37 weeks and 5 days' gestation age was born to a 29-year-old gravida 2, para 1 woman as the second baby of the twin, and as the third child of the family. The pregnancy was uneventful and the infant was delivered in a local hospital by a cesarean section, due to a previous history of cesarean section. Apgar scores were 7 and 8 at 1 and 5 minutes, respectively, but shortly after birth, the infant showed signs of tachypnea and moaning sound along with mild chest retractions. The infant required 5 liters of oxygen to maintain adequate blood gas oxygen saturation and was brought to our NICU 2 hours after birth. The first baby of the twin did not have any immediate perinatal problems.

Physical examinations of the infant showed tachypnea of over 80 respiration rate per minute and chest retractions. Chest X-ray revealed sun-burst pattern and the infant was diagnosed of transient tachypnea of the newborn. Nasal CPAP was applied and respiration

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rate was normalized, however after 3 hours, respiration rate suddenly increased to 80 breaths per minute again and follow-up chest x-ray showed pneumothorax of left lung. Chest tube was promptly inserted and on the 5th day of admission, pneumothorax was resolved and chest tube was removed. The infant was discharged on the 8th day of admission.

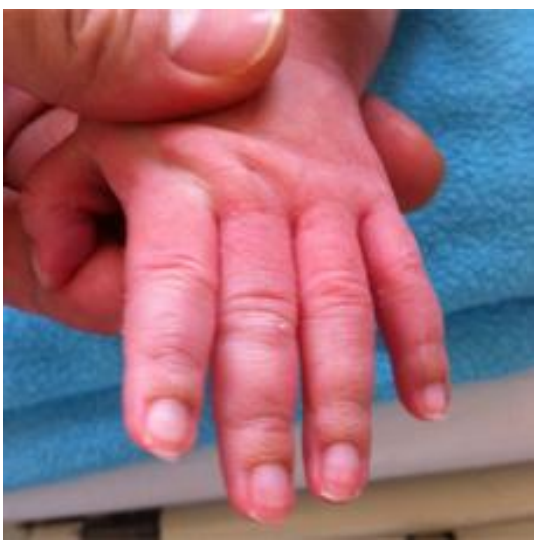

Fig. 1. Arachnodactyly of right hand is shown.

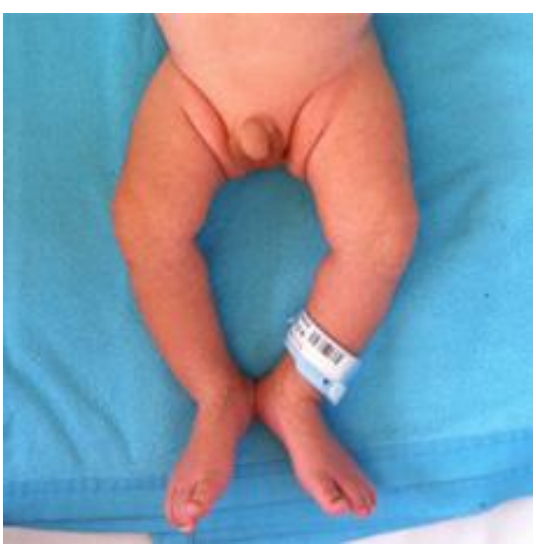

Fig. 2. Prominently long limbs and toes are notable and flexion contractures of knees, limited to 20 degrees on full extension, is shown.

The infant had a birth weight of 3,170 g. He was presented with a long and narrow face, prominently long limbs, long phalanges and toes leading to initially suspect Marfan syndrome (Fig. 1, 2). On closer physical examination, bilateral crumpled inferior helix and prominent antihelix of the ears, high-arched palate, caput quadratum, tense anterior fontanelle, short neck, clenched position of the hands, and bilateral arachnodactyly were noted (Fig. 3). Mild flexion contractures of the elbows and knees were examined. X-rays of the upper extremities revealed elongation of phalanges and accelerated bone age of up to 1 1/2 years. However there were no signs of scoliosis on whole spine x-rays and bone density was normal. Echocardiographic, fundoscopic, brainstem audiometry findings were unremarkable. Tandem mass screening and TORCH results were negative. Chromosomal karyotype analysis was normal and screening for Marfran syndrome was negative. Genetic assay of Beals syndrome was done on exon 23-35 of the *FBN2* gene, representing the middle region and the most commonly found mutation on literature, however, no mutations were found. Ultra-

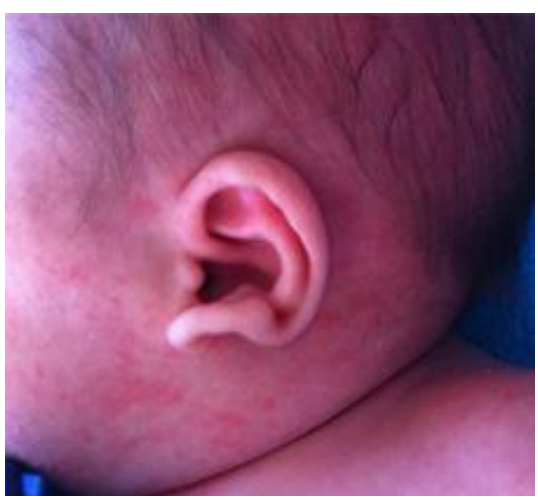

Fig. 3. Crumpled inferior helix and prominent antihelix of the left ear is shown; The patient had bilaterally similar morphology of ears.

sonography of the brain showed left lateral ventricle dilatation of 0.5 cm, and follow-up ultrasonography showed increased ventricular dilation to 1.2 cm. Brain MRI revealed diffuse cortical atrophy and confirmed asymmetric dilation of the left ventricle (Fig. 4).

Physical examination of the first baby of the twin showed no dysmorphic appearance with normal face and ear morphology, and there were no signs of arachnodactyly or flexion of joints.

Bilateral crumpled ear, profound arachnodactyly, congenital contractures along with normal findings on echocardiogram and fundoscopy, and negative results on screening of Marfan syndrome led to diagnosis of Beals syndrome. The infant was discharged in good condition and was closely followed up for progression of hydrocephalus.

After discharge, the infant had constant increase in the size of the ventricles and was consulted to the Neurosurgery department. Ventriculoperitoneal shunt was recommended to prevent further damage to the brain, and an insertion of the shunt was promptly done, at 3 months of age. On 12 months of follow-up, the infant showed normal growth with height and weight of 25th percentile. Mild motor delay was noted with just sitting and crawling possible. Language development was normal, and the infant was able to pronounce 'Mom' and 'Dad'. Flexion contractures of both the elbows were improved from maximum extension of 35 degrees to 15 degrees, and the knees from 45 degrees to 20 degrees. The infant maintained clenched posture of the fist, but full extensions of the fingers were possible. Follow-up brain MR, at 12 months, revealed consistent ventriculomegaly on both ventricles, and ventriculo-peritoneal shunt was maintained (Fig. 5).

Discussion

Beals syndrome is also known as Beals-Hecht syndrome or congenital contractural arachnodactyly. It shares the same skeletal features of Marfan syndrome and should be questioned on any patients with such an impression. Beals syndrome patients are distinguished by the presence of crumpled ear helix, arachnodactyly, congenital contractures and pro-

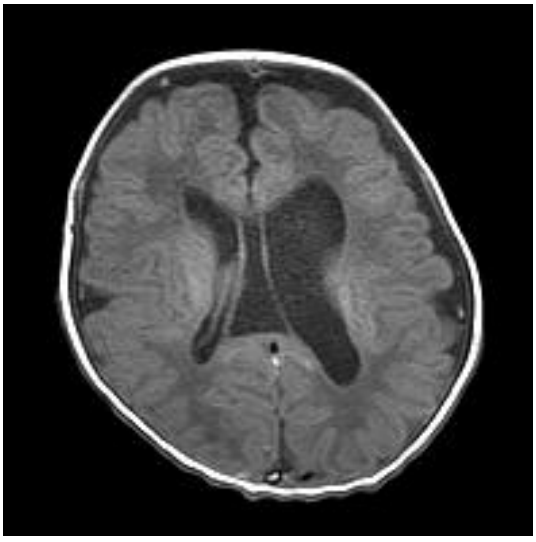

Fig. 4. T1-weight brain MRI at 2 months after birth shows diffuse cortical atrophy and asymmetric dilation of left ventricle.

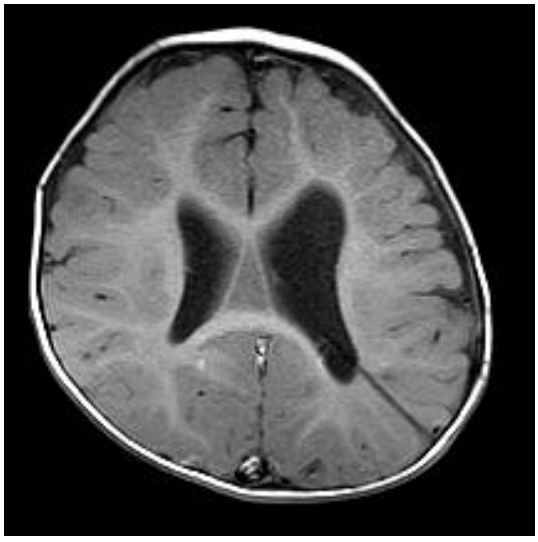

Fig. 5. Follow-up brain MR at 12 months revealed consistent ventriculomegaly on both ventricle, and ventriculo-peritoneal shunt inserted on left ventricle.

gressive kyphoscoliosis. Also, ocular and cardiovascular complications are very rare, compared to the Marfan syndrome.[1] Beals syndrome have theses distinct features, and while it maybe be difficult to differentiate from that of Marfan syndrome, differentiation must be made because the two syndromes have different prognosis.

Beals syndrome is an autosomal dominant disorder, caused by a mutation in the *FBN2* (Fibrillin-2) gene, situated on the 5q23-31 chromosome, while the Marfan syndrome by FBN1 on the 15q15-21.3 chromosome.[4, 5] Encoded fibrillins are cysteine-rich glycoproteins that polymerize extracellularly, and form macro aggregates called microfibrils. Microfibrils provide force-bearing structural support, and form elastic fibers with elastin to provide elasticity.[6, 7] Microfibrils also control the release of transforming growth factor beta (TGFb), which is also an important mechanism of Marfan syndrome.[8] Less than 30 mutations of the *FBN2* gene have been published to date and all of the found mutations were located on the middle region, exon 23-35 of the gene. Even when all exons of the *FBN2* gene were screened, only 14 out of the 32 probands were identified, and all of the exons found were in the middle region, except for one in exon 17. Clinical characteristics of the *FBN2* gene mutation positive and negative groups did not show significant difference.[9] Our case was screened for the middle region of the *FBN2* gene, and owing it to its known low detection rate, the mutation was not detected.

Contractures involving large joints, elbows, knees and fingers are seen from birth, and may partially resolve with growth.[10] However, camptodactyly may remain. Pectus excavatum or cavinatum are seen. Hands show a clenched fist appearance and fingers are long and phalanges are elongated on X-rays. Aggravating scoliosis and kyphoscoliosis have high influence on the overall prognosis of disease.[11]

Cardiac manifestations are very rare. However, cases of the atrial septal defect and mitral valve prolapse have been reported and may involve up to 14.7%.[1, 5, 12, 13] There have been reports of lethal cases of aortic root dilations. Ophthalmologic manifestations, especially heterotropia, are found in 20% of the cases.[5, 14] Rare cases of ectopia lentis, keratoconus and myopia have also been reported.[15, 16]

There are no reported cases of Beals syndrome associated with ventriculomegaly in the literature, to date. In our patient, antenatal and postnatal evaluation for possible causes of ventriculomegaly has revealed negative results. If ventriculomegaly is a possible manifestation of Beals syndrome, it is of great significance as a prompt intervention is necessary to prevent its complications.

Beals syndrome patients are expected to live a relatively normal life, with normal mental intelligence and normal lifespan. Screening for ventriculomegaly and other central nervous system diseases should be considered. Evaluation of the cardiac and ocular manifestations is necessary. The treatment of camptodactyly and contractures are confined to physiotherapy and mainly symptomatic. Spinal deformity and scoliosis should be followed-up for surgical intervention, should it become necessary.

In conclusion, we present a case of a newborn male with Beals syndrome accompanied by ventricular dilatation and progression to hydrocephalus, which has not been reported before with a review of the literature.

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= 국 문 초 록 =

수두증을 동반한 Beals 증후군 1례

아주대학교 의과대학 소아과학교실
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Beals 증후군은 Beals-Hect 증후군 또는 거미손가락증으로도 알려져 있으며 상염색체 우성으로 유전되는 드문 결체조직 질환이다. 이 질환은 구겨진 귀, 거미손가락증, 선천적 관절 구축, 척추 측만증의 특징을 보인다. 재태기간 37주 5일, 출생 체중 3,170 g의 남자 환아가 길고 좁은 얼굴, 양측 구겨진 귀, 뚜렷한 귀의 대륜, 양측 거미손가락증, 양손의 주먹을 지고 있는 자세, 슬관절과 주관절의 구축 등을 보였다. 환아는 출생 후 빈호흡 및 흉각 함몰을 보였으며, 기흉을 동반한 일과성 신생아 빈맥으로 진단되어 양압 환기 및 흉관 삽입등의 치료를 하였다. 유전자 핵형 검사는 정상이였으며 Marfan 증후군 관련 검사는 음성이였다. 심초음파 검사상 이상소견은 없었으나, 두부 초음파 검사상 좌측 뇌실이 0.5 cm 으로 확장되어 있었으며, 추적 검사상 1.2 cm 으로 증가되어 있었다. 두부 MRI 상 좌측 뇌실 확장이 더욱 진행되어 출생 3개월경 뇌실복강션트를 삽입하였다. 저자들은 이전에 발표되지 않은 뇌실 확장 및 수두증을 동반한 Beals 증후군 환아 1례를 보고하는 바이다.

중심 단어 : Beals 증후군, 거미손가락증, FBN2 protein, 수두증