CLINICAL IMAGE

Hajdu-Cheney syndrome: the first case report in Poland?

Agnieszka Walczak[1], Marta Bladowska[2], Jan Walczak[3], Piotr M. Burak[4], Elżbieta Jurkiewicz[5], Tomasz Stompór[6]

1 Department of Pediatric Surgery, Prof. dr Stanisław Popowski Regional Specialist Children's Hospital in Olsztyn, Olsztyn, Poland
2 Department of Radiology, Prof. dr Stanisław Popowski Regional Specialist Children's Hospital in Olsztyn, Olsztyn, Poland
3 Pantamed – the General Practitioners Group, Olsztyn, Poland
4 Faculty of Medicine, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland
5 Department of Diagnostic Imaging, Children's Memorial Health Institute, Warsaw, Poland
6 Department of Nephrology, Hypertension and Internal Medicine, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland

Hajdu-Cheney syndrome (HCS) is a very rare genetic disorder (less than 50 cases described to date) of an autosomal dominant inheritance, or developing as a result of a de novo mutation in the *NOTCH2* gene encoding the notch2 protein. The mutation results in an enhanced notch2 signaling.[1] Notch is a transmembrane protein involved in several physiological processes, contributing to the cell fate determination and critically influencing tissue development. Notch2 positively regulates receptor-activated nuclear factor–κB ligand–induced osteoclastogenesis which results in bone deformations upon enhancement of this signaling pathway.[1]

The disease affects many body systems with predominant skeletal involvement. Acro-osteolysis is most characteristic of this disease, but other health issues can occur including osteoporosis, skull abnormalities (eg, facial bones), dental problems, hearing loss, deep gravelly voice due to recurrent infections, cardiac defects, and kidney abnormalities (mainly multiple renal cysts). Most serious manifestations include: platybasia (abnormal flattening of the skull base) and basilar invagination. These complications can lead to severe headaches, hydrocephalus, breathing disorders, and even sudden death.[2-5]

A woman aged 21 years at presentation was diagnosed with HCS at the age of 6 years. The diagnosis was based on several imaging techniques that revealed a dolichocephalic skull and the typical facial features: widely spaced eyes, low-set ears, and midface hypoplasia. Other abnormalities included: patent ductus arteriosus (closed shortly after birth), multiple renal cysts, hearing loss, and bone lesions. The latter comprised: wormian bones, platybasia, widened sella turcica, abnormally shaped (shortened and arched) all long bones, pathological fractures of metatarsal bones, acro-osteolysis of phalanges, and delayed bone age (by 5 years). Vertebral lesions were also noticed: biconcave "fish" vertebrae and spondylolisthesis. The medulla oblongata and pons were modelled from the front by bone structures. Other symptoms included hydrocephalus and syringomyelia. The mentioned kidney disorder led to chronic and then end-stage renal failure at the age of 10, and consequently, to a kidney transplant at the age of 12. The patient suffered from recurring respiratory infections and finally respiratory failure that required mechanical ventilation. She died at the age of 21 due to respiratory failure and cardiac arrest. Genetic testing (search for mutation) was not done because of a very typical clinical and imaging phenotype. All the deformities are presented in **FIGURE 1A–1F**.

The patient presented with symptoms considered typical of HCS but their intensity seemed to be higher than in other cases described in the literature. To the best of our knowledge, the case described herein is the first report of the disease in Poland and was the result of a de novo mutation. A causative therapy does not exist for HCS, so the patients can only be treated symptomatically. Cranial base reconstruction was considered but due to high risk, the surgery was cancelled.

Correspondence to:
Prof. Tomasz Stompór, MD, PhD, Department of Nephrology, Hypertension and Internal Medicine, University of Warmia and Mazury in Olsztyn, ul. Żołnierska 18, 10-561 Olsztyn, Poland, phone: +48 89 538 63 73, email: stompin@mp.pl
Received: April 4, 2021.
Revision accepted: April 26, 2021.
Published online: April 29, 2021.
Pol Arch Intern Med. 2021; 131 (6): 571-573
doi:10.20452/pamw.15981
Copyright by the Author(s), 2021

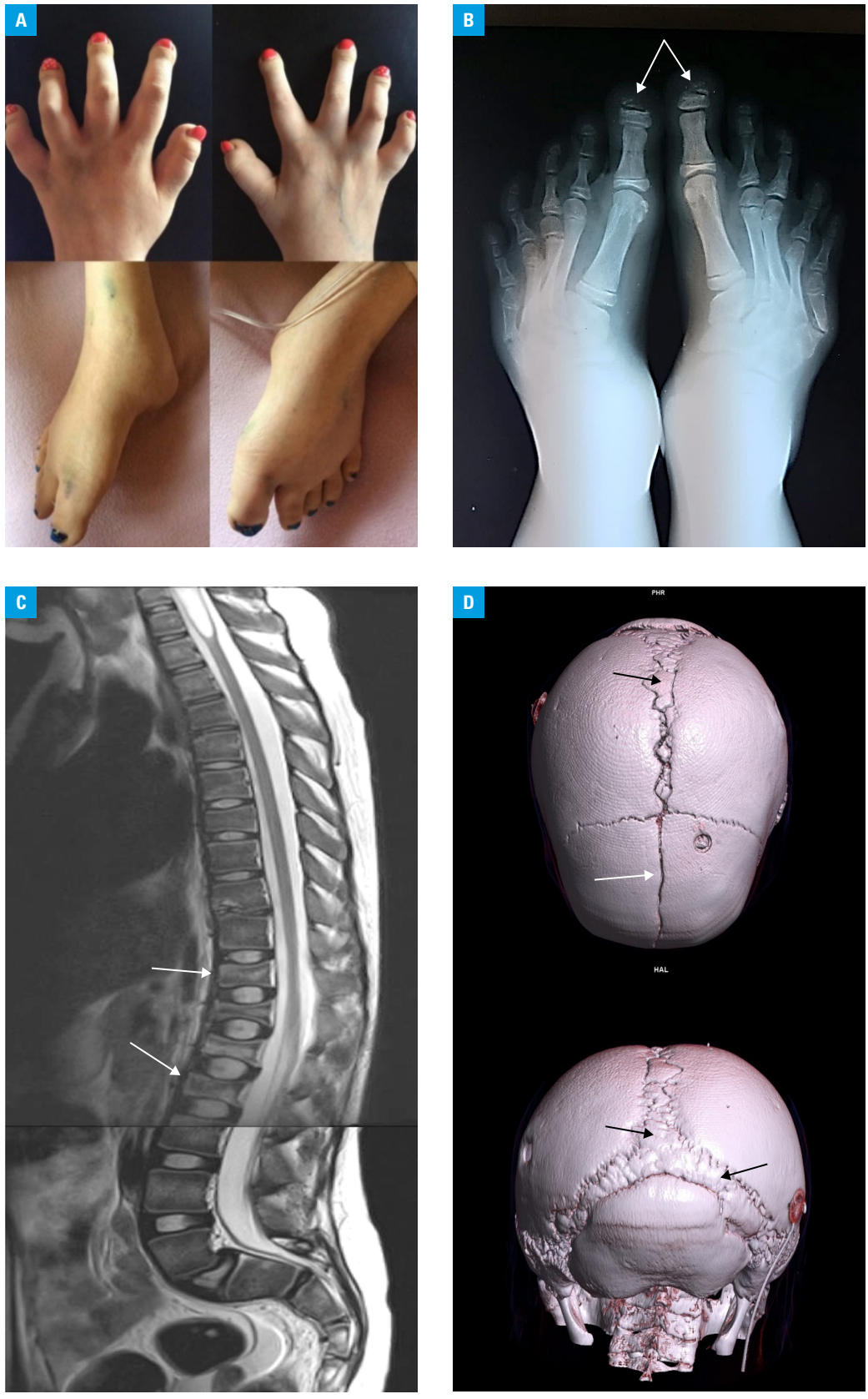

FIGURE 1 **A** – short and broad toes and fingers at the age of 15 years (patent's private archive); **B** – radiograph of feet showing midphalangeal resorption of the terminal phalanges, fractures due to osteoporosis, and joint deformities at the age of 14 (reproduced with permission from the Department of Radiology, Lipno County Hospital, Lipno, Poland); **C** – magnetic resonance imaging of the spine showing osteoporotic compression fractures (white arrows) of T11, T12, L1, and L2 vertebrae at the age of 15 (reproduced with permission from the Department of Diagnostic Imaging, Children's Memorial Health Institute, Warsaw, Poland); **D** – a 3-dimensional computed tomography reconstruction of the skull showing numerous wormian bones (black arrows) filling the significantly widened lambdoid suture and posterior part of the sagittal suture; an anatomical variant, metopic suture (white arrow), can be observed; age of 15 years (reproduced with permission from the Department of Radiology, Children's Memorial Health Institute)

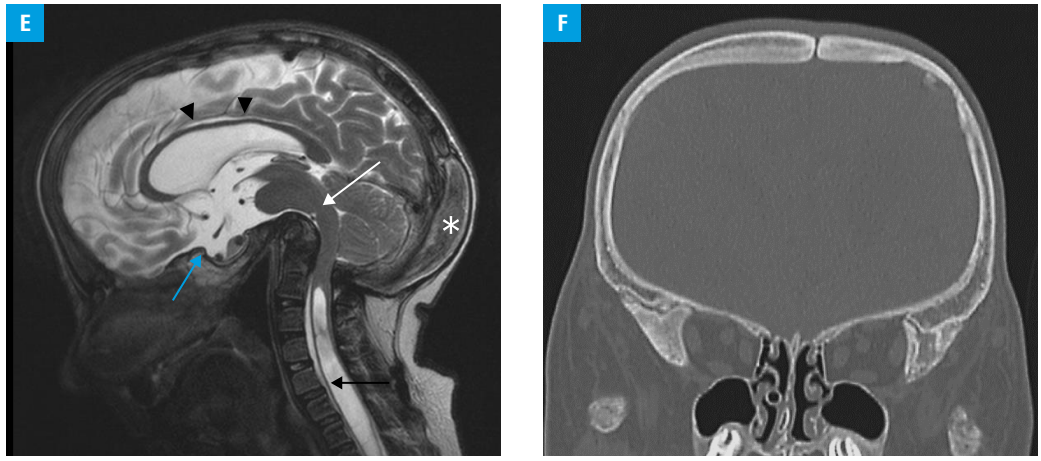

FIGURE 1 **E** – brain magnetic resonance showing platybasia and basilar invagination with J-shaped enlarged sella (blue arrow), bathrocephaly (asterisk), severe brainstem distortion (white arrow) due to the basilar invagination, thin corpus callosum (black arrowheads), hydrosyringomyelia in C2 through T2 vertebrae (black arrow) at the age of 16 years (reproduced with permission from the Włocławek Oncology Center, Włocławek, Poland); **F** – cranial computed tomography showing aplasia of the frontal and sphenoid sinuses, and hypoplasia of the ethmoid sinuses at the age of 16 years (reproduced with permission from the Department of Diagnostic Imaging, Children's Memorial Health Institute, Warsaw, Poland)

ARTICLE INFORMATION

ACKNOWLEDGMENTS The authors would thank to the following institutions for their permissions to use the images: Department of Radiology, Lipno County Hospital, Lipno, Poland; Department of Radiology, Włocławek Regional Specialist Hospital, Włocławek, Poland; Włocławek Oncology Center, Włocławek, Poland.

The authors would like to express their special thanks and appreciation to Mrs MT, the mother of the patient, who kindly shared with us her late daughter's clinical data and asked one of the authors (AW), a close friend of the family, to publish the patient's images for teaching purposes.

CONFLICT OF INTEREST None declared.

OPEN ACCESS This is an Open Access article distributed under the terms of the Creative Commons AttributionNonCommercialShareAlike 4.0 International License (CC BY-NC-SA 4.0), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material, provided the original work is properly cited, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at pamw@mp.pl.

HOW TO CITE Walczak A, Bladowska M, Walczak J, et al. Hajdu-Cheney syndrome: the first case report in Poland? Pol Arch Intern Med. 2021; 131: 571-573. doi:10.20452/pamw.15981

REFERENCES

1 Canalis E, Zanotti S. Hajdu-Cheney syndrome: a review. Orphanet J Rare Dis. 2014; 9: 200.

2 Rodríguez L, Piqueras-Sola B, Rodríguez-Blanque R, et al. Hajdu-Cheney syndrome: a systematic review of the literature. Int J Environ Res Public Health. 2020; 17: 6174.

3 Cheney WD. Acro-osteolysis. Am J Roentgenol Radium Ther Nucl Med. 1965; 94: 595-607.

4 Hajdu N, Kauntze R. Cranio-skeletal dysplasia. Br J Radiol. 1948; 21: 42-48.

5 Brennan AM, Pauli RM. Hajdu-Cheney syndrome: evolution of phenotype and clinical problems. Am J Med Genet. 2001; 100: 292-310.