Radiology Case Reports 19 (2024) 5569–5574

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Sinusitis-associated ischemic stroke in an adolescent patient with Cornelia de Lange syndrome ☆,☆☆

Motoki Yamataka, MD, Satoshi Tsutsumi, MD, Natsuki Sugiyama, MD, Hideaki Ueno, MD, Hisato Ishii, MD*

Department of Neurological Surgery, Juntendo University Urayasu Hospital, Urayasu, Chiba, Japan

ARTICLE INFO

Article history:
Received 18 July 2024
Revised 12 August 2024
Accepted 14 August 2024

Keywords:
Cornelia de lange syndrome
Sinusitis
Ischemic stroke
Internal carotid artery

ABSTRACT

A 17-year-old boy presented with a high-grade fever. The patient had been previously diagnosed with Cornelia de Lange syndrome (CdLS). The patient visited a local physician and was diagnosed with sinusitis. Owing to persistent fever, the patient was referred to our hospital. At the initial presentation, his body temperature was 38.2°C, while maintaining previous living activities and neurological function. Despite changing the antibiotic to amoxicillin, the patient's fever persisted with worsened activity. At the second presentation, the patient presented with left hemiparesis. Blood examination revealed increased white blood cell count and serum C-reactive protein level. Emergency magnetic resonance imaging revealed acute cerebral infarcts in the right cerebral hemisphere, with evident stenosis in the right paraclinoid segment of the internal carotid artery (ICA). In addition, an abscess was found in the cerebellar hemisphere, which was punctured through the burr hole. Computed tomography performed after the completion of antibiotic therapy revealed a restored diameter of the stenotic ICA. Sinusitis can cause ischemic stroke due to compressive stenosis of the paraclinoid ICA, particularly in patients with CdLS. Sinusitis should be preferentially managed in patients with CdLS.

Introduction

Cornelia de Lange syndrome (CdLS) is a rare and complex genetic disorder affecting approximately 1/10,000–100,000 newborns. Patients with CdLS present distinct craniofacial features, growth limitations, limb anomalies, and brain dysgenesis. Mutations associated with CdLS were identified in 7 genes [1–6]. Cerebral atrophy, white matter changes, cerebellar hypoplasia, enlarged ventricles, pituitary tumors or cysts,

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☆☆ Acknowledgments: The authors have no conflicts of interest to declare regarding the materials or methods in this study or the findings specified in this paper.

* Corresponding author.
E-mail address: shotaro@juntendo-urayasu.jp (S. Tsutsumi).

https://doi.org/10.1016/j.radcr.2024.08.071

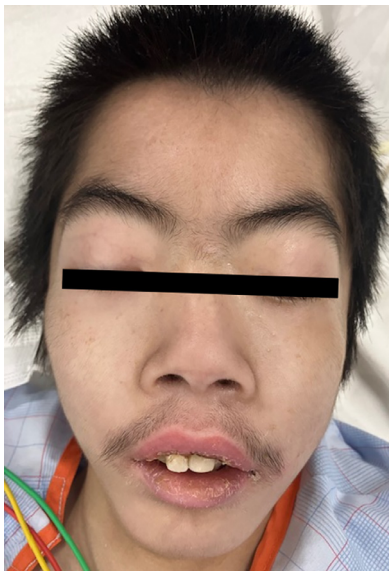

Fig. 1 – Photograph of the patient at the initial presentation showing hypertrichosis and saddle nose, frequent characteristics of patients with Cornelia de Lange syndrome.

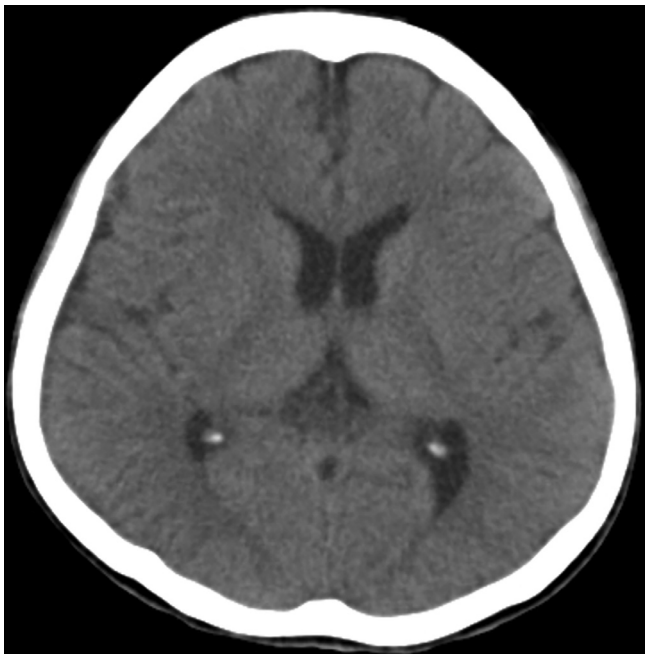

Fig. 2 – Noncontrast axial computed tomography at the initial presentation showing the lateral ventricles with intact appearance.

Chiari I malformation, and gliosis have been documented as characteristic findings on cerebral magnetic resonance imaging (MRI). Jones et al. [7] reported a patient with CdLS and hypoplastic external carotid arteries. Recurrent sinus infections are frequent in patients with CdLS [8,9]. A study has suggested that decreased percentages of regulatory and helper

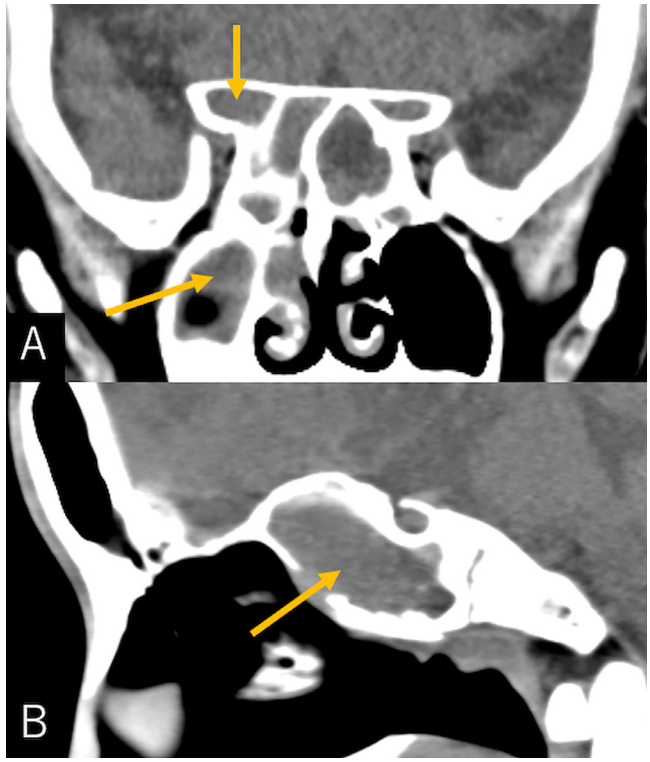

Fig. 3 – Noncontrast coronal (A) and midsagittal (B) computed tomography at the initial presentation showing findings of sinusitis in the maxillary sinus, sphenoid sinus, and unusually developed aeration formed in the anterior clinoid process (*arrow*).

T-lymphocytes and a high frequency of antibody deficiency predispose patients to infections [8].

Most sinus infections are viral, and only a small proportion of patients develop secondary bacterial infections. *Staphylococcus aureus* and anaerobic bacteria, such as *Porphyromonas, Prevotella, Fusobacterium*, and *Peptostreptococcus* species, are thought to be the main isolates of chronic sinusitis [10–12]. Paranasal sinus infections can lead to intracranial abscesses [13]. Sinusitis-associated ischemic stroke is a rare entity, with only a few reported cases to date [14,15].

Here, we present the unique case of an adolescent patient with CdLS who was assumed to have developed sinusitis-associated ischemic stroke.

Case report

A 17-year-old boy presented with a high-grade fever for 5 days. The patient was previously diagnosed with CdLS, presented with severe intellectual disability, and was living in an orphanage with a modified Rankin Scale (mRS) score of 3. His parents had intellectual disabilities and lived in another facility. The patient initially visited a local physician who prescribed levofloxacin for acute exacerbation of chronic sinusitis. The patient was referred to our hospital because of a persistent fever. He presented a body temperature of 38.2°C, while

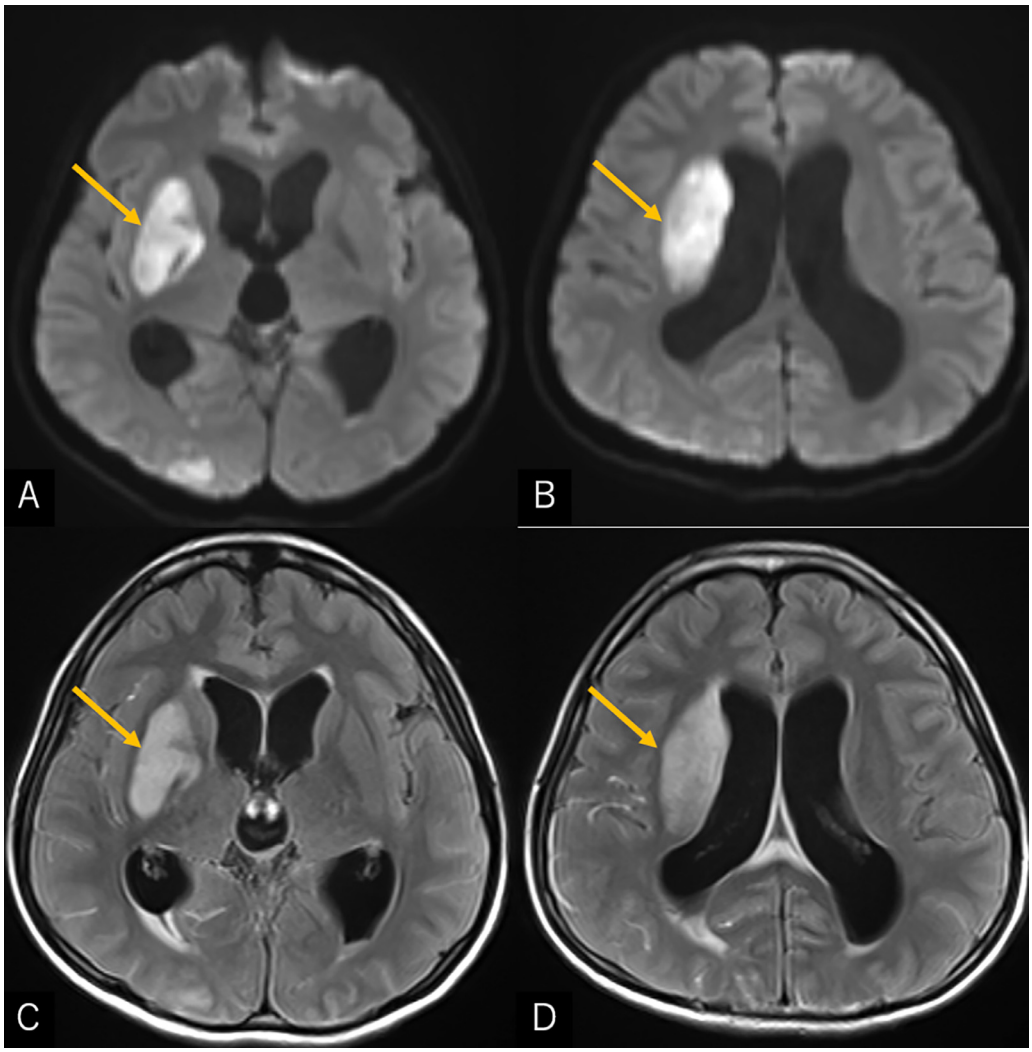

Fig. 4 – Axial diffusion weighted (A, B) and fluid-attenuated inversion recovery (C, D) sequences performed at the second presentation, at the level of the foramina of Monro (A, C) and the body of the lateral ventricles (B, D), showing hyperintense areas in the right putamen and periventricular white matter, suggesting infarcts in acute phase (*arrow*). Ventriculomegaly is also observed.

maintaining his usual living activities and neurological function. Body height and weight were 151 cm and 23.5 kg, respectively. Hypertrichosis and saddle nose, which frequently appear in patients with CdLS, were observed (Fig. 1). Cranial computed tomography (CT) did not detect dysgenesis or lesions in the cerebrum, cerebellum, or brainstem, and the cerebral ventricles appeared intact (Fig. 2). However, findings consistent with chronic sinusitis were observed in the paranasal sinuses, with unusually developed aeration in the anterior clinoid processes (Fig. 3). The patient was diagnosed with persistent sinusitis and was subsequently prescribed amoxicillin. Despite this change in the antibiotic agent, the patient's fever persisted with deteriorating activity. On the second visit to our hospital. His blood pressure was 122/77 mmHg and he showed motor weakness in the left upper and lower extremities. The blood examination showed increased white blood cell count (15900 /μl) and level of serum C-reactive protein (12.7 mg/dL). Chest CT revealed diffuse infiltrative shadows in both lungs, whereas a lumbar cerebrospinal fluid tap suggested neither viral nor bacterial meningitis. The patient underwent emergent cerebral magnetic resonance imaging (MRI), which showed hyperintense areas in the right putamen and periventricular white matter on diffusion-weighted and fluid-attenuated inversion recovery sequences, in addition to ventriculomegaly (Fig. 4). Postcontrast images revealed stenosis of the right paraclinoid segment of the internal carotid artery (ICA). In addition, MR angiography revealed tapered flow in the right paraclinoid ICA (Fig. 5). Furthermore, a cystic mass with a rim-like enhancement was identified in the right cerebellar hemisphere (Fig. 6). Under the diagnosis of cerebellar abscess, an emergency cyst puncture was performed through a burr hole. The cyst was filled with pus containing *Porphyromonas* and *Prevotella* species. Two days later, the patient underwent endoscopic sinus surgery, followed by intravenous administration of piperacillin (4 g/day) for 4 weeks. CT performed at the completion of antibiotic therapy showed

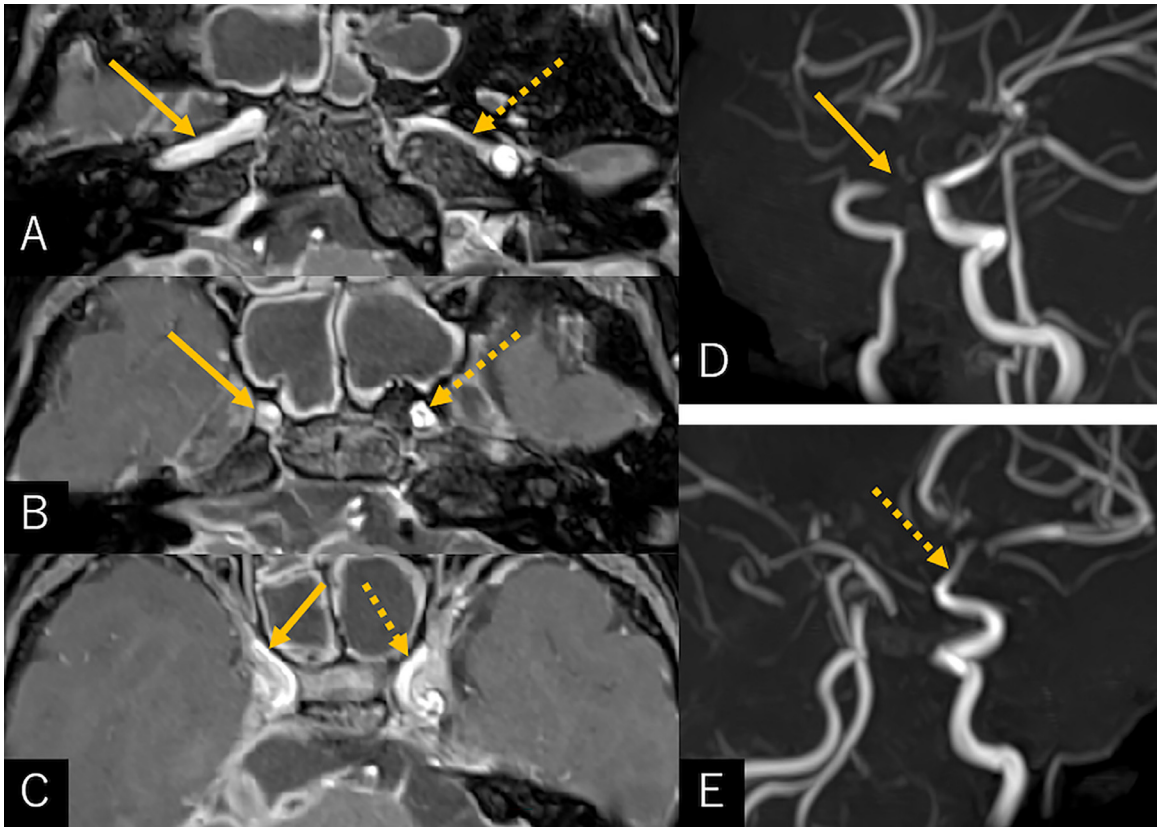

Fig. 5 – (A-C) Postcontrast axial T1-weighted magnetic resonance images at the levels of the petrous (A), cavernous (B), and paraclinoid (C) segments of the internal carotid arteries, performed at the second presentation, showing evident stenosis in the paraclinoid segment of the right internal carotid (C, arrow). (D, E) Cerebral magnetic resonance angiography, oblique views, showing tapered flow of the right paraclinoid ICA (D, arrow). *Arrow:* right internal carotid artery; *dashed arrow:* left internal carotid artery.

significant resolution of the sinusitis (Fig. 7). Post-contrast CT revealed a restored diameter of the right paraclinoid ICA (Fig. 8). The patient underwent ventriculoperitoneal shunting for slowly progressive ventriculomegaly. Eventually, the patient was transferred to an orphanage with an mRS score of 5.

Discussion

CdLS is a rare congenital disorder encountered in clinical practice. Due to the common accompaniment of intellectual disability, the detection of slight neurological deterioration in the early stages of central nervous system involvement may be challenging in patients with CdLS. The present patient experienced hemiparesis after persistent sinusitis. Brain MRI revealed cerebral infarcts in the acute phase and stenotic changes in the ipsilateral paraclinoid segment of the ICA. In addition, the ICA segment was adjacent to the sphenoid sinus. Furthermore, the ICA stenosis resolved after antibiotic treatment for sinusitis. Therefore, we assumed that the ICA stenosis was associated with sinusitis.

Anatomically, the paraclinoid segment of the ICA is surrounded by 3 bony structures in the superior, medial, and inferior aspects: the lower wall of the anterior clinoid process, the lateral wall of the ethmoidal sinus, and the upper wall of the sphenoid sinus, respectively [16]. In our patient, the unusually aerated anterior clinoid processes, ethmoidal sinus, and sphenoid sinus were filled with inflammatory byproducts (Fig. 3). Thus, the paraclinoid ICA may be compressed by the bony walls of these structures during persistent sinusitis. Alternatively, sinusitis adjacent to the paraclinoid ICA may cause vasculitis, resulting in ICA stenosis and consecutive infarctions in perfusion areas [14]. These hypotheses can be strengthened when combined with “CdLS” commonly accompanied by immune deficiency [8]. Symptomatic sinusitis in patients with CdLS should be preferentially managed to avoid ischemic stroke.

In the present case, *Porphyromonas* and *Prevotella* spp. were thought to be the causative organisms of the sinusitis and cerebellar abscesses. These anaerobic bacteria are most frequently isolated in chronic sinusitis; however, they were not isolated in 10 patients with cerebellar abscesses secondary to sinus infections [10,11,13]. Patients with CdLS are at a high risk of infection with atypical pathogenic organisms owing to immune deficiency.

The treatment outcome in our patient was unpromising, with a decreased mRS score. Timely surgical intervention and prompt identification of the causative organism, followed by the administration of effective antibiotics, are crucial when treating infectious diseases in patients with CdLS.

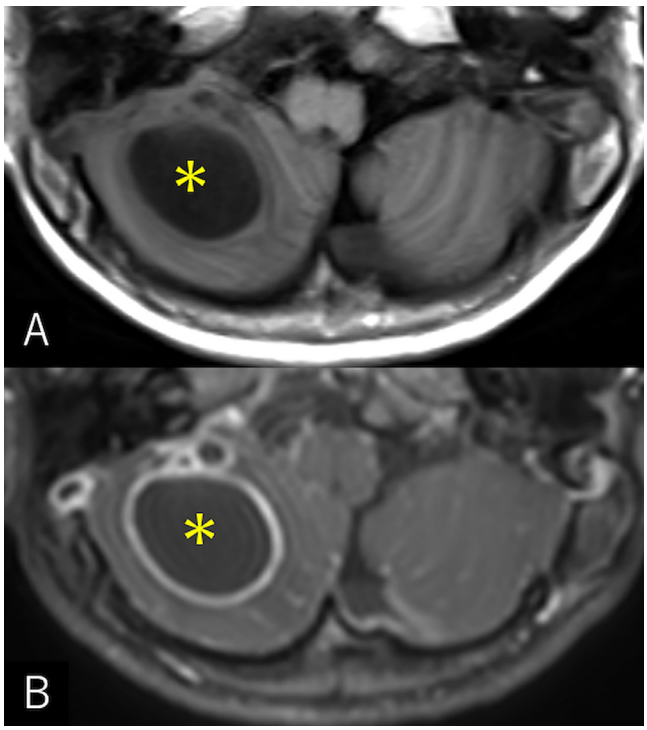

Fig. 6 – Pre- (A) and postcontrast (B) T1-weighted magnetic resonance images at the same level, performed at the second presentation, showing a cystic mass in the right cerebellar hemisphere (*asterisk*) with rim-like enhancement.

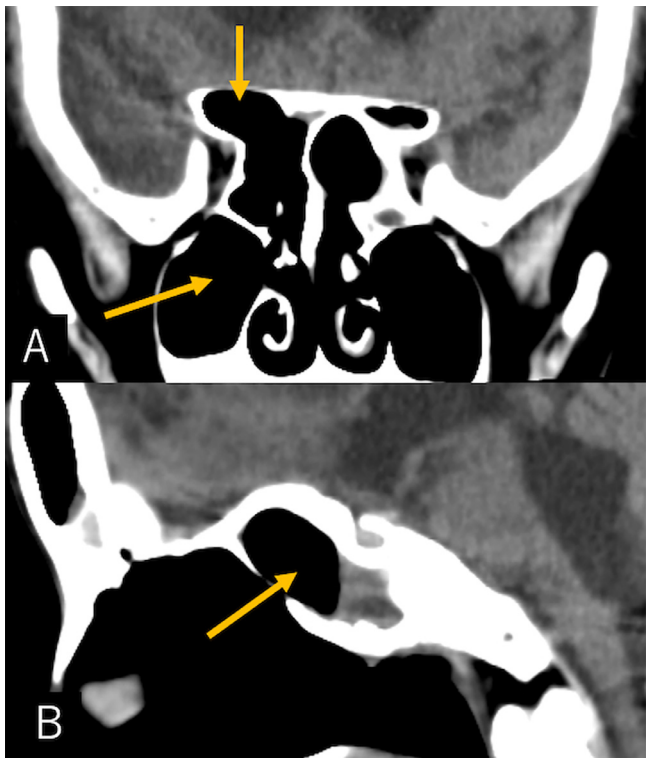

Fig. 7 – Noncontrast coronal (A) and midsagittal (B) computed tomography performed at the completion of antibiotic therapy showing resolution of the sinusitis (*arrow*).

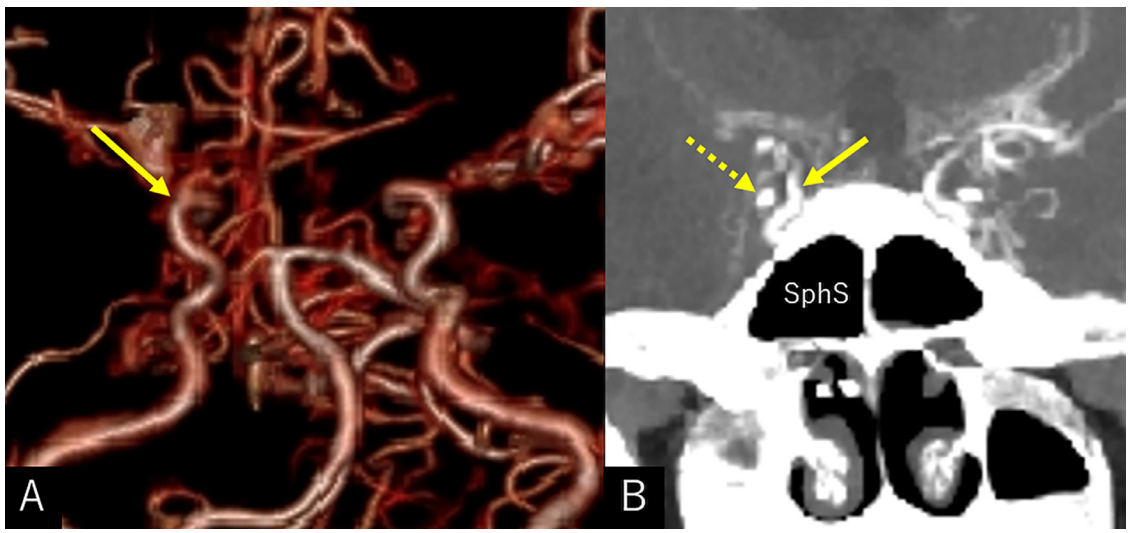

Fig. 8 – Anteroposterior view of the 3-dimensional computed tomography angiography (A) and postcontrast coronal computed tomography (B) performed at the completion of antibiotic therapy showing the paraclinoid segment of the right internal carotid artery restored to normal diameter (arrow). *SphS*: sphenoid sinus; *dashed arrow:* anterior clinoid process.

Conclusion

Sinusitis can cause ischemic stroke due to compressive stenosis of the paraclinoid ICA, particularly in patients with CdLS. Sinusitis should be preferentially managed in patients with CdLS.

Ethical standards

We declare that all procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments.

Patient consent

Written informed consent was obtained from the patient.

Author contributions

All the authors contributed equally to the study.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2024.08.071.

REFERENCES

[1] Deschamps GN. Cornelia de Lange syndrome. Neonatal Netw 2022;41(3):145–9. doi:10.1891/NN-2021-0011.

[2] Gruca-Stryjak K, Doda-Nowak E, Dzierla J, Wróbel K, Szymankiewicz-Bręborowicz M, Mazela J. Advancing the clinical and molecular understanding of Cornelia de Lange syndrome: a multidisciplinary pediatric case series and review of the literature. J Clin Med 2024;13(8):2423. doi.org/10.3390/jcm13082423.

[3] Olioso G, Passarini A, Atzeri F, Milani D, Cereda A, Cerutti M, et al. Clinical problems and everyday abilities of a group of Italian adolescent and young adults with Cornelia de Lange syndrome. Am J Med Genet A 2009;149A(11):2532–7. doi:10.1002/ajmg.a.33075.

[4] Roshan Lal TR, Kliewer MA, Lopes T, Rebsamen SL, O'Connor J, Grados MA, et al. Cornelia de Lange syndrome: correlation of brain MRI findings with behavioral assessment. Am J Med Genet C Semin Med Genet 2016;172(2):190–7. doi:10.1002/ajmg.c.31503.

[5] Yamaguchi K, Ishitobi F. Brain dysgenesis in Cornelia de Lange syndrome. Clin Neuropathol 1999;18(2):99–105.

[6] Yamamoto K, Horiuchi K, Uemura K, Shohara E, Okada Y, Sugimura M, et al. Cornelia de Lange syndrome with cleft palate. Int Oral Maxillofac Surg 1987;16(4):484–91. doi:10.1016/s0901-5027(87)80090-5.

[7] Jones J, Duckwiler G, Tateshima S. Rare cerebrovascular anomalies in a patient with Cornelia de Lange syndrome. Surg Neurol Int 2015;6:74. doi:10.4103/2152-7806.156772.

[8] Jyonouchi S, Orange J, Sullivan KE, Krantz I, Deardorff M. Immunologic features of Cornelia de Lange syndrome. Pediatrics 2013;132(2):e484–9. doi:10.1542/peds.2012-3815.

[9] Kline AD, Grados M, Sponseller P, Levy HP, Blagowidow N, Schoedel C, et al. Natural history of aging in Cornelia de Lange syndrome. Am J Med Genet C Semin Med Genet 2007;145C(3):248–60. doi:10.1002/ajmg.c.30137.

[10] Brook I. Prevotella and porphyromonas infections in children. J Med Microbiol 1995;42(5):340–7. doi:10.1099/00222615-42-5-340.

[11] Brook I. Microbiology of sinusitis. Proc Am Thorac Soc 2011;8(1):90–100. doi:10.1513/pats.201006-038RN.

[12] Stapleton AL, Shaffer AD, Morris A, Li K, Fitch A, Methé BA. The microbiome of pediatric patients with chronic rhinosinusitis. Int Forum Allergy Rhinol 2021;11(1):31–9. doi:10.1002/alr.22597.

[13] Maniglia AJ, VanBuren JM, Bruce WB, Bellucci RJ, Hoffman SR. Intracranial abscesses secondary to ear and paranasal sinuses infections. Otolaryngol Head Neck Surg 1980;88(6):670–80. doi:10.1177/019459988008800608.

[14] Kiramira D, Uphaus O, Othman A, Heermann R, Deschner J, Müller-Heupt LK. Stroke caused by vasculitis induced by periodontitis-associated oral bacteria after wisdom teeth extraction. Brain Sci 2024;14(6):550. doi:10.3390/brainsci14060550.

[15] Righini CA, Bing F, Bessou P, Boubagra K, Reyt E. An acute ischemic stroke secondary to sphenoid sinusitis. Ear Nose Throat J 2009;88(11):E23–8.

[16] Rhoton AL Jr. The sellar region. Neurosurgery 2002;51(4 Suppl):S335–74.