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Original Article

Neuroepidemiology of Porencephaly, Schizencephaly, and Hydranencephaly in Miyagi Prefecture, Japan

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ABSTRACT

BACKGROUND: No population-based surveys of porencephaly, schizencephaly, and hydranencephaly have been conducted in Japan or other Asian countries. We performed a neuroepidemiologic analysis to elucidate the incidence of porencephaly, schizencephaly, and hydranencephaly in Miyagi prefecture, Japan, during 2007-2011. **METHODS:** We sent inquiry forms in February 2012 to three neonatal intensive care units, 25 divisions of orthopedic surgery in municipal hospitals, 33 divisions of pediatrics including one university hospital, municipal hospitals, pediatric practitioners, and institutions for physically handicapped children located in Miyagi prefecture. These covered all clinics related to pediatric neurology and orthopedic surgery in Miyagi prefecture. In the inquiry, diagnostic criteria for porencephaly, schizencephaly, and hydranencephaly were described and representative images of magnetic resonance imaging were shown. We obtained an 82% (27 of 33) response rate from the divisions of pediatrics, a 100% (3 of 3) response rate from the neonatal intensive care units, and a 68% (17 of 25) response rate from orthopedic surgery clinics. The magnetic resonance imaging scans of each patient were retrieved and inspected. **RESULTS:** Five, one, and two individuals developed porencephaly, schizencephaly, and hydranencephaly, respectively. The estimated incidence rates of porencephaly, schizencephaly, and hydranencephaly were 5.2 (95% confidence interval [CI], 0.6-9.8), 1.0 (95% CI, 0.0-3.1), and 2.1 (95% CI, 0.0-5.0) per 100,000 live births, respectively. **CONCLUSIONS:** The prevalence rates of porencephaly, schizencephaly, and hydranencephaly at birth reported herein are compatible with results reported previously in the United States and European countries. The overall prevalence rate of these three diseases was 8.3 (95% CI, 2.6-14.1) per 100,000 live births.

Keywords: porencephaly, schizencephaly, hydranencephaly, epidemiology, prevalence rate

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Introduction

The destructive brain lesions of porencephaly, schizencephaly, and hydranencephaly have long been considered to be related to prenatal vascular events with unknown cause, except for some genetic and infectious causes.[1,2] The term schizencephaly was coined by Yakovlev and Wadsworth[3] in 1946 to describe true clefts formed in the brain as a result of failure of development

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of the cortical mantle in the zones of cleavage of the primary cerebral fissures. Schizencephaly is distinguished from encephaloclastic porencephalies, now known simply as porencephaly.[3] Schizencephaly is a neuronal migration disorder, because the clefts are lined by abnormal gray matter, described as polymicrogyria. In contrast, porencephaly is a postmigration stroke resulting in lesions without gray matter lining the clefts.[3] However, in large infarcts that appear before 6 months of gestation, clastic lesions form cavity or cleft, which is bordered by polymicrogyria.[1,2] Therefore, it has been suggested that both schizencephaly and porencephaly are caused by encephaloclastic regions and can be distinguished depending on the time of insult.[1,2,4,5] A recent study demonstrated that *COL4A1* mutations cause both porencephaly and schizencephaly, as 16% (10 of 61) of porencephaly and 50% (5 of 10) of schizencephaly cases had a heteroplasmic mutation in the *COL4A1* gene.[6] These findings suggest that the same pathologic mechanism results in two conditions as suggested in the previous studies.[1,2,4]

On the other hand, hydranencephaly has long been considered as the most severe end of encephaloclastic porencephaly.[7,8] Diffuse insults to the developing brain, at a time when the brain reacts by liquefaction necrosis, can result in hydranecephaly.[8] Barkovich[9,10] stated that some examples of severe bilateral schizencephaly are similar to hydranencephaly, suggesting a spectrum of encephaloclastic disorders ranging from hydranencephaly to schizencephaly.

No population-based surveys of porencephaly, schizencephaly, and hydranencephaly have been conducted in Japan or other Asian countries. Furthermore, the overall prevalence rate of these three diseases was not studied in the literature. This prompted us to evaluate the incidence of porencephaly, schizencephaly, and hydranencephaly in Miyagi prefecture, Japan.

Method

We studied patients with porencephaly, schizencephaly, and hydranencephaly who lived in Miyagi prefecture and whose illness began between January 1, 2007, and December 31, 2011. First, we sent inquiry forms in February 2012 to three neonatal intensive care units (NICUs), 25 divisions of orthopedic surgery in municipal hospitals, 33 divisions of pediatrics including one university hospital, municipal hospitals, pediatric practitioners, and institutions for physically handicapped children located in Miyagi prefecture, where the population in 2012 was 2,326,957. These covered all clinics related to pediatric neurology and orthopedic surgery in Miyagi prefecture. In the inquiry, diagnostic criteria for porencephaly, schizencephaly, and hydranencephaly were described and representative images of magnetic resonance imaging (MRI) were shown based on the previous reports (Suppl 1, 2).[4,7,11] We obtained an 82% (27 of 33) response rate from the divisions of pediatrics, a 100% (3 of 3) response rate from the neonatal intensive care units, and a 68% (17 of 25) response rate from orthopedic surgery clinics. The MRIs of each patient were retrieved and reviewed independently by two of the authors (KH, NH-F). A disagreement in diagnosis was resolved by the opinion of a third author. The kappa coefficient for porencephaly, schizencephaly, and hydranencephaly was 0.7, 1.0, and 1.0, respectively. A total of 96,136 babies were born between January 1, 2007, and December

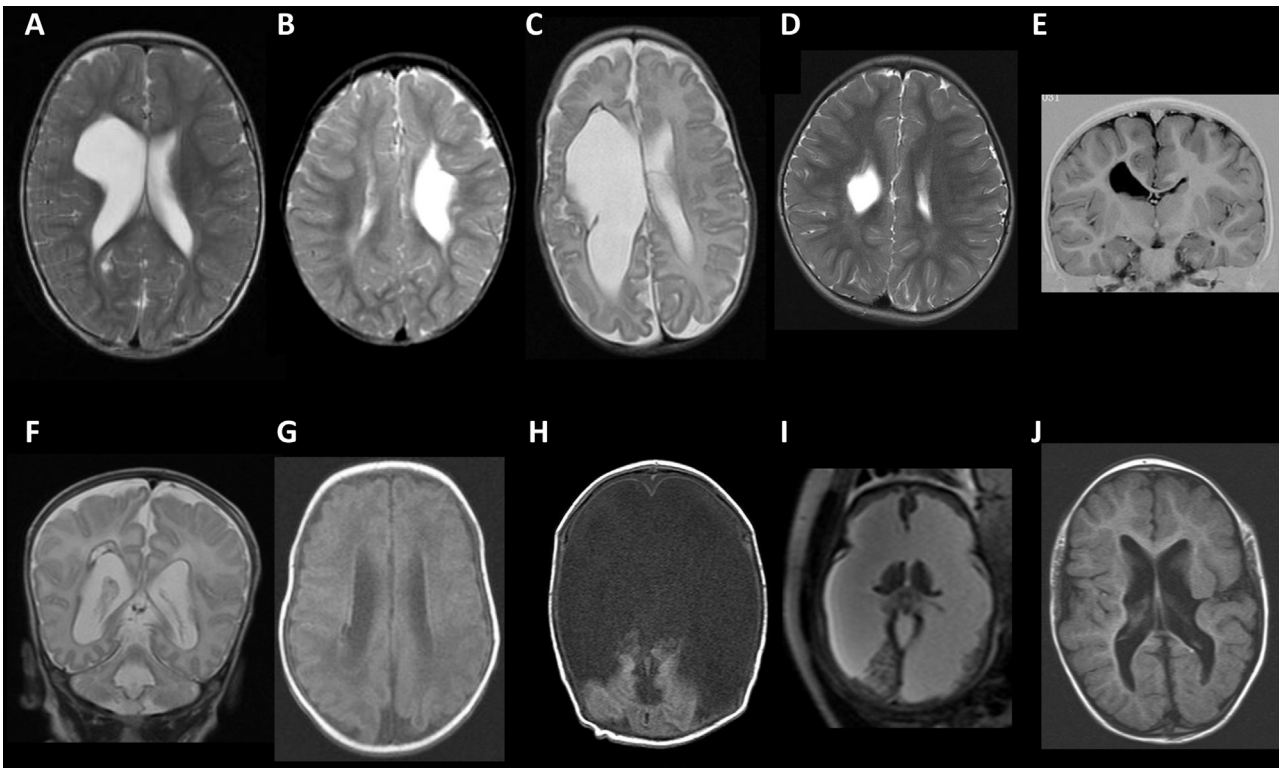

FIGURE.
Magnetic resonance images of patients with porencephaly (Patients 1-5), hydranencephaly (Patients 6 and 7), and schizencephaly (Patient 8). (A) Patient 1 (1 year 10 months), axial T2-weighted image (T2WI); (B) Patient 2 (3 years), axial T2WI; (C) Patient 3 (3 months), axial T2WI; (D, E) Patient 4 (2 years), axial T2WI (D) and coronal short T1-inversion recovery image (E); (F, G) Patient 5 (0 years). Coronal T2*-weighted gradient-echo image (F) and T1WI (G); (H) Patient 6 (7 days), axial T1WI; (I) Patient 7 (32 weeks of pregnancy), fetal axial T1WI; (J) Patient 8 (2 years), axial T1WI.