Sebaceous Nevus Syndrome as the Underlying Cause of Intractable Seizures in a One-Month-Old Infant

ANANNIT VISUDTIBHAN, M.D.*,
AMORNSRI CHUNHARAS, M.D.*,
PONGSAKDI VISUDHIPHAN, M.D.*
SURANG CHIEMCHANYA, M.D.*,
DUANGRAT KITIVIRIYAKUL, M.D.*,

Abstract

A one-month-old male infant with generalized seizures since 2 days old was evaluated at the Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. His seizures were initially characterized as focal movement of the right upper and lower limbs followed by generalized tonic. Initially, phenobarbital was administered but failed to control his seizures. Physical examination revealed generalized mild hypotonia with a hyperpigmented brownish patch affecting the left side of his face. The initial diagnosis was sebaceous nevus syndrome which is one of the neurocutaneous syndromes. The diagnosis was confirmed by skin biopsy of the affected lesion. The literature was reviewed and discussed. The authors emphasized the importance of thorough physical examination including evaluation of specific skin lesion which would be a leading clue in making the diagnosis of symptomatic epilepsy in infants.

Key word : Sebaceous Nevus Syndrome, Intractable Seizures

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Neurocutaneous syndrome is one of the common underlying causes of seizure in infants and children[1]. Among them, tuberous sclerosis and neurofibromatosis are the most recognized disorders. Seizure is not commonly found in neurofibromatosis. An ontogeny of epilepsy in neurofibromatosis which was not different from the general population. From a case-series study, the prevalence of epileptic seizure was 4.2 per cent[2]. There are many types of seizures observed in tuberous sclerosis at various ages. Seizures might occur in young infants during the perinatal period[3]. However, it will not be difficult

* Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

to recognize if there is an awareness of this syndrome. A thorough physical examination with the aid of a wood-lamp would be able to reveal the clue for the diagnosis[4]. However, there are some syndromes which are not common and physicians might not be able to make the diagnosis if they are not aware of their existence. Sebaceous nevus syndrome or epidermal nevus is one of these syndromes. Recognition of these syndromes will be helpful in making clinical diagnosis and will assist physicians in avoiding performing unnecessary investigations. The authors report a case of this syndrome to create awareness among physicians.

CASE REPORT

A one-month-old male infant was referred from a provincial hospital located 50 kilometers from Bangkok because of uncontrolled seizures. He was a normal-delivered, full-term first son of the family. There was no problem observed during his prenatal period. His initial physical examination was normal and was discharged home with his mother on the second day. One day later, he developed two episodes of generalized tonic seizures lasting around 3 minutes without any precipitating factor. He was then admitted to the provincial hospital where his physical and neurological examinations were reported within normal limits. His blood tests which consisted of serum electrolytes, glucose, calcium, magnesium and complete blood counts were within normal limits. Despite normal complete septic work-up including lumbar puncture for cerebrospinal fluid analysis, cefotaxime 200 mg/kg/day was administered for 14 days. However, multiple episodes of focal motor seizures affecting his right upper and lower limbs followed by generalized tonic seizures continued. Phenobarbital was the initial antiepileptic drug but it failed to control the seizures. Because of uncontrolled seizures, he was then transferred to our institution for diagnosis and treatment.

His physical examination upon arrival revealed normal body weight, length, head circumference and vital signs. There was a brownish hyperpigmented patch over the left side of his face (Fig. 1). Neurological examination disclosed an alert and wakeful male infant, normal cranial nerve functions, and slight spasticity of the right upper and lower limbs. Deep tendon reflexes were 3+ on the right side and 2+ to 3+ on the other side.

Repeated blood tests were within normal limits. Urine ferric chloride did not demonstrate any change in color. An EEG recording demonstrated a suppression-burst like pattern (Fig. 2). A magnetic resonance imaging of the brain was performed which revealed hemimegalencephaly of the left hemisphere (Fig. 3).

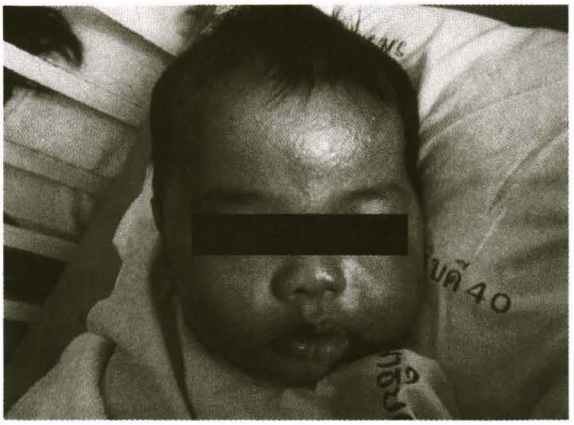

Fig. 1. Skin lesion of the reported patient.

Owing to his clinical presentation and skin lesion, sebaceous nevus syndrome which is one of the neurocutaneous syndromes was the presumptive diagnosis. Finally, skin biopsy was performed and demonstrated mild hyperkeratosis and mild papillary hyperplasia which supported the clinical diagnosis.

His seizures, however, did not fully respond to antiepileptic drugs which consisted of high dosages of phenobarbital and nitrazepam. The seizures were a combination of myoclonic, focal motor, generalized tonic and spasm-like seizures. His development was profoundly delayed for age. Because the prognosis of his underlying disease was poor, further aggressive measures to control the seizures including additional antiepileptic drug was not deployed. He had serial follow-up evaluation at the pediatric neurology clinic in our institution till he was 1 year and 9 months old when he was transferred to a nearby hospital for continuation of treatment. He still has one to three episodes of seizures daily which were characterized as a brief period of generalized tonic type.

DISCUSSION

Neurocutaneous syndrome is one of the common causes of symptomatic epilepsy in childhood [1]. Being able to recognize this syndrome would ease pediatricians in managing the children especially in investigation of any associated anomaly and in pre-

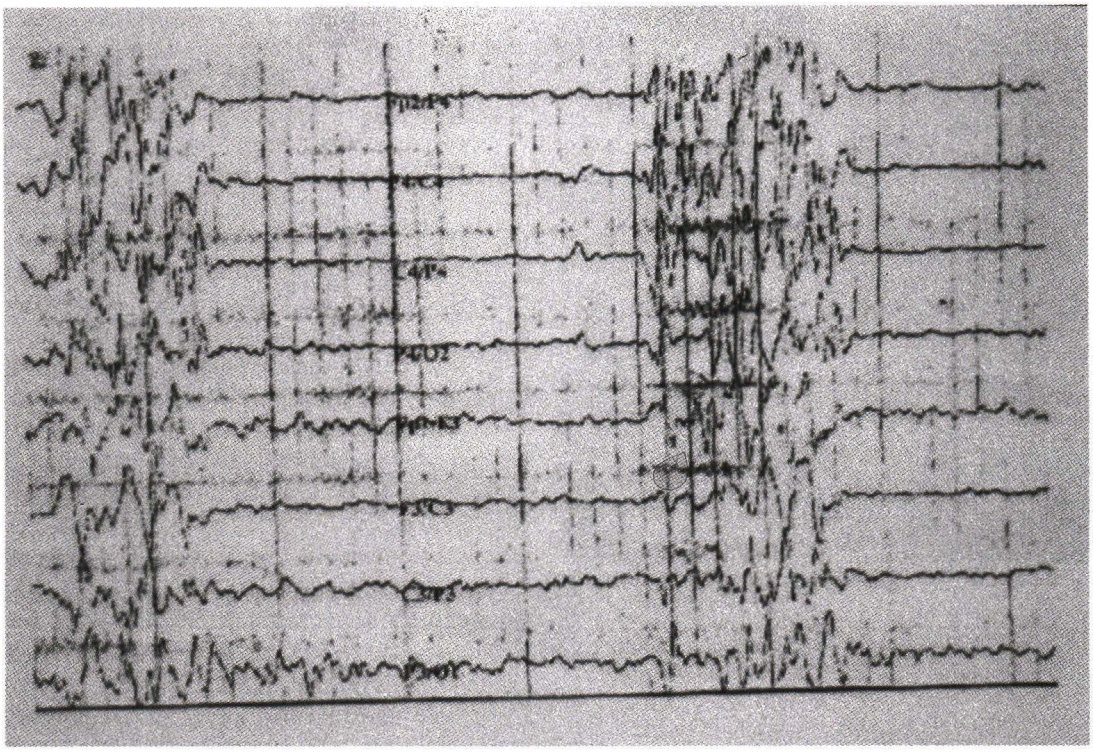

Fig. 2. EEG recording demonstrates a suppression-burst like pattern.

diction of the prognosis. There are many syndromes categorized in this entity. Tuberous sclerosis and neurofibromatosis are two examples which pediatricians are familiar with. However, there are some syndromes of which the prevalence may be less frequent and may be slightly difficult to recognize when the affected child is very young, especially in the infancy period. Sebaceous nevus syndrome, also called epidermal nevus syndrome, is among these syndromes. It is a rare sporadic neurocutaneous syndrome which was first described by Schimmelpenning in 1957 and defined by Feuerstein and Mims in 1962[5]. The phenotypes of this syndrome were characterized as a triad of midline skin lesions, seizures and mental retardation[6]. Since then, there have been more reports describing a wide spectrum of developmental defects and neurological disorders found in this syndrome which involved eyes, skeleton and the central nervous system[7-10]. Hemimegalencephaly and cerebellar hypoplasia were two neurological defects which were commonly found[8,11]. To make it simple, this syndrome was the combination of sebaceous nevus, cerebral, ocular and skeletal abnormalities[12]. However, this syndrome might remain unrecognized early in infancy because of the clinical appearance which was influenced by histological pattern, hormone and environment[13]. Hemihypertrophy of the face, which might be found in up to 50 per cent of the patients, was usually ipsilateral to the nevus[14]. Patients without facial hemihypertrophy might be difficult to recognise during infancy because the only clue for diagnosis was the nevus that might be barely visible until puberty. Because this phenotype was not a constant feature of the patients, a hypothesis that there was a separate subgroup of patients affected by this without facial hypertrophy was suggested[15].

Concerning seizures observed in this syndrome, many types of seizure were observed in infants and children, which might be focal, multifocal and generalized. Myoclonic seizures and infantile spasms were also reported[11,14,15]. However, seizure was not a persistent clinical presentation of all patients despite a demonstrable abnormal EEG recording

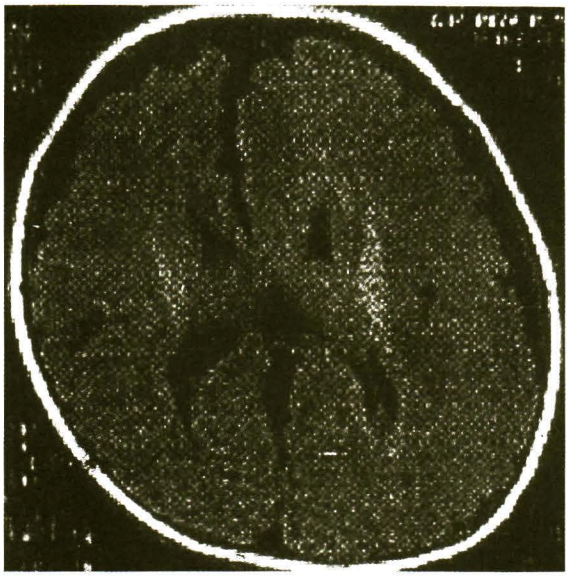

Fig. 3. MRI of the brain demonstrates hemimegalencephaly of the left cerebral hemisphere.

(16,17). In the presented patient, a suppression-burst pattern was the initial finding which, however, was not a specific finding in this syndrome. Seizure and developmental delay that occurred in these patients were related to anomaly of migratory defects(18). The most common striking pathological features was the presence of giant neurons with abnormal dendritic branching in the cortex which might be seen in cortical dysplasia(19,20). However, there was no hemispheric enlargement found in focal cortical dysplasia (20). Seizures occurring in this syndrome were usually protracted and unresponsive to antiepileptic drugs(5). Hemispherectomy was another option in managing intractable seizures which was demonstrated to be beneficial in the control of seizure frequency and severity(21).

In approaching an infant or a child presenting with seizures, diagnosis of the underlying disease might be made simply by thorough evaluation of the skin. Early diagnosis of sebaceous nevus syndrome must be based on the accurate clinical examination to detect a typical skin lesion(15). Though, it was not a common neurocutaneous syndrome and there were some variants, clinical diagnosis of this syndrome could still be made if there was an awareness of its existence. For a patient with classic clinical presentation, prediction of associated anomaly of the CNS such as hemimegalencephaly was also possible(15, 16). MRI is one of the diagnostic tools which would be very helpful in providing more clues for diagnosis. Apart from hemimegalencephaly, focal thickening of the calvarium, hypoplasia of the white matter, cortical calcification and enhanced leptomenigeal drape with contrast injection were other findings(20, 22). For definite diagnosis, skin biopsy should be done to separate this syndrome from others(23).

Concerning the prognosis of this condition, there is a high mortality in the neonatal period. Seizures which occurred in the first month of life was one of the poor prognostic factors(19). With increasing age, there was an increased incidence of tumors including cancers of the skin, breast, salivary gland, stomach, esophagus and ameloblastoma(14). It was also reported to be associated with rickets caused by excretion of a phosphaturic agent(24).

In the presented infant, presumptive diagnosis was made upon admission according to clinical presentation, skin lesion, and exclusion of other possible causes of epilepsy in young infants. Skin biopsy was performed to confirm the diagnosis according to the parent's request for definite diagnosis and for prediction of the prognosis. His seizures remain intractable and developmental milestones were delayed which was similar to the previously reported patients(11,12,15).

In conclusion, the authors reported the case of a one-month-old infant presenting with uncontrolled seizures caused by an uncommon neurocutaneous syndrome. However, the diagnosis was made according to the dermatologic finding and the absence of other causes of seizure. Therefore, with a thorough physical examination and awareness of this syndrome, it would not be difficult for any physician to make the diagnosis. For a patient with typical presentations, recognition of this syndrome would reduce performing any unnecessary investigation that might be a burden for the family.

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โรคลมชักที่ไม่ตอบสนองต่อยากันชักซึ่งเกิดจากกลุ่มอาการซีบาเซียส นีวัสในทารกอายุหนึ่งเดือน

อนันต์นิตย์ วิสุทธิพันธ์, พ.บ., สุรางค์ เจียมจรรยา, พ.บ.*, อมรศรี ชุณหรัศมิ์, พ.บ.*, ดวงรัตน์ ธนกิติวิริยกุล, พ.บ.*, พงษ์ศักดิ์ วิสุทธิพันธ์, พ.บ.**

รายงานผู้ป่วยเด็กทารกอายุ 1 เดือนซึ่งมีอาการชักแบบทั้งตัวตั้งแต่อายุ 2 วัน และไม่ตอบสนองต่อยากันชักที่ได้รับการวินิจฉัยเป็นกลุ่มซีบาเซียส นีวัส จากการตรวจร่างกายที่พบมีความผิดปกติของผิวหนังบริเวณใบหน้า การตรวจภาพสมองด้วยสนามแม่เหล็กไฟฟ้าซึ่งพบขนาดของส่วนคอร์เท็กใหญ่เฉพาะซีก และการตรวจวิเคราะห์ผิดหนัง คณะผู้รายงานได้ทบทวนรายงานการศึกษาจากต่างประเทศ และได้ย้ำถึงความสำคัญที่แพทย์และกุมารแพทย์ที่จะต้องตระหนักถึงกลุ่มอาการความผิดปกติของผิวหนังที่เกิดร่วมกับความผิดปกติของระบบประสาท ซึ่งจะเป็นสาเหตุของการเกิดอาการชักชนิดที่ไม่ตอบสนองต่อยากันชัก

คำสำคัญ : อาการชัก, กลุ่มอาการความผิดปกติของผิวหนัง

อนันต์นิตย์ วิสุทธิพันธ์, สุรางค์ เจียมจรรยา, อมรศรี ชุณหรัศมิ์, ดวงรัตน์ ธนกิติวิริยกุล, พงษ์ศักดิ์ วิสุทธิพันธ์
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* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400