A Novel Neonatal Michelin Tire Baby Syndrome with Craniosynostosis and Gigantism

Yeni bir Michelin Lastik Bebek Sendromlu Yenidoğanda Kraniositoz ve Gigantizm Birlikteliği

Michelin Lastik Bebek Sendromu ve Gigantism / Michelin Tire Baby Syndrome and Gigantism

İbrahim Akalın[1,2], Didem Armangil[3], Alper Han Cebi[4], Yunus Alp[4], Kemal Süleyman[5]
[1]Istanbul Medeniyet University, Faculty of Medicine, SB Göztepe Training and Research Hospital, Medical Genetics, Istanbul,
[2]Trabzon Women's and Children's Hospital, Genetic Diseases Diagnosis Center, Trabzon, [3]Trabzon Women's and Children's Hospital,
Neonatology Unit, Trabzon, [4]Karadeniz Technical University, Faculty of Medicine, Department of Medical Genetics,
[5]Trabzon Numune Training and Research Hospital, Dept. of Pediatrics, Trabzon, Turkey

Özet

Michelin Lastik Bebek Sendromu, klinik olarak iyi tanımlanmış özellikle çoklu halka şeklinde deri katlantıları ile karakterize nadir bir konjenital anomalidir. Hastamız, 38 yaşında akrabalık olmayan ailenin 3. çocuğu olarak sağlıklı anneden son adet tarhine göre olaysız 40 haftalık gebelikten belirgin deri katlantıları ve devlik ile doğdu. Doğumda kilosu 4950 gr (>90 persentil), boyu 57.5 cm,(>90 persentil) ve baş çevresi 39,5 cm (>90 persentil) idi. Fizik muayenede kaba yüz, brakisefali ve kraniosinoztoz saptandı. Doğumda vital ve laboratuar bulguları normal sınırlarda idi. Kraniyel ve renal ultrasonogramlar, X-ray grafiler ve karyotip analizi normal idi. Ekokardiyografide küçük patent duktus arteriosus ve patent foramen ovale saptandı.

Bu yazımızda, eşlik eden gigantizm ve kraniosinostoz bulguları olan literatürdeki ilk Michelin Lastik Bebek Sendromlu bir yenidoğan olguyu, detaylı literatür incelemesi ile birlikte sunduk.

Anahtar Kelimeler

Michelin Lastik Bebek Sendromu; Deri Katlantıları; Kraniosinoztoz; Gigantizm

Abstract

Michelin Tire Baby Syndrome is a rare congenital disorder and characterized clinically well defined multiple ring shaped skin creases. Our patient was born to non-consanguineous healthy parents as the third child of the family at 40 weeks of uneventful gestation with distinctive skin creases and gigantism. He was 4,950 g in weight (>90 percentile), 57.5 cm in length (>90 percentile), and had a head circumferences of 39.5 cm (>90 percentile) at birth. The physical examination showed a rough face, brachicephaly and craniosynostosis. His vital and laboratory findings were within normal limits at birth. Cranial and renal ultrasonograms, X-ray graphics and cytogenetic analyses were normal. Echocardiography revealed small patent ductus arteriosis and patent foramen ovale.

In this report, we present a new case of Michelin Tire Baby Syndrome who is the first neonate associated with severe gigantism and craniosynostosis, in the literature. A review of the related literature has also been presented.

Keywords

Michelin Tire Baby Syndrome; Skin Creases; Craniosynostosis; Gigantism

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Corresponding Author: İbrahim Akalın, İstanbul Medeniyet Üniveritesi, S.B. Göztepe Eğitim ve Araştırma Hastanesi, Tıbbi Genetik Anabilim Dalı, İstanbul 34730, Turkey. F.: +90 2165664023 GSM.: +905066613542 E-Mail: ibrahimakalin@yahoo.com

Introduction

Michelin Tire Baby Syndrome (MTBS) is characterized as clinically well defined multiple ring shaped skin creases on extremities. It was first described by Ross et al. [1] as a generalized folded skin and announced as a congenital anomaly syndrome by Wiedemann at 1987 [2]. It's a rare disorder and multiple anomalies may accompany to circumferential skin creases. Eighteen cases have been reported in the literature so far [1-18].

According to the literature, our patient is the first neonate of Michelin Tire Baby Syndrome associated with severe gigantism and craniosynostosis.

Case Report

In this paper, we report a new case of 'Michelin Tire Baby Syndrome' [OMIM, %156610]. The patient was born to non-consanguineous healthy parents at 40 weeks of gestation with C/S in Trabzon Women's and Children's Hospital, and referred to Genetic Diseases Diagnosis Center of Trabzon Women's and Children's Hospital at birth with multiple congenital abnormalities and distinctive gigantism and skin creases. The index patient was the third child of the family. The pedigree did not reveal any other abnormalities. Physical findings are presented at Table 1 and compared with previous reports and Bechwith-Wiedemann Syndrome (BWS). He was 4,950 g in weight (> 90 percentile), 57.5 cm in length (> 90 percentile), and had a 39.5 cm of head circumferences (> 90 percentile) at birth.

The physical examination showed a rough face, brachicephaly, craniosynostosis and gigantism with folded skin on limbs and body (Figures 1A, 1B, 1C). His vital findings were normal at birth, but followed up for three days at Neonatology Unit due to his abnormal appearance. Laboratory investigation showed normal biochemical findings including hematological parameters. Growth Hormone 13,4 ng/mL, insulin (7.08 uIU/mL), Insulin-Like Growth Factor-1 (<25.0), Insulin-Like Growth Factor Binding Protein-3 (0.551) ug/mL were within normal ranges at his 2nd day. Echocardiography revealed small patent ductus arteriosus and patent foramen ovale. Cranial and renal ultrasonographies were normal. Audiometric examination was normal. Cytogenetic studies were performed on 72-hr cultured peripheral blood at Karadeniz Technical University, Faculty of Medicine, Department of Medical Genetics. Peripheral blood sample was harvested and treated by conventional cytogenetic method. Chromosomes were analyzed on G-banding and showed normal 46, XY karyotype.

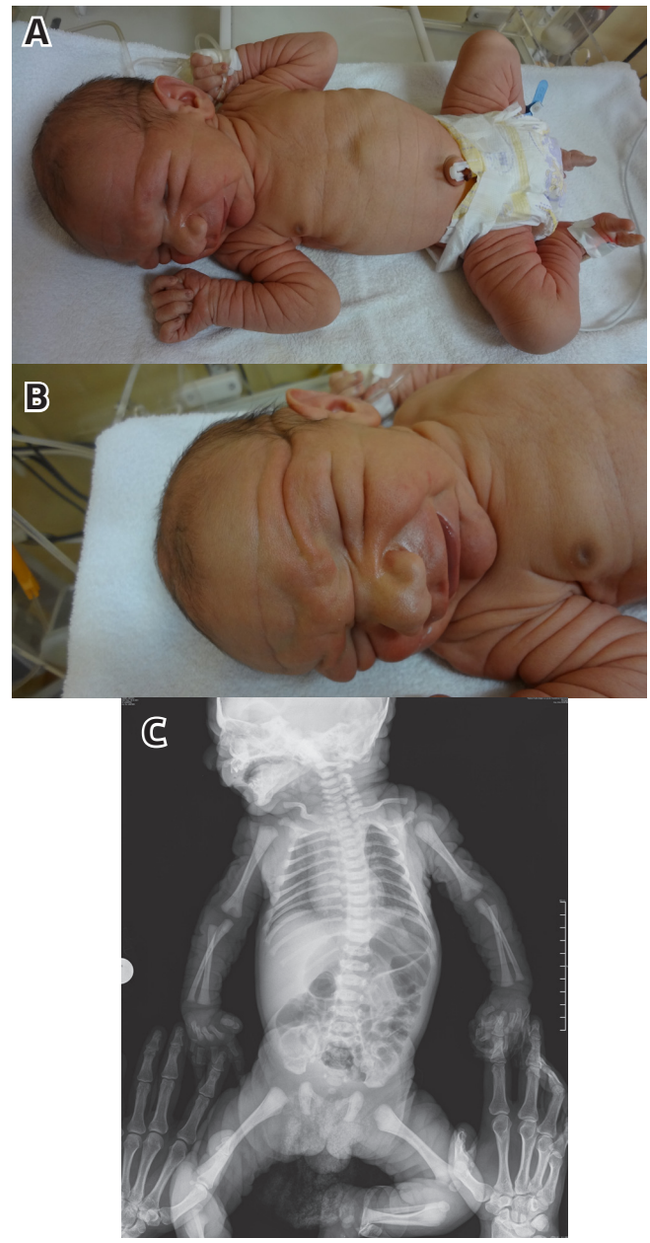


Figure 1. General view of the patient representing gigantism, multiple ring shaped skin creases on body and extremities (A). Close view on head and upper limb showing fine skin creases on upper extremity and gigantic facial appearance (B). Plain X ray graphy of the patient representing normal skeletal structure, but definite skin creases (C).

Discussion

Congenital symmetrical circumferential skin creases are a rare feature and have occasionally been associated with frequent congenital anomalies such as hypotelorism, epicanthal folds, upward slanting of the palpebral fissures, malformed ears, cleft palate, micrognathia, hemihypertrophy, ureterocele, mental retardation, convulsion, and/or neuroblastoma [1,2,7,9,17]. However, in our case most striking anomalies were gigantism and craniosynostosis which were firstly described in association with MTBS.

Craniosynostosis is one of the most frequent craniofacial anomalies known as the premature fusion of paired frontal bones [19]. Craniosynostosis could be isolated or accompany to other malformations. Skeletal, facial and cranial nervous system abnormalities are usually seen with craniosynostosis [20]. Genetic causes of the craniosynostosis are the mutations occurred basically in the fibroblast growth factor receptors (FGFR 1,2 and 3), TWIST1 and MSX2 genes [21]. Craniosynostosis Type1 and 2 are familial and autosomal dominant in manner having mutation in TWIST1 and MSX gene, respectively representing scaphocephaly, dolichocephaly and beaten copper appearance of skull. Our patient had no family history and Kleeblattschaedel deformity (cloverleaf skull) at X-ray graph (Figure 2). Crouzon syndrome, Muenke syndrome, Apert syndrome are well defined congenital malformation syndromes associated with FGFR gene mutations. Crouzon syndrome has been diagnosed mainly by cranial manifestations like progressive hydrocephalus. However, our patient did not have manifestations of holoprosencephaly. Apert and Baller-Gerold syndromes have characteristic facial appearance with finger anomalies like syndactly and radial

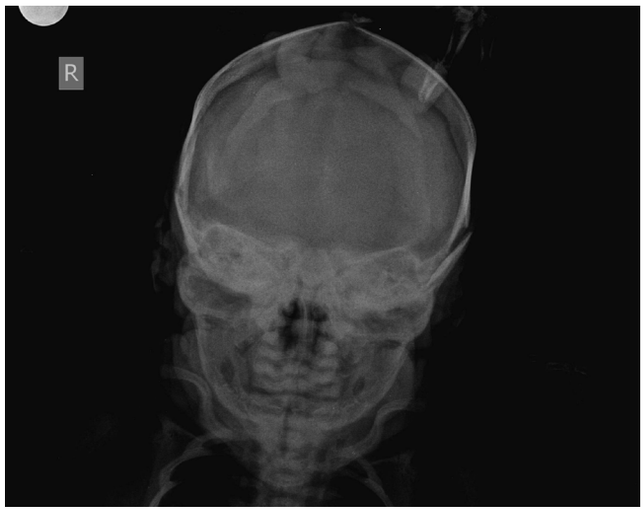


Figure 2. Plain X ray graphy of sculp showing absence of cloverleaf skull appearance.

aplasia which were also absent in our case. Moreover, those syndromes mentioned above have neither been reported with gigantism nor dermal creases. The clinical findings of previously reported cases were summarized and compared with index at Table 1.

In the literature, there is only one case of craniosynostosis reported with skin creases [22]. But the patient was within less to normal percentiles and the authors have focused on the diverse craniofacial abnormalities and unlike skin folds from our case.

The presence of gigantism in our patient has reminded us a pediatric overgrowth disorder Beckwith Wiedemann Syndrome which has a variable clinical presentation including characteristic triad of abdominal wall defects (omphalocele, umbilical hernia, and diastasis recti), macroglossia, and gigantism [23-25]. The growth may also manifest itself as hemihypertrophy and visceromegaly in addition to a pathognomonic finding of

Table 1. Clinical features of Michelin Tire Baby Syndrome (MTBS): comparison with previous reports and Beckwith Wiedemann Syndrome

CATEGORY	SUB-CATEGORY	FEATURES	MTBS PREVIOUS REPORTS	BECKWITH WIEDEMANN	OUR CASE
Inheritance	-	Autosomal dominant	+?	+	?
Growth	Height	Average birth length,	N/A	52.6 cm	57.5 CM
	Weight	Average birth weight	3000 g (At most 75 percent)	4000 g	4950 g (>95 %)
	Head cicumference	Average	Normal to small	N/A	39.5 cm (>90 %)
	Growth	at birth	Normal	Generalized overgrowth	Generalized overgrowth
		Postnatal	Normal (At most 75 percent)	Parallel curve at or above 95 %	Parallel curve at or above 95 %
		Hemihypertrophy	-	+	-
Head and Neck	Head	Metopic ridge	-	+	-
		Large fontanelle	N/A	+	Craniosynostosis
		Prominent occiput	N//A	+	+
	Face	Coarse facial features	+	+	+
		Broad nasal bridge	+	-	+
		Short neck	+	-	+
		High forehead	+/-	N/A	+
	Ears	Malformed ears,	+	-	-
		Low set	+	-	-
		Posteriorly angulated	+	-	-
		Linear ear lobe creases	-	+	-
		Posterior helical indentations	-	+	-
		Conductive hearing Loss	+/-	-	-
	Eyes	Epicanthal folds	+	-	-
		Mongoloid slant of the eyes	+	-	-
		Hypertelorism	+	-	-
		Microphtalmia	+	-	-
		Prominent	-	+	-
	Mouth	Macroglossia	-	+	-
		Median Palate Cleft	+/-	-	-
		High Arched palate	-	N/A	+
		Micrognathy	+	-	-
		Microstomia	+/-	-	-
		Thick lips	-	+/-	+
		Smooth Filtrum	-	N/A	+
	Imaging	Dilated Ventricles	+	N/A	-
		Hypoplastic Corpus Callosum	+	N/A	-
Cardiovascular	Heart	Cardiomyopathy	N/A	+	-
		Cardiomegaly		+	-
		PDA		-	+
		Patent Foramen Ovale		-	+
Abdomen	External Features	Omphalocele (exomphalos)	-	+	+
		Diastasis recti	-	+	-
	Liver	Hepatomegaly	N/A	+	-
	Pancreas	Pancreatic hyperplasia	N/A	+	-

Genitourinary	External Genitalia (Male)	Overgrowth of external genitalia	-	+	-
	Internal Genitalia (Male)	Cryptorchidism	+	+	-
		Hypoplastic Scrotum	+/-	-	-
	Kidneys	Renal medullary dysplasia Large kidneys	-	+	-
Endocrine Features		Adrenocortical cytomegaly Pituitary amphophil hyperplasia	N/A N/A	+ +	- -
Neoplasia		Wilms tumor Hepatoblastoma Adrenal carcinoma Gonadoblastoma Neuroblastoma	- - - - +	+ + + + -	- - - - -
Cytogenetic Abnormalities			Normal	duplication or deletion at 11p15.5	46,XY
Laboratory Abnormalities		Hypoglicemia Hyperinsulinemia Growth Hormon IGH-1, IGH-2 IGH Binding Protein	- - N/A N/A N/A	+ + N/A -, high N/A	- - Normal Normal Normal
Molecular Basis			Not Known	Genetic Heterogeneity	Not Known

fetal adrenocortical cytomegaly. The presence of 3 major findings (macroglossia, pre- or postnatal growth greater than the 90th centile, and abdominal wall defects) or 2 major findings plus minor manifestations were set for the diagnostics criteria [26-28]. However, our patient did not reveal any other accompanying anomaly present in the Beckwith-Wiedemann syndrome except gigantism. The pregnancy of our patient was uneventful. There was neither polyhydromnios nor excessive umbilical cord length being reported to suspect BWS at birth unlike Wang et al (1995). Absence of primary renal malformations such as renal medullary dysplasia, nephrocalcinosis, and nephrolithiasis on renal ultrasonography has also put our diagnosis away from BWS. Hypoglycemia has also been reported in 30 to 50% of BWS patients [24]. In view of the fact that neonatal hypoglycemia is frequent and prospectively harmful for the central nervous system, [29] the monitoring of the glucose levels has been proposed in BWS newborns at every 6 hours during the first 3 days, but our patient did not developed hypoglycemia during and after his first three days of follow up at neonatology unit.

Since BWS has genotypic heterogeneity, no cytogenetic abnormality was detected in general or specifically for critical region 11p13-p15. Since the 11p15 region presumably contains the locus for insulin-like growth factor-2 (IGF2) besides insulin locus (INS), laboratory findings of Insulin, IGF-1, IGFBP and GH were within normal range.

In conclusion, we diagnosed the patient as Michelin Tire Baby Syndrome with characteristic skin folds although there was an accompanying gigantism which let us to focus on the common overgrowth syndromes. Hence, we kept in mind whether as an overgrowth syndrome Beckwith-Wiedemann might be overlapped with skin creases due to its genetic heterogeneity, but, we concluded to report the neonate to be a new case of MTBS associated with gigantism and craniosynostosis.

Competing interests

The authors declare that they have no competing interests.

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