

# 출생 후 커다란 두혈종과 혈소판감소증을 보인 Jacobsen Syndrome 1예

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## A Case of Jacobsen Syndrome Presenting with a Huge Cephalhematoma and Thrombocytopenia after Birth

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Jacobsen syndrome (JS) is a contiguous gene syndrome resulting from a deletion of chromosome 11q, with various clinical manifestations. A post-term small for gestational age infant was born by normal vaginal delivery without trauma or vacuum extraction. On day 5, right parietotemporal scalp swelling developed, with petechiae on the right cheek and thrombocytopenia (platelets: 63,000/ $\mu$ L). A prominent forehead, wide-set eyes, short and upturned nose were noted. Karyotyping and microarray analysis demonstrated del(11)(q24q25), consistent with Jacobsen syndrome. Brain magnetic resonance imaging (MRI) revealed a huge cephalhematoma. The patient is scheduled to receive periodic evaluations for thrombocytopenia and heart, kidney, abdominal malformations, ophthalmologic and auditory problems. There are lots of newborns with cephalhematoma or petechiae after birth. Not all newborns with these symptoms need evaluations, but if they have these symptoms with suspect features or appearances, we need to go through further evaluations.

**Key Words:** Jacobsen syndrome, 11q deletion, Paris-Trousseau syndrome, Thrombocytopenia, Distal 11q deletion syndrome

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### Introduction

Jacobsen syndrome (JS) is a contiguous gene syndrome resulting from a deletion of chromosome 11q, mostly distal to 11q23 [1]. The deletion usually extends to the telomere [2]. The prevalence of JS is estimated at 1:100,000 births [3]. The female/male ratio is about 2:1 [4]. The clinical features of JS are quite variable, and include heart and skeletal abnormalities, and growth and developmental delay [4,5].

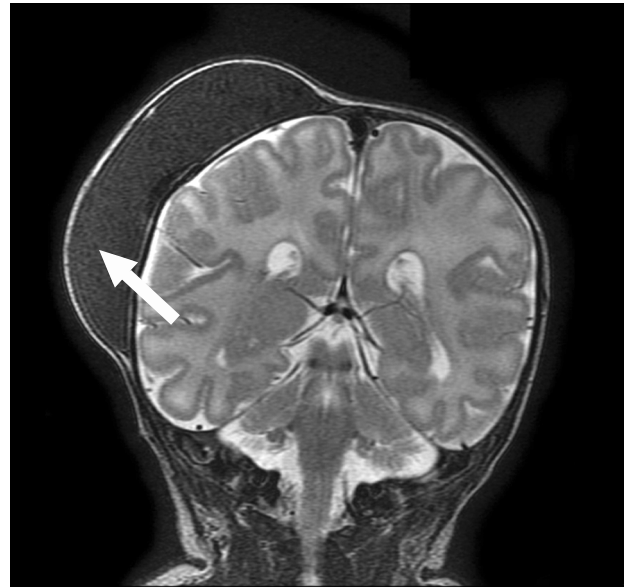
Typical facial features include skull deformities, ptosis, strabismus, a prominent nasal bridge, and low-set ears. Cutaneous syndactyly, and a large and long first toe can be seen [5]. Many patients have thrombocytopenia or pancytopenia at birth, also called Paris-Trousseau syndrome (PTS) [6]. Of 3 reported in Korea, 1 was diagnosed before birth [7-9]. We report a case of JS in a 13-day-old, full-term infant who represented with a cephalhematoma and petechiae and was found to have an 11q24q25 deletion.

## Case Report

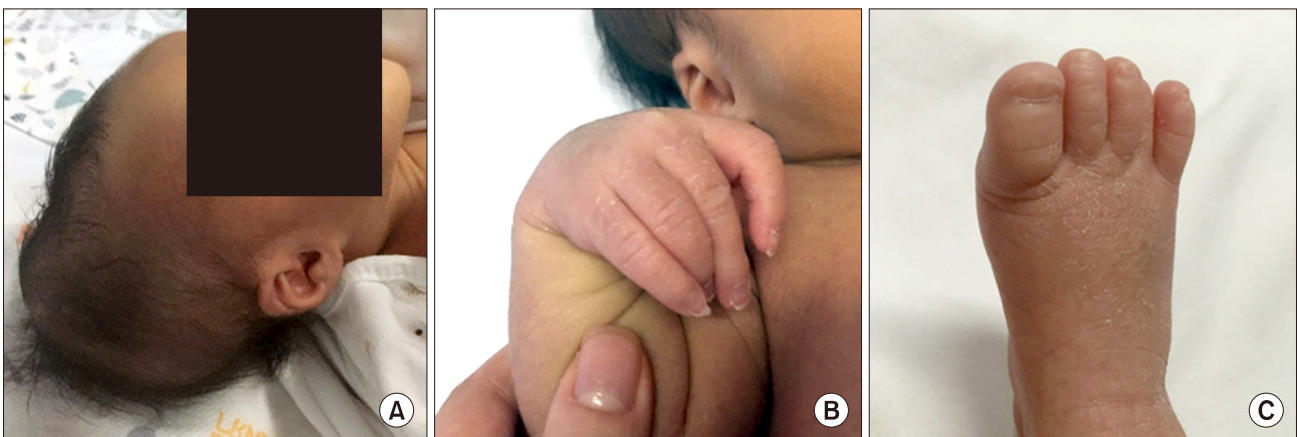
This study was approved by the institutional review board of Keimyung University Dongsan Medical Center (Approval No. 2018-03-051). A 13-day-old female infant was transferred to our hospital and admitted with a history of petechiae on the right cheek and a right parietotemporal cephalhematoma. She was born at 41 weeks by normal vaginal delivery. There was no history of asphyxia or premature rupture of membranes. The birth weight was 2,560 g, consistent with post term small for gestational age (SGA) and intrauterine growth restriction (IUGR). There was no history of trauma or vacuum extraction. Neonatal screening with tandem mass spectrometry was unremarkable. On day 3 after birth, right parietotemporal scalp swelling gradually developed. On day 9, right cheek petechiae were observed. On day 13 when she was transferred, the scalp swelling had reached about 8×7 cm and the right cheek petechiae were still present (Fig. 1A). A prominent forehead, wide-set eyes, short and upturned nose, slightly triangular face, and camptodactyly were observed. Her right third and fourth fingers were flexed and difficult to extend (Fig. 1B). Her fourth right toe was thinner than the others (Fig. 1C). There was no hepatosplenomegaly or palpable abdominal mass. The heart beat was regular with no murmur.

Initial blood tests revealed thrombocytopenia (platelets:

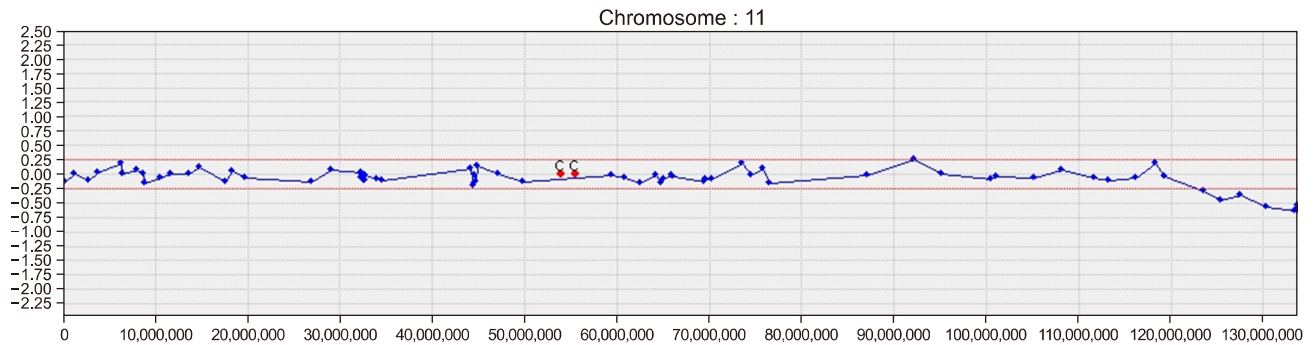
63,000/ $\mu$ L). She had no family history of coagulation disorder. Anti-platelet antibody, prothrombin time, activated partial thromboplastin time, fibrinogen, platelet function analyzer-100, coagulation factor, and von Willebrand factor test results were normal. Blood and urine cytomegalovirus polymerase chain reaction test were negative. Skull radiography showed cortex tearing and a huge biparietal cephalhematoma. Ultrasonography and MRI revealed a



**Fig. 2.** Brain magnetic resonance imaging findings revealing a large cephalhematoma in the right parietal lobe (arrow) in an infant with Jacobsen syndrome.



**Fig. 1.** An infant with Jacobsen syndrome and a large cephalhematoma. (A) Scalp swelling reached about 8×7 cm in the right parietotemporal area. (B) The right third and fourth fingers were flexed, showing camptodactyly. (C) The fourth right toe was thinner than the other toes.



**Fig. 3.** The chromosomal microarray analysis (G-scanning, MGmed, Korea) showing arr11q24q25(123630374\_135054016)x1 in an infant with Jacobsen syndrome.

large, right parietal lobe cephalhematoma (Fig. 2).

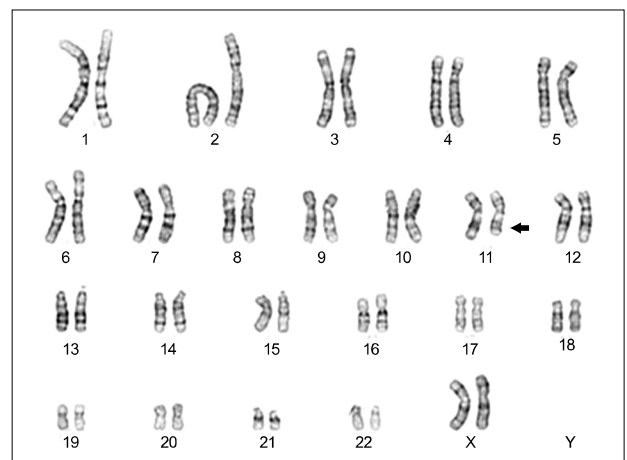
Based on the symptoms and physical examination, karyotyping and chromosomal microarray analysis (G-scanning, MGmed, Korea) were performed and identified 46, XX, del(11)(q24q25) and arr11q24q25(123630374\_135054016)x1, respectively (Fig. 3, 4). Accordingly, this patient was diagnosed with JS.

Cephalhematoma aspiration yielded 55 mL without pre-treatment. Serial testing showed slightly improved thrombocytopenia (platelets: 96,000-115,000/ $\mu$ L) and no other symptoms were noted. No other treatment was performed, but gentle care was done. Periodic evaluation for thrombocytopenia was scheduled as an out-patient. Pediatric orthopedics was consulted. Further necessary evaluation included echocardiography, developmental assessment, renal ultrasonography for malformations and abdominal ultrasonography to exclude pyloric stenosis. Ophthalmologic and auditory evaluation will be needed.

### Discussion

JS is a variable phenotypic, heterogeneous disorder that is confirmed by cytogenetic analysis of a deletion on chromosome 11q extending to the telomere [5]. Most deletions occur at 11q23, with some cases reportedly occurring at q24, q22, and q21 [1,10]. More severe clinical features can be seen with larger deletions [5]. JS occurs 1 in 100,000 births and roughly 50% cases diagnosed by age 1-year have more obvious clinical manifestations [5,11].

JS is known to show varying degrees of skeletal dis-



**Fig. 4.** Karyotype result showing deletion of distal 11q24q25 (arrow) in an infant with Jacobsen syndrome.

orders, hormonal abnormalities including growth hormone deficiency (GHD) or hypothyroidism, and cognitive impairment [2-6]. The severity of neurocognitive deficiency depends on the size of deletion [4]. Short stature is found in 75% of cases and mild to severe mental retardation in 97% of cases [5]. Because GHD and central hypothyroidism are characteristic and common hormonal defects in JS, growth hormone or thyroid-stimulating hormone testing should be performed [3]. Most patients have dysmorphic features as a prominent forehead, low-set ears, trigonocephaly, a flat nasal bridge, and a large and long first toe as in our case [2,5]. Cardiac anomaly is observed in 56% of cases and include ventricular septal defects, aortic or mitral valve abnormalities, coarctation of the aorta, and hypoplastic left heart syndrome, which is rare in the general population [2,5]. Cardiac abnormalities can lead to severe complications and

an electrocardiogram and echocardiography should be performed. Abdomen and kidney ultrasonography can be useful to evaluate gastrointestinal and renal anomalies. Pyloric stenosis is the most common gastrointestinal malformation, occurring in 56% of cases [2,5]. Feeding difficulty and chronic constipation can be present. Kidney dysplasia, double ureters, multicystic kidney, and cryptorchidism are frequently observed [2,5]. An ophthalmologic examination and auditory testing should be performed [5].

Our patient had thrombocytopenia and many JS patients have thrombocytopenia at birth [5]. Up to 47-94% of JS patients are reported with thrombocytopenia [4,5,12], although severe bleeding such as intraventricular hemorrhage (IVH) is rarely reported [13]. Some cases were reported with coagulopathy, which may be related with preterm birth, SGA, or IUGR [13]. It includes intraluminal bleeding and IVH which can lead to death [13]. In this patient, the presence of thrombocytopenia with SGA, IUGR, facial characteristics and skeletal anomalies helped the diagnosis. If there is thrombocytopenia with morphologic abnormalities, genetic syndrome should be suspected and chromosomal studies should be proceeded accordingly [14].

Paris-Trousseau syndrome is a mild phenotypic form, with chronic thrombocytopenia, giant alpha granules in abnormal giant platelets deletion of 11q23.3, abnormal platelet function, and abnormal megakaryocytes [4,12]. Paris-Trousseau thrombocytopenia normalizes with time while platelet function is maintained [6]. This phenotype is highly penetrant, affects at least 88.5 to 92% of patients, and can also be seen in JS [6]. In the Paris-Trousseau syndrome, friend leukemia virus integration 1 (*FLI1*) is strongly associated with dysmegakaryocytopoiesis and thrombocytopenia [5].

One study reported a patient with JS and 15% giant alpha granules presenting as Paris-Trousseau syndrome [12]. Another study found that the genomic 11q24.2q24.3 deleted region present in JS contains 8 OMIM genes: *ETS1*, *FLI1*, *SENCR*, *KCNJ1*, *KCNJ5*, *ARHGAP32 (RICS)*, *TP53AIP1*, and *BARX2* [2]. As *FLI1* is included in the deleted portion of JS, the Paris-Trousseau syndrome can present with thrombocytopenia [2]. Accordingly, a study suggested that the Paris-Trousseau syndrome is either a variant of JS or

the same disease [15].

Many neonates with a cephalhematoma or petechiae have no risk factors such as vacuum extraction or trauma. Based on our case findings, although there is no risk factor for newborns, we suggest that neonates with petechiae or cephalhematoma may go through further evaluations such as blood test or image work up to screen a case like our case. And if these test have any doubts, we recommend to do karyotyping and microarray analysis to confirm the disease related to thrombocytopenia like JS.

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