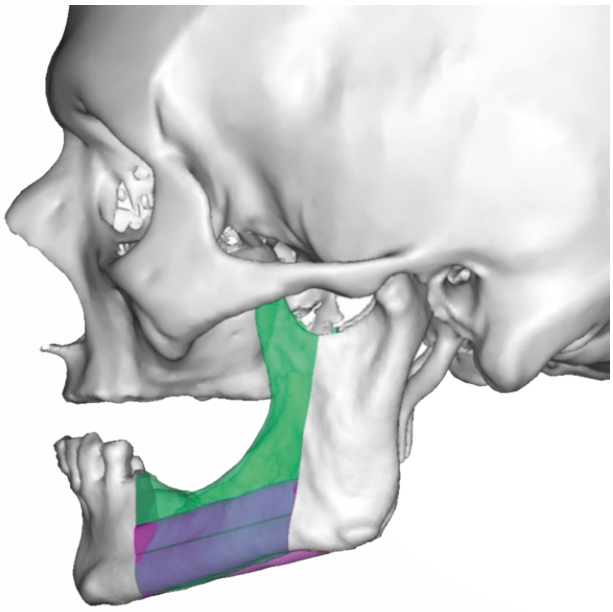
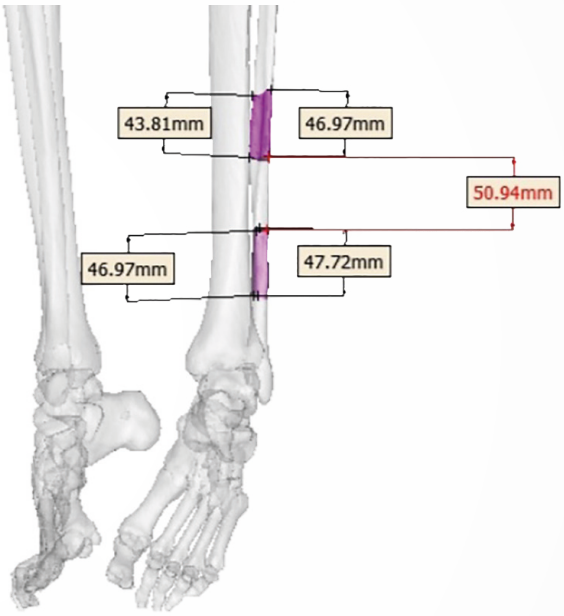
VOLUME 3 • ISSUE 2 • 2019 ISSN 2519-2086

Journal of DIAGNOSTICS & TREATMENT of Oral & Maxillofacial Pathology

2 2019





Section Editor
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Official Journal of the
Ukrainian Association for
Maxillofacial and Oral Surgeons

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щодо медичних виробів

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Goals & Scope

Journal of Diagnostics & Treatment of Oral & Maxillofacial Pathology goals to publish the cutting-edge and peer-reviewed articles on work in oral and maxillofacial surgery and neighboring specialties. The journal includes the following topics: implants surgery, head and neck imaging, microvascular and reconstructive surgery, oral and maxillofacial pathology, head and neck surgery/oncology, TMJ lesions/disorders, head and neck trauma, plastic surgery, pharmacology/drugs.

Official Registered Multilingual Journal Name
Journal of Diagnostics and Treatment of
Oral and Maxillofacial Pathology
Журнал "Діагностика і лікування оральної
та щелепно-лицевої патології"
Журнал "Диагностика и лечение оральной
и челюстно-лицевой патологии"

Registered in Ministry of Justice (Ukraine)
Registration Certificate: КВ №22251-12151P
Issued on July 28, 2016
ISSN 2522-1965 (Online)
ISSN 2519-2086 (Print)

3 (2) 2019

Frequency: 12 times a year

The *Journal* is included to the list of scientific professional publications (issued on December 28, 2017; protocol #1714) of Ministry of Education and Science of Ukraine. In that *Journal* the results of dissertation papers can be published for obtaining the degrees of Candidate and Doctor of Medical Sciences.

Citations
CrossRef, Google Scholar

Founders
Shupyk National Medical Academy of Postgraduate Education
Private Higher Educational Establishment
"Kyiv Medical University"
OMF Publishing, LLC

Investments
Ellet E. (Ukraine)

Marketing and Advertising
Dushyna A.I. (Canada)

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UAMOS webpage: *www.uamos.org*

Is Recommended by
Ukrainian Association for Maxillofacial and Oral Surgeons.

Published by
OMF Publishing, LLC
13-A Simferopolska Street, office 121, Kyiv, Ukraine, 02096
Tel: +38 (097) 301 55 92,
E-mail: *omfpublishing@ukr.net*
Instagram: *omf_publishing*
www.omfpublishing.com
Printed in Ukraine

SUBSCRIPTION INDEX IN UKRAINE: 60077

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February 2019 · VOLUME 3 · ISSUE 2
www.dtjournal.org

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Continued from page EB A2

TANTUM VERDE®

INFORMATION LEAFLET
for the medicinal product

Composition:
active substance: **benzydamine hydrochloride**;
100 mL of solution contain benzydamine hydrochloride 0.15 g;
excipients: ethanol 96%, glycerol, methyl parahydroxybenzoate (E 218), flavor (menthol), saccharin, sodium hydrocarbonate, Polysorbate 20, Quinoline Yellow (E 104), Patent Blue V (E 131), purified water.

Dosage form. Oromucosal solution.
Basic physical and chemical properties: a clear green liquid with a typical mint flavor.

Pharmacotherapeutic group. Dental preparations. Other agents for local oral treatment.
ATC code: A01A D02.

Pharmacological properties.
Pharmacodynamics.
Benzydamine is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and antiexudative properties.

Clinical studies have shown that benzydamine is effective in the relief of symptoms accompanying localized irritation conditions of the oral cavity and pharynx. Moreover, benzydamine has anti-inflammatory and local analgesic properties, and also exerts a local anesthetic effect on the oral mucosa.

Pharmacokinetics.
Absorption through the oral and pharyngeal mucosa has been proven by the presence of measurable quantities of benzydamine in human plasma. However, they are insufficient to produce any systemic pharmacological effect. The excretion occurs mainly in urine, mostly as inactive metabolites or conjugated compounds.

When applied locally, benzydamine has been shown to cumulate in inflamed tissues in an effective concentration due to its ability to permeate through the mucous membrane.

Clinical particulars.
Indications.
Symptomatic treatment of oropharyngeal irritation and inflammation; to relieve pain caused by gingivitis, stomatitis, pharyngitis; in dentistry after tooth extraction or as a preventive measure.

Contraindications.
Hypersensitivity to the active substance or to any other ingredients of the product.

Interaction with other medicinal products and other types of interaction.
No drug interaction studies have been performed.

Warnings and precautions.
If sensitivity develops with long-term use, the treatment should be discontinued and a doctor should be consulted to get appropriate treatment.

In some patients, buccal/pharyngeal ulceration may be caused by severe pathological processes. Therefore, the patients, whose symptoms worsen or do not improve within 3 days or who appear feverish or develop other symptoms, should seek advice of a physician or a dentist, as appropriate.

Benzydamine is not recommended for use in patients hypersensitive to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).

The product can trigger bronchospasm in patients suffering from or with a history of asthma. Such patients should be warned of this.

For athletes: the use of medicinal products containing ethyl alcohol might result in positive antidoping tests considering the limits established by some sports federations.

Use during pregnancy or breast-feeding
No adequate data are currently available on the use of benzydamine in pregnant and breastfeeding women. Excretion of the product into breast milk has not been studied. The findings of animal studies are insufficient to make any conclusions about the effects of this product during pregnancy and lactation.

The potential risk for humans is unknown.

TANTUM VERDE should not be used during pregnancy or breast-feeding.

Effects on reaction time when driving or using machines
When used in recommended doses, the product does not produce any effect on the ability to drive and operate machinery.

Method of administration and doses.
Pour 15 mL of TANTUM VERDE solution from the bottle into the measuring cup and gargle with undiluted or diluted product (15 mL of the measured solution can be diluted with 15 mL of water). Gargle 2 or 3 times daily. Do not exceed the recommended dose.

Children.
The product should not be used in children under 12 years due to a possibility of ingestion of the solution when gargling.

Overdosage.
No overdose has been reported with benzydamine when used locally. However, it is known that benzydamine, when ingested in high doses (hundreds times higher than those possible with this dosage form), especially in children, can cause agitation, convulsions, tremor, nausea, increased sweating, ataxia, and vomiting. Such acute overdose requires immediate gastric lavage, treatment of fluid/salt imbalance, symptomatic treatment, and adequate hydration.

Adverse reactions.
Within each frequency group, the undesirable effects are presented in order of their decreasing seriousness.

Adverse reactions are classified according to their frequency: very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000); frequency unknown (cannot be estimated from the available data).

Gastrointestinal disorders: rare – burning mouth, dry mouth; *unknown* – oral hypesthesia, nausea, vomiting, tongue edema and discoloration, dysgeusia.

Immune system disorders: rare – hypersensitivity reaction, *unknown* - anaphylactic reaction.

Respiratory, thoracic and mediastinal disorders: very rare – laryngospasm; *unknown* – bronchospasm.

Skin and subcutaneous tissue disorders: uncommon – photosensitivity; *very rare* – angioedema; *unknown* – rash, pruritus, urticaria.

Nervous system disorders: unknown – dizziness, headache.

TANTUM VERDE contains methyl parahydroxybenzoate, which can cause allergic reactions (including delayed-type reactions).

Shelf life. 4 years.

Storage conditions.
Do not store above 25°C. Keep out of reach of children.

Packaging.
120 mL of solution in a bottle with a measuring cup; 1 bottle per cardboard box.

Dispensing category.
Over-the-counter medicinal product.

Manufacturer.
Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Italy.

Location of the manufacturer and its business address. Via Vecchia del Pinocchio, 22 – 60100 Ancona (AN), Italy.

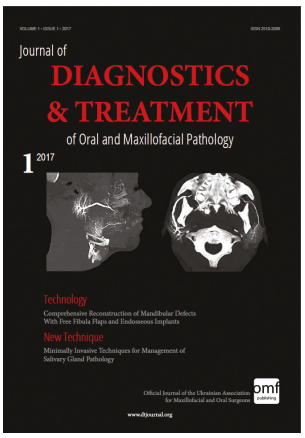
Date of the last revision of the text.
September 26, 2018.

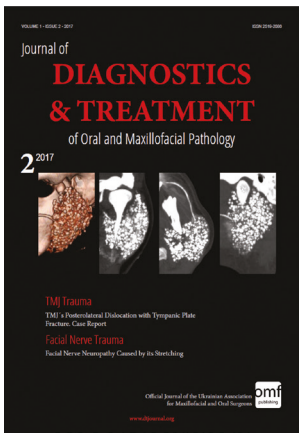
Information leaflet is
APPROVED by
Order of the
Ministry of Health of Ukraine
No. 636 dated 01.10.2015
Registration Certificate
No. UA/3920/01/01

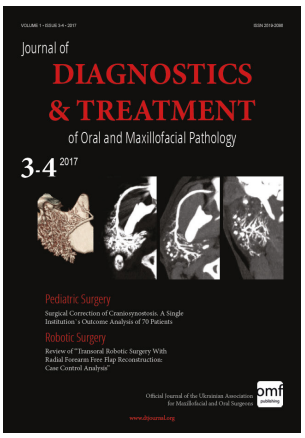
Subscription in Ukraine

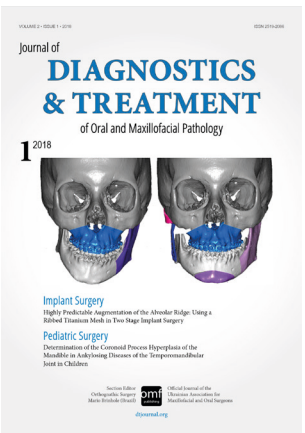
A *Journal of Diagnostics & Treatment of Oral & Maxillofacial Pathology* is published monthly. A subscription for individuals and institutions to the print version of the *Journal* is performed both in any state post offices of Ukrposhta at the territory of Ukraine and online via website www.presa.ua

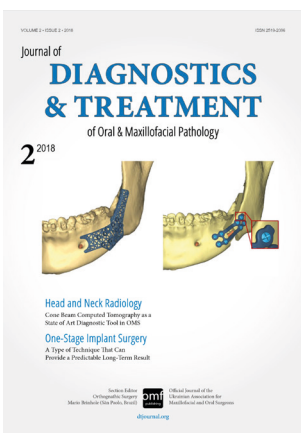
SUBSCRIPTION INDEX IS: 60077

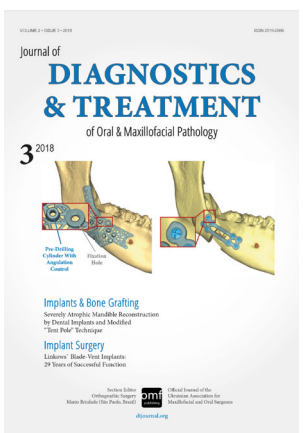


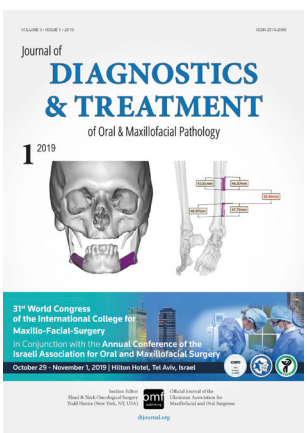


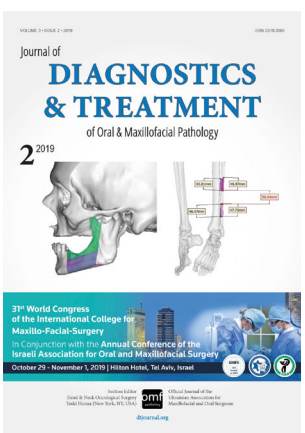












From a January 2019 the *Journal* becomes a monthly publication. Taking into account that individuals or institutions who have already subscribed 4 Issues (in 2019) or will subscribe the *Journal* in 2019 will receive additional 8 Issues free of charge.

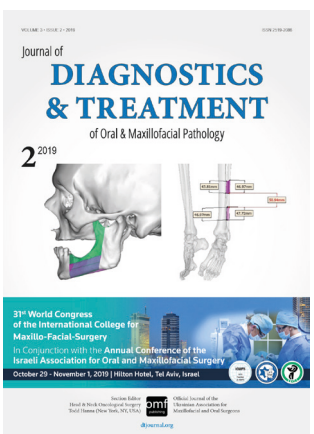
From the end of 2019 it will be possible to subscribe all 12 of 2020-year Issues.

ANOUNCMENT: At the end of the 2019 it will be possible subscribe the *Journal* from any corner of the globe via Journal`s website.

Number of Issues (Numbers)	Cost
4 issues in 2019 (March, June, September, December)	US $ 27.68 (UAH 782.00)
12 issues in 2020	US $ 83.95 (UAH 2 325.12)

Content

of the Volume 3 (Issue 2) 2019



Journal`s cover images
(virtual surgical planning for a bilateral segmental mandibular reconstruction with single fibula segmented transplants) are courtesy of:

Todd Hanna, MD, DDS, FACS (on the *upper image)*

Private Surgical Practice; Todd Hanna, MD, DDS, PC
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WELCOME LETTER

Dear Colleagues,

Tradition and progress coming together.

Maxillofacial surgery is one of the most diverse and challenging professions. We operate while influencing on a person's facial appearance, some of the times unintentionally while at other times in order to improve appearance. We treat bony tissue and soft tissue, functional structures and aesthetic structures, healthy people and sick ones, children and adults. Our field includes numerous procedures; from minor oral surgery and implantology up to major head & neck surgery and reconstruction.

Due to the diversity of our field, an increased number of technological developments are introduced constantly, starting from minimal invasive endoscopic instrumentation up to virtual 3D pre planning of operations and personalized surgical guides and implants.

Research is an important part of our field and completes the clinical activity.

All of the above require us to exchange experiences and developments in our field in order to allow the best possible care for our patients.

In light of the importance of these scientific meetings it is my pleasure to invite you to the 31st World Congress of the International College for Maxillo-Facial-Surgery (ICMFS), which will be held in Tel Aviv, Israel between the 29th of October and the 1st of November 2019 (www.icmfs2019.com).

This congress will include keynote lectures from some of the most experienced and well known surgeons of our field.

In addition, we want this congress to act as a platform for all of you to exhibit your experience as well as your research accomplishments while conducting discussions to improve you as a clinician and researcher.

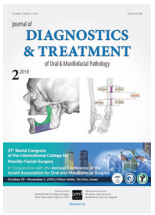
In this congress you will be exposed to keynote lectures, oral presentations, poster presentations, masterclasses, panel discussions, evening receptions and more. You will get the chance to meet new people in your field and form collaborations.

You will have the opportunity to see Israel with all of its historical past and numerous beaches and cultural experience as well as great food and great weather.

We are looking forward to meet you all in the congress and have a wonderful time together in Israel.

Adi Rachmiel, Professor
President, 31st ICMFS World Congress 2019

Dr. Yoav Leiser
President Elect, Israeli Association for Oral and Maxillofacial Surgery



GRATEFUL
WORD

Helpful Hand of a Canadian Medical Team for the Severely Wounded Ukrainian Defenders

"*We must accept finite of the disappointment, but never lose infinite hope*"
—Martin Luther King, Jr.
American Baptist minister and activist

FIGURE. Dr. Antonyshyn and his Ukrainian colleagues performing reconstructive surgery in Military Hospital; Canada-Ukrainian Foundation Mission, Kyiv, 2016. Image is courtesy of Adriana Luhovy.[3]

Oleh M. Antonyshyn, MD, FRCS(C) is a Professor in the Division of Plastic Surgery (University of Toronto) with a subspecialty practice in craniomaxillofacial surgery. Dr. Antonyshyn established a Clinical Fellowship in Adult Craniofacial Surgery in 1993, providing post-residency specialized training in adult craniofacial surgery to candidates from Canada, the United States, Ireland, Israel and the Middle East.[1] In 2008 he was awarded the A. Freiberg Plastic Surgery Resident Teaching Award.[2]

Also, Dr. Antonyshyn serves as:

- Head, Adult Craniofacial Program (founded by Dr. Antonyshyn in 1996), Sunnybrook Hospital (Toronto, ON, Canada).
- Affiliate Scientist, Physical Sciences, Trauma, Emergency & Critical Care Research Program, Sunnybrook Research Institute (Toronto, ON, Canada).[2]
- Full time clinical staff, Division of Plastic Surgery, Sunnybrook Health Sciences Centre (Toronto, ON, Canada).[2]
- Member, Global Advisory Board of the Advanced Cranio-Maxillo-Facial Forum.
- Member, Examination Board in Plastic Surgery for the Royal College.

The impact of contribution of Dr. Antonyshyn, his medical team (Fig), and a Canada-Ukrainian Foundation Mission is enormous. A lot of saved faces, given hope for a better quality of life due to novelty complex rehabilitation operations, multiple prosthesis and plenty of minor esthetic procedures for the Ukrainian defenders.

The statistics of the Canadian and the Ukrainian teams` cooperation from 2014 to 2018 is numerous, and keeps increasing. In the National Military Medical Clinical Center "Main Military Clinical Hospital" (Kyiv, Ukraine) together with the Ukrainian team of Maxillofacial, Neurocranial, Orthopedic, and Otorhinolaryngology Departments were performed 346 consultations and 239 surgeries to the severely wounded defenders of Ukraine.[4, 5] Predominant amount

of patients (85 percent) consists of patients with post-traumatic defects, maxillofacial deformities, cranial, and limbs` injuries[4]. So, the grateful words for Dr. Antonyshyn and Canadian team are endless.

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http://dx.doi.org/10.23999/j.dtomp.2019.2.1

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Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology
2(2019)38-51

Free online article at www.dtjournal.org

Craniofacial Deformities: Report of Cases

Muenke Syndrome: Variable Expressivity between Family Members

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ABOUT ARTICLE

Article history:
Paper received 12 February 2019
Accepted 22 February 2019
Available online 28 February 2019

Keywords:
Muenke syndrome
Coronal suture
Oral anomalies
FGFR3

SUMMARY

Muenke syndrome (MS) is the most common syndromic form of craniosynostosis with an incidence of 1 in 30,000 births, it corresponds to 8 percent of all craniosynostosis.[1, 2] We report a data of a 5-year-old male patient with syndromic craniosynostosis and his father. Clinical view of patient and his father is analyzed. The 3D computed tomography scans are also discussed. A single surgery has been performed as a treatment for coronal craniosynostosis with bilateral frontoorbital advancement with bone grafts.

"A new clinical syndrome is being defined on the basis of the molecular finding in 61 individuals."
—Maximilian Muenke et al, 1997[1]
USA and UK

Craniosynostosis occurs in approximately 1 in 3,000 live births and is characterized by the premature fusion of one or more cranial sutures resulting in malformation of the skull and face. They usually occur as an isolated and sporadic anomaly; however, craniosynostosis is a component in more than 150 described syndromes.

Muenke syndrome (MS) [OMIM #602849] is the most common syndromic form of craniosynostosis with an incidence of 1 in 30,000 births, it corresponds to 8% of all craniosynostosis.[1, 2] This condition has autosomal dominant inheritance with incomplete penetrance and variable expressivity, the classic presentation includes unilateral or bilateral craniosynostosis of the coronal suture,[3, 4] wide thumbs, carpal and tarsal fusion and presence of the c.749C> G mutation (p.Pro250Arg) in the FGFR3 gene[1, 4-6] affecting more severely women.[7]

The clinical phenotype is heterogeneous and varies from few detectable clinical manifestations, "isolated" craniosynostosis, to more complex findings that overlap with other classic craniosynostosis syndromes such as Crouzon syndrome, Pfeiffer or Saethre-Chotzen syndrome. Subtle phenotypes with this mutation such as macrocephaly or minor facial anomalies have also been reported.[7, 8] Some individuals heterozygous for the mutation in the *FGFR3* gene may be clinically and radiographically asymptomatic.[9]

The spectrum of clinical presentation includes unilateral or bilateral synostosis of the coronal suture, occasionally associated with synostosis of other sutures, resulting in maxillary and orbital hypoplasia, associated to bone involvement of the extremities. In unilateral synostosis, the phenotype is presented with plagiocephaly, facial asymmetry (hypoplasia of the middle facial third, dystopia, palpebral ptosis, ogee palate, cleft lip and/or palate, dental malocclusion and mild retrognathia), flattening of the frontal region and anterior implantation of the ear. In contrast to bilateral synostosis in which the facial phenotype is presented with brachycephaly, bulging of the temporal bone and facial asymmetry.[1-3, 5, 6] Conductive hearing loss caused by stenosis or atresia of the external auditory canal and/or malformations of the ossicles has been described[6] and sensorineural hearing loss has been related to impaired maintenance of homeostasis of the inner ear.[10] Additionally, mild osteopenia, scoliosis

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(Mary García–Acero)

http://dx.doi.org/10.23999/j.dtomp.2019.2.2.

and changes in the joints have been described without compromising size.[6] Cognitive development is usually normal, although cases with cognitive impairment have been described in relation to the presence of intracranial hypertension, age of surgical correction, socioeconomic status of the family and schooling of the child.[1] The oral findings described in patients with MS include dental crowding, malocclusion, crossbite and open bite, probably due to the combined effect of high arched palate and the side effects of craniosynostosis in the skull, facial bones and dental architecture.[4]

Patients with syndromic craniosynostosis require multidisciplinary management that includes geneticist, ophthalmologist, otorhinolaryngologist, pediatrician, psychologist, maxillofacial surgeon, and speech therapist.[4] In severe cases of craniosynostosis with elevated intracranial pressure, the mainly treatment is the surgery. For children with less severe problems, the shaping orthoses can help to reorganize the skull to facilitate the normal growth of the brain and improve the general appearance of the head.[11] The surgical correction should be ideally done between 6 to 12 months. The surgical decision should be made based on the aspects that involve: the capacity of brain development for cranial synostosis and the repercussion of intracranial hypertension, as well as the effects generated by mid-facial hypoplasia on the airway, and the commitment of other systems and organs.[12]

MOLECULAR PHYSIOPATHOLOGY

The family of fibroblastic growth factor receptors (*FGFR*) plays an important role in the craniofacial development during endochondral ossification of the skull and face, when interrelated with three receptors in the facial mesenchyme. *FGFR1* is expressed continuously during the development of the craniofacial complex, *FGFR2* is expressed exclusively in the mass of the medial frontonasal mesenchyme, and *FGFR3* is expressed in the caudal portion of the frontonasal region and in the lateral portion of the maxillary prominences.[3, 4] The molecular defects in *FGFR* are related to disorders of the bone tissue, due to changes that produce gain-of-function, through a ligand in a dependent or independent way. Mutations in the *FGFR1*, *FGFR2* and *FGFR3* genes are mainly associated with syndromic craniosynostosis, in which around 500 different syndromes have been described, among which the syndromes of Apert, Crouzon, Pfeiffer, Beare-Stevenson, Jackson-Weiss, and Muenke are highlighted.[2, 3]

The mutation c.749C>G (Pro250Arg) responsible for MS is one of the most common transversions in humans,[6] with a calculated mutational rate of 8×10^{-6} per haploid genome, in addition, there is evidence of the exclusive paternal origin of the mutation, as well as the association with advanced paternal age.[13, 14] Molecular confirmation of the Pro250Arg mutation is not only important for genetic counseling, also for patient management purposes. In the study reported by Thomas et al[15] in individuals with unicoronal or bicoronal synostosis and nonspecific phenotype, it was found that those with MS with molecular confirmation tended to require reoperation due to increased intracranial pressure after surgery.

Case

We report a 5-year-old male patient, product of first pregnancy of non-consanguineous parents, with history of sensorineural hearing loss in hearing aid management and neurodevelopmental delay. Evidence at physical examination of brachycephaly with temporary overlapping of bones, triangular face, broad forehead, broad metopic suture, facial asymmetry (hypertelorism, oblique palpebral fissures directed downward, scarce eyebrows, palpebral ptosis, mediofacial hypoplasia, depressed nasal bridge), auricular pavilions facing posterior, nasal wing hypoplasia, flat philtrum, high arched palate, microrethrognathia, thin upper lip (Fig 1A and B). The rest of the physical examination evidenced low height and brachydactyly (Fig 1C).

Computed tomography (CT) with three-dimensional reconstruction of the skull showed bilateral synostosis of the coronal suture (*synonym*: coronal synostosis), increase of the posterior digital marks, and increase of the space of metopic suture (Fig 2).

Regarding the coexistence of craniosynostosis and brachydactyly, syndromic craniosynostosis was considered. Genomic DNA was isolated from a peripheral blood sample to perform the next-generation sequencing panel of genes associated with syndromic craniosynostosis, this test revealed heterozygous variant c.749C>G (p.Pro252Arg) in the *FGFR3* gene, previously reported as pathogenic associated to MS. The study of segregation of the variant exhibited that the father was the carrier of the variant, physical evaluation revealed (Fig 3) a slight spectrum of the condition with broad forehead, brachycephaly, facial asymmetry (hypertelorism, oblique palpebral fissures directed downward, scarce eyebrows, palpebral ptosis), flat philtrum and thin upper lip.

A single surgery has been performed as a treatment for coronal craniosynostosis with bilateral frontoorbital advancement with bone grafts. Currently, the patient is in multidisciplinary monitoring by geneticist, maxillofacial surgeon, neurosurgeon, endocrinologist, and otorhinolaryngologist. Comprehensive management with language therapies is also indicated.

Discussion

The main characteristic of MS is coronal synostosis that can be unilateral or bilateral. Since the syndrome was

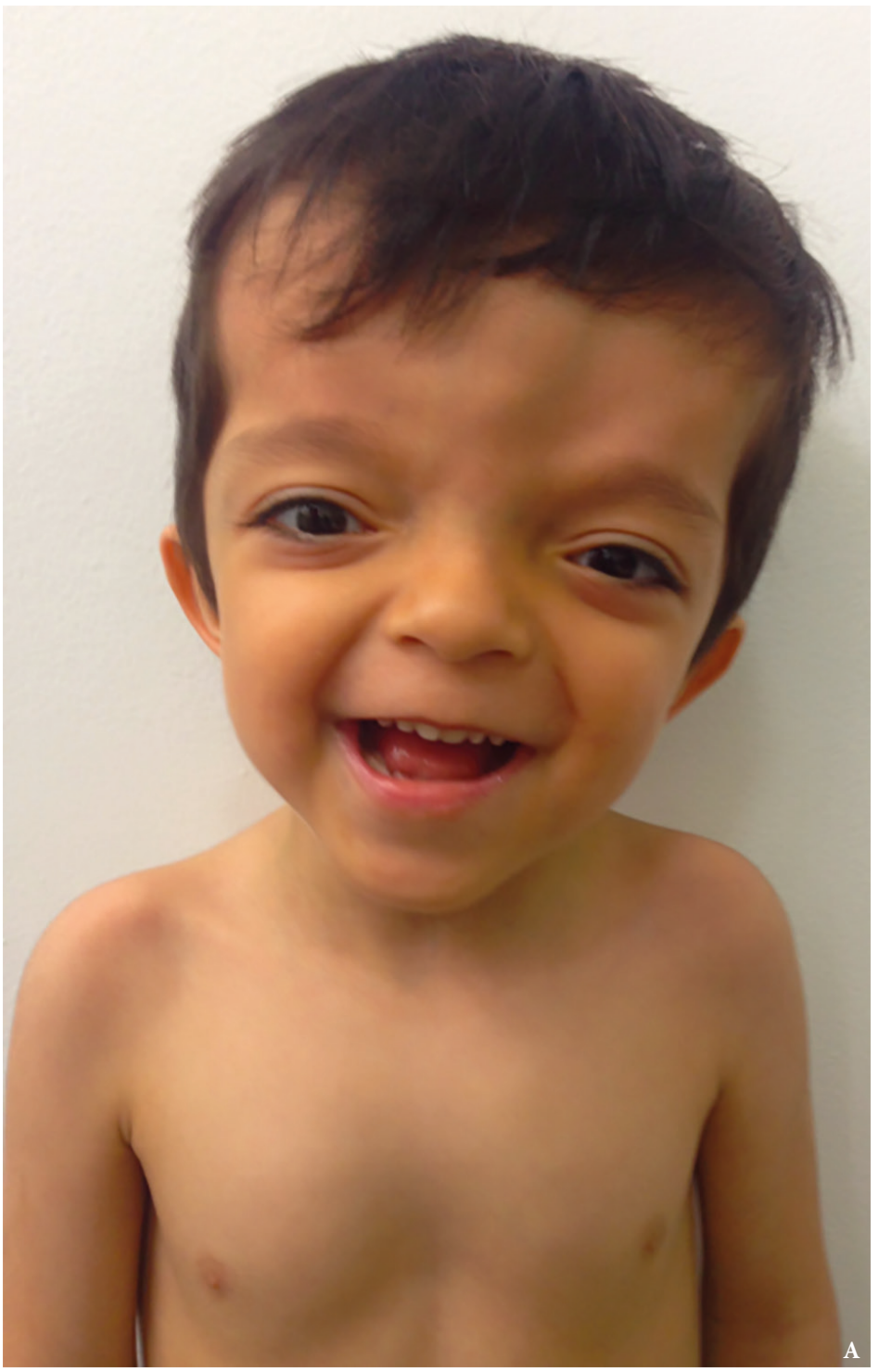

FIGURE 1. Frontal (**A**) of a 5-year-old patient with brachycephaly (the shape of a skull shorter than typical skull), triangular face, broad forehead, facial asymmetry (hypertelorism, oblique palpebral fissures directed downward, scarce eyebrows, palpebral ptosis, and depressed nasal bridge), flat philtrum, thin upper lip and micrognathia. **(Fig 1 continued on next page.)**

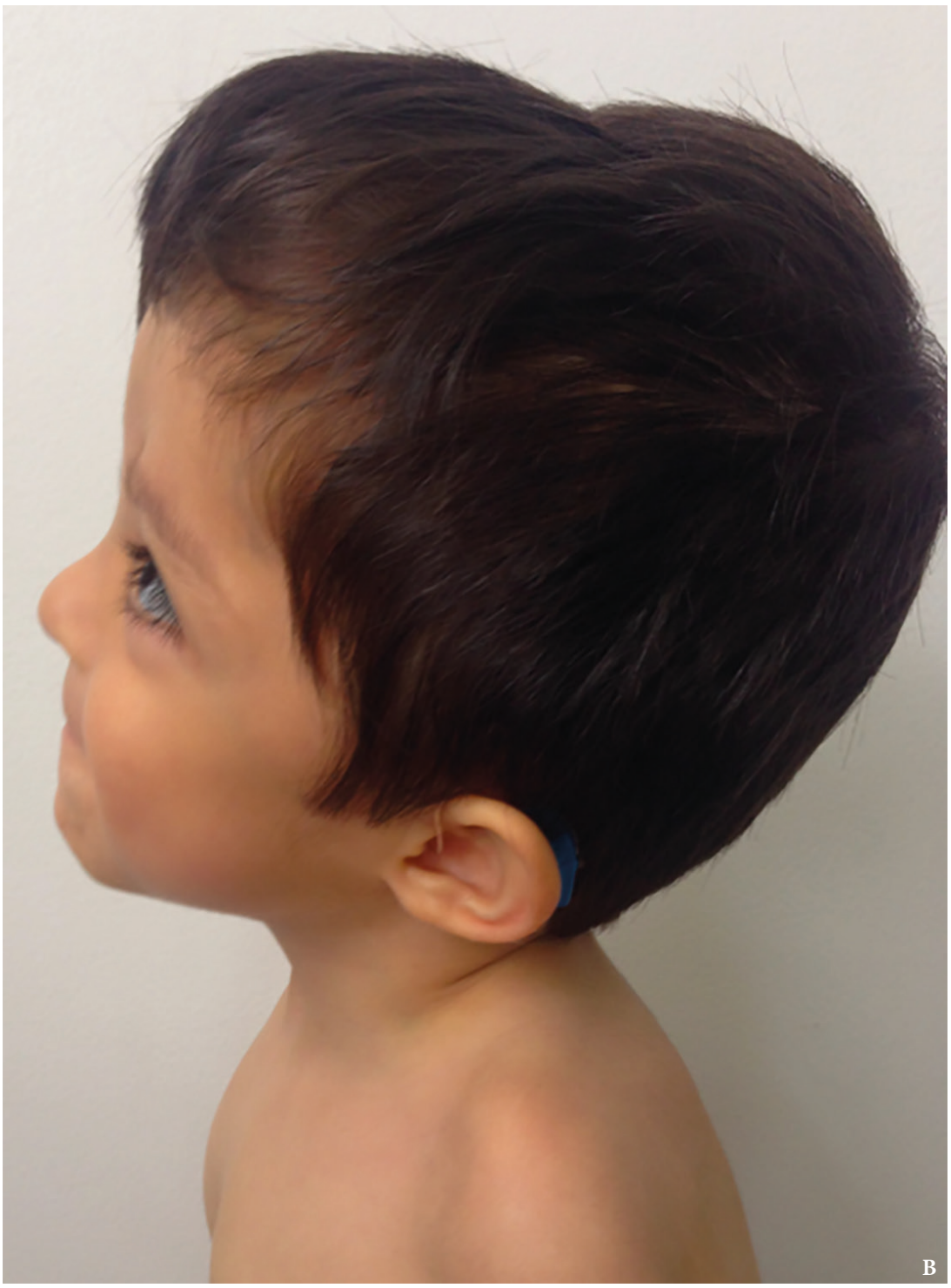

FIGURE 1 (cont'd). Left side view (**B**) of a 5-year-old patient with brachycephaly (the shape of a skull shorter than typical skull), triangular face, broad forehead, facial asymmetry (hypertelorism, oblique palpebral fissures directed downward, scarce eyebrows, palpebral ptosis, and depressed nasal bridge), flat philtrum, thin upper lip and micrognathia. **(Fig 1 continued on next page.)**

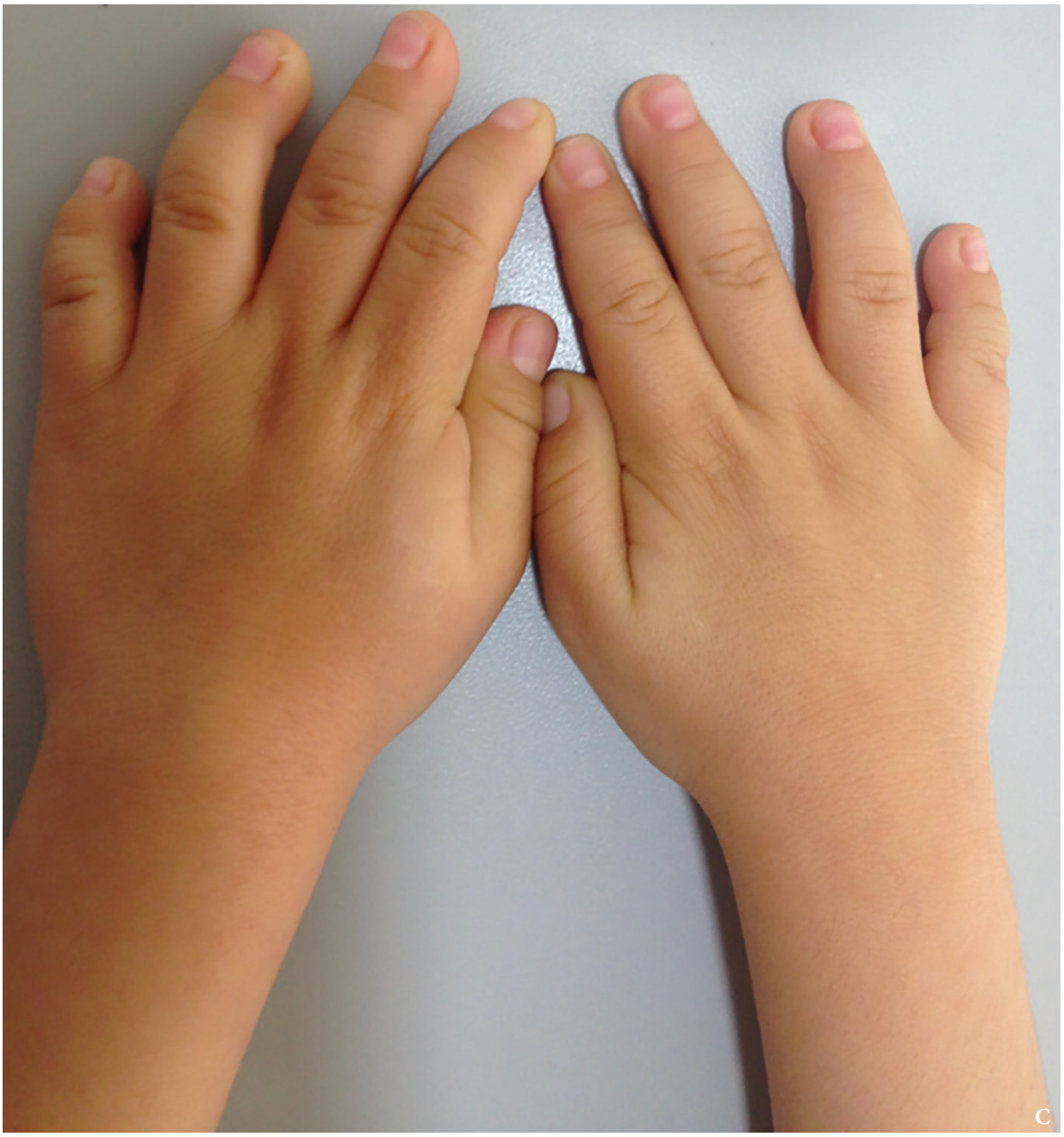

FIGURE 1 (cont'd). Photograph of a 5-year-old patient's hands. (**C**) A brachydactyly (a shortening of the fingers) is noted.

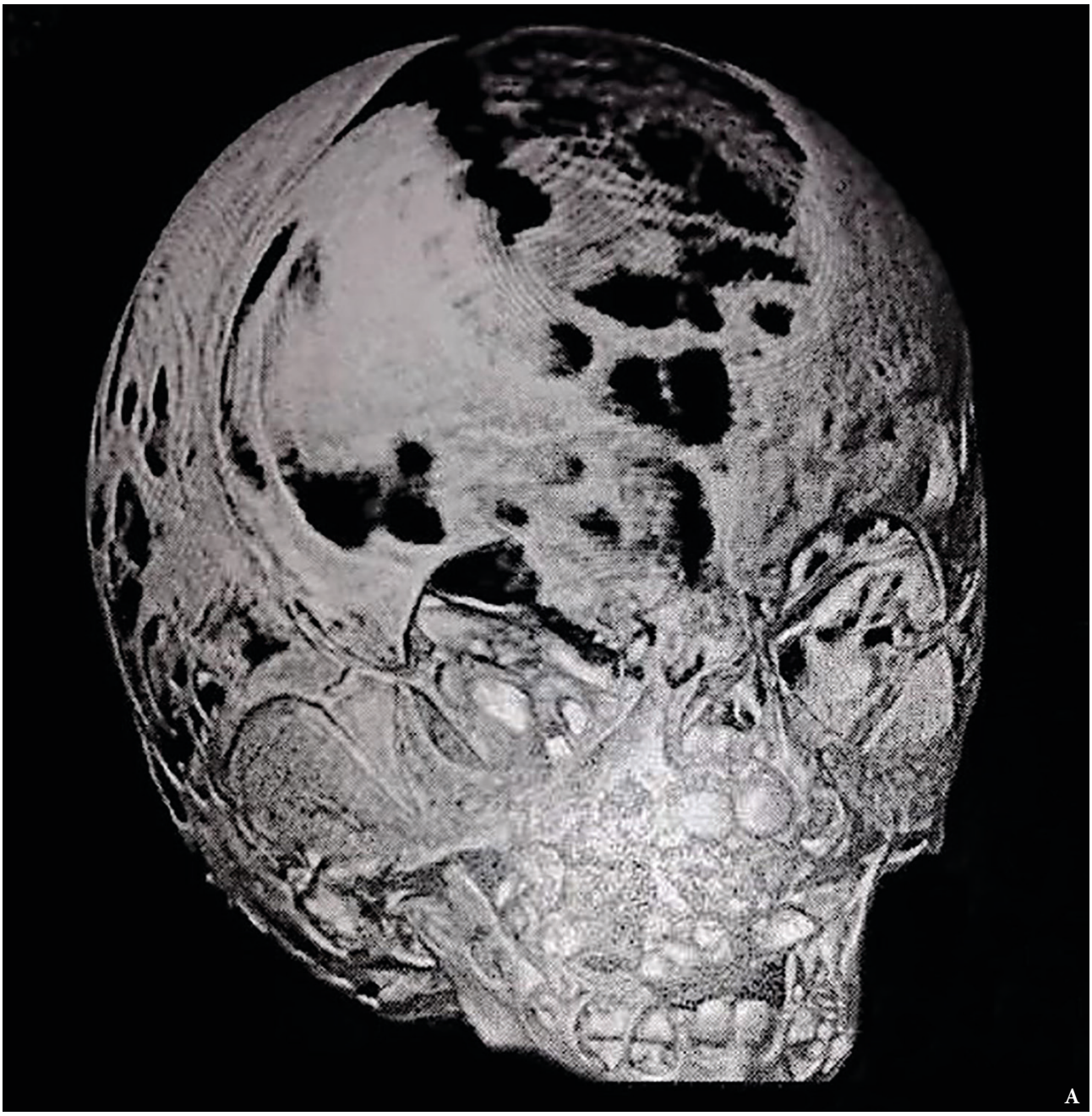

FIGURE 2. (**A**) Three-dimensional (3D) reconstruction CT scan of the skull evidence bilateral synostosis of the coronal suture, increase of the posterior digital marks. Noted the increase of the space of metopic suture. **(Fig 2 continued on next page.)**

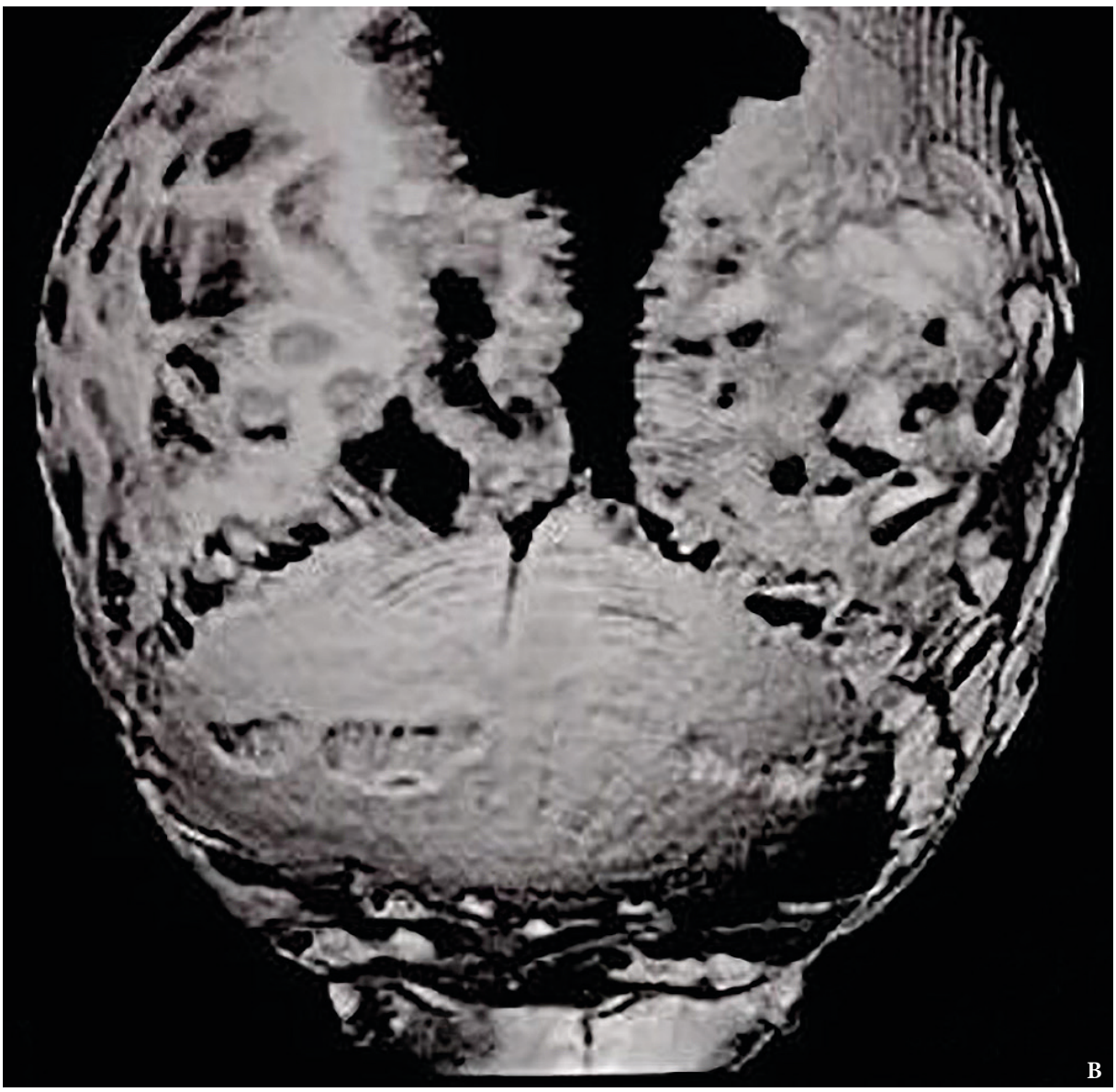

FIGURE 2 (cont'd). 3D reconstruction CT scans of the skull: posterior view (**B**). The increase of the space of metopic suture (*asterisk*) is noted. **(Fig 2 continued on next page.)**

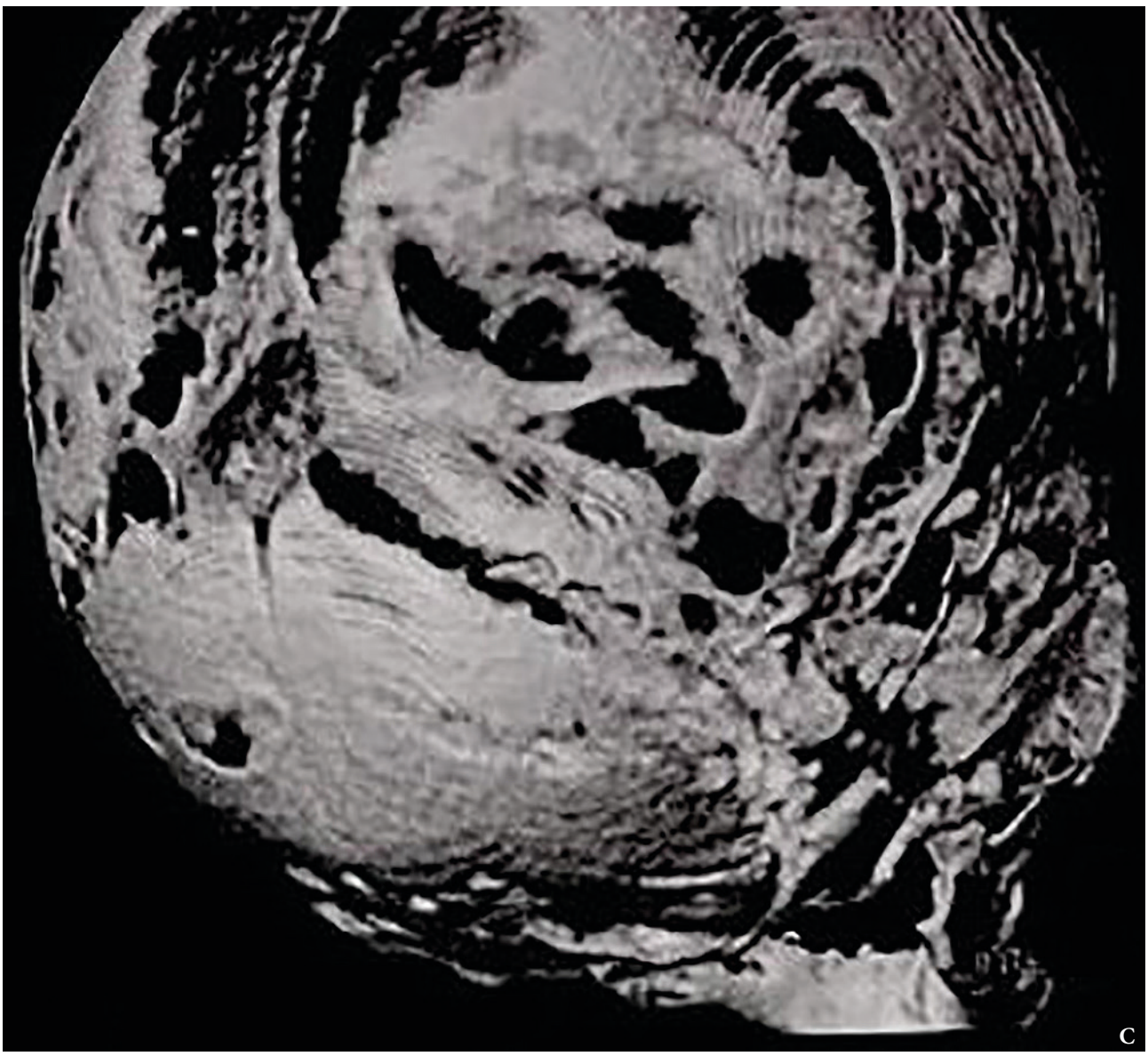

FIGURE 2 (cont'd). 3D reconstruction CT scans of the skull: left posterolateral view (**C**). The increase of the space of metopic suture (*asterisk*) is noted. **(Fig 2 continued on next page.)**

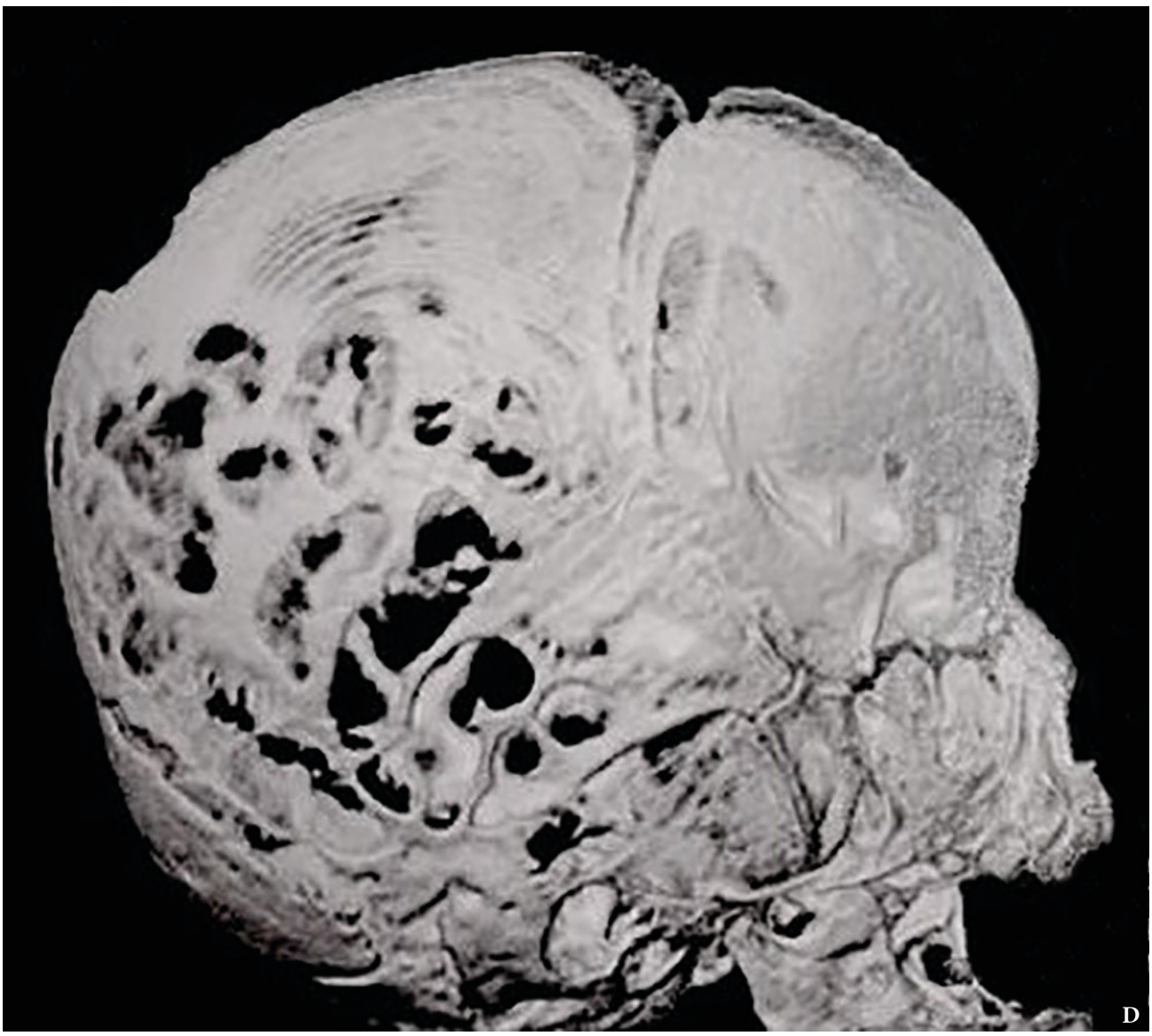

FIGURE 2 (cont'd). 3D reconstruction CT scans of the skull: left lateral view (**D**). **(Fig 2 continued on next page.)**

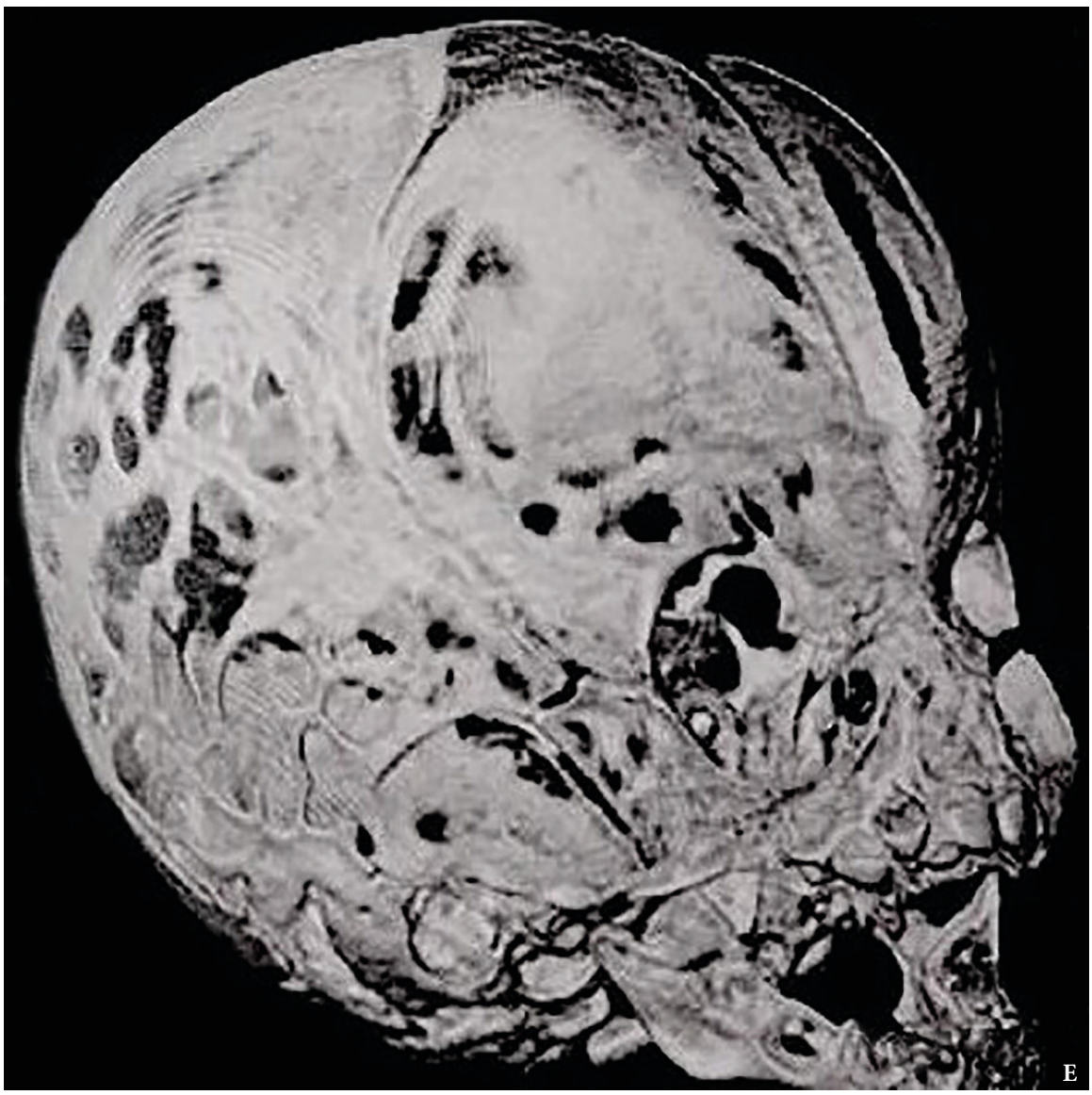

FIGURE 2 (cont'd). 3D reconstruction CT scans of the skull: left anterolateral view (**E**).

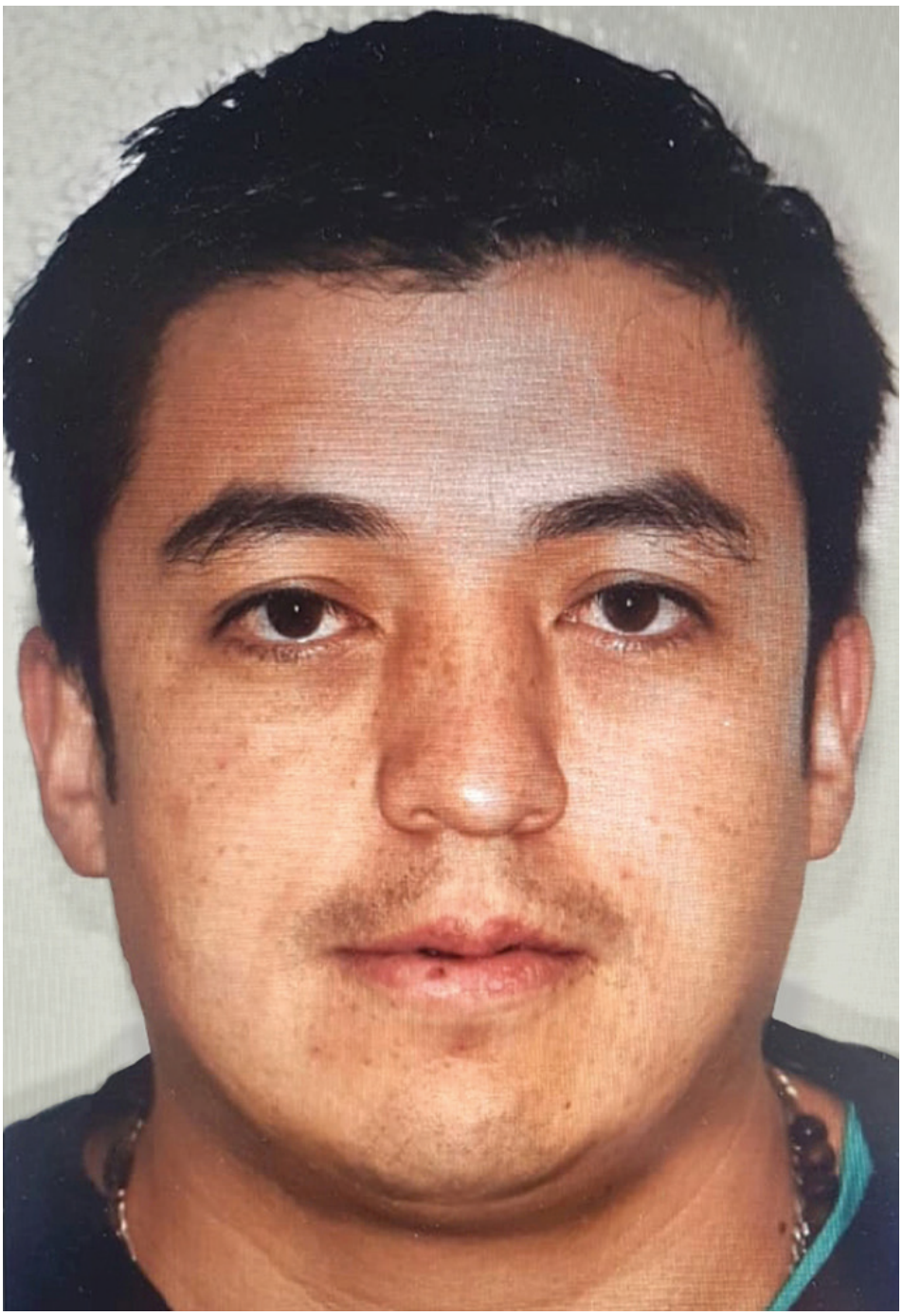

FIGURE 3. Patient´s father. Frontal view with broad forehead, brachycephaly, facial asymmetry (hypertelorism, oblique palpebral fissures directed downward, scarce eyebrows, palpebral ptosis), flat philtrum, thin upper lip, and micrognathia. Slight expression of MS related to the son.

described for the first time,[1] several cases have been described[5, 6, 16] that have contributed to the broader description of the phenotype originally described.

People with Muenke syndrome have the lowest incidence of cleft palate among the most common craniosynostosis syndromes. However, the high and/or cleft palate has been reported in some cohorts,[4, 17] therefore, orofacial anomalies should merit clinical attention, since palatal alterations cause interference with the tensor veli palatini muscle and predispose to recurrent and long-term chronic otitis media with increased risk of conductive hearing loss, among other complications.

The cranial surgical procedure is often delayed until facial growth is completed, decreasing the rate of reoperation by excessive frontal bulging. Affected individuals with significant degrees of orbital hypertelorism will require medial accommodation of their orbits through surgical osteotomies, a procedure carried out beyond 5 years of age to ensure adequate surgical correction. Malocclusion`s problems are treated with maxillary and orthodontic orthopedics to allow establish an adequate occlusion.

TABLE 1. Clinical Management Suggested in Individuals With Muenke Syndrome.

Three-dimensional CT images of the skull
Monitoring of measured head circumference and simple CT
Initial skeletal radiographs[a]
Auditory evoked potentials*
Multidisciplinary evaluation[b,*]
Sleep study
Neurodevelopment monitoring
Consider teaching supports
Orthodontic/dental evaluation

[a] Discard associated skeletal anomalies (eg, brachydactyly).
[b] Multidisciplinary team should include: neurosurgeon, otorhinolaryngologist, ophthalmologist, phonoaudiologist, maxillofacial surgeon, geneticist, psychologist, and pediatrician.
** Perform periodically.*

As the occlusion is related to the position of the jaw and maxilla, a treatment plan must be formulated not only to achieve a normal dental occlusion, but also to optimize the aesthetic result of the individual's appearance.

Historically, the care of individuals with syndromic craniosynostosis has focused purely on the correction of the cranial defect and the monitoring of neurological, ocular and auditory complications. However, the literature and this case demonstrate the importance of other associated anomalies, which is why it is suggested in all cases of craniosynostosis to perform routine oral examination and orthodontic evaluations, as well as to follow the clinical management suggested in Table 1.

Given the variable expressivity of the MS and the reduced penetrance of the gene, it is recommended that the parents of the patients be carefully evaluated by radiographic and molecular study to identify the affected relatives. The genetic risk of recurrence depends on the state of the parents with respect to the variant, if a parent has the pathogenic variant FGFR3 p.Pro250Arg, the risk of inheriting this variant to their offspring is 50%. When the parents are not affected clinically and do not have the pathogenic variant, the risk for the offspring is low, but not null, due to the possibility of germinal mosaicism. The proband's offspring have 50% risk of inheriting the variant.

Role of the Co-authors
The co-authors are eaqully contributed to that paper. All of them read and approved the final manuscript.

Fundings

No funding was received for this study.

Acknowledgements

We thank to the patient and his family for their kind cooperation and their permission to publish this report.

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Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology
2(2019)52-75

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Craniofacial Deformities: Original Research

Three-Dimensional Computed Tomography Imaging in the Evaluation of the Child With Craniosynostosis: Study of 60 Patients*

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ABOUT ARTICLE

Article history:
Paper received 08 February 2019
Accepted 18 February 2019
Available online 28 February 2019

Keywords:
Craniosynostosis
Cranial sutures
Neuroimaging
3D CT
Scaphocephaly
Brachycephaly

ABSTRACT

Purpose. The aim of this article is to describe and illustrate the appearance of craniosynostosis on CT scan images.
Methods. A total of 60 children during the years 2014-2018 were included. The medical and radiographic records of patients less than 3 years of age, clinically diagnosed with nonsyndromic craniosynostosis were studied. They underwent CT imaging examination in order to confirm the diagnosis and to accurately establish the surgical treatment plan.
Results. The high diagnostic performance of CT with 3D surface-rendered reconstructions was pointed out together with the most common findings.
Conclusion. 3D CT appears as the imaging modality with the best diagnostic performance in children with craniosynostosis. However, large prospective studies and further research are needed, in order to clearly define the role of 3D CT and minimize the unnecessary exposure of infants to radiation.

"CT imaging is currently considered the criterion standard for diagnosing craniosynostosis."
—Jeffrey A. Fearon, 2012[1]
USA

Craniosynostosis is an important clinical entity in the pediatric population resulting in significant cosmetic and functional effects. This pathological condition of infancy, characterized by partial or complete premature fusion of one or multiple cranial sutures, leads to characteristic skull shape deformities and facial asymmetry.[1] It occurs in approximately 3.5–4.5 out of 10,000 live births worldwide. It can affect one or multiple sutures, occur as an isolated defect or be associated with a craniofacial syndrome. The incidence of non syndromic cases is higher compared to syndromic.[2]

Premature fusion of a suture leads to growth restriction of the skull perpendicular to the suture`s axis. This results in characteristic anomalies of skull shape, which can be readily diagnosed clinically and with imaging. The main causes of morbidity in craniosynostosis are increased intracranial pressure, headaches, neurodevelopmental delay, visual defects and cosmetic deformities.[3]

Although the diagnosis of craniosynostosis can be clinical, all imaging techniques contribute to the accurate diagnosis of the entity. The overall goal of neuroimaging for infants with craniosynostosis is the early detection and description of this entity to enable appropriate treatment.[4] Delayed diagnosis and treatment may lead to cosmetic calvarial deformity which may be difficult to correct, or may require more extensive cranial reconstruction. In addition, may cause a potentially irreversible neurological impairment. Specific imaging aims include detailed characterization of the number of sutures, exact extent of the suture fusion, demonstration of the resulting

* This manuscript has not been presented

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http://dx.doi.org/10.23999/j.dtomp.2019.2.3.

craniofacial deformities, as well as the underlying structural brain changes and the coexisting anomalies or complications.[5]

Classically, plain skull radiography is the initial technique used in the evaluation of a child with an abnormal head shape due to its greater availability, low cost and reduced risk.[6] Three-dimensional computed tomography (3D CT) is considered the gold standard for the diagnosis of craniosynostosis in the assessment of infants with abnormal skull shape, as it can provide highly detailed 3D images of the skull, along with information about the possible coexisting anomalies of the brain.[7]

As a rule, 3D CT is the imaging modality of choice for syndromic cases, provided that the number and extent of suture fusion are described in detail.[8] On the other hand, for nonsyndromic cases, the suggested diagnostic algorithm includes plain radiographs for the initial assessment, followed by 3D CT only to establish the complex surgical treatment plan. With all this theoretical background, the objective of the current article is to present the characteristic radiologic features of craniosynostosis on 3D CT imaging.

Methods

At the Department of Pediatric Surgery, Division of Pediatric Craniofacial Surgery at the National Institute of Children Diseases, a total of 60 children (36 males and 24 females) with nonsyndromic craniosynostosis have been monitored by 3D CT while creating the treatment plan according to the guidelines of the World Medical Association (Declaration of Helsinki). In addition, a standard measurement protocol, examined and approved by the Institutional Ethical Committee was used.

The average age at the time of first presentation was 5.2 months, with a range between 3.2 and 9.4 months (Chart 1). All patients underwent primary surgery with open cranial vault reconstruction, with the minimum requirement for 3D CT examination preoperatively to confirm the diagnosis and to create the ideal surgical protocol. Evaluation of each case was performed clinically and radiographically by the author in consultation with a pediatric neuroradiologist. Every CT scan was examined carefully and all characteristic radiographic features were pointed out in addition to the clinical picture of each child.

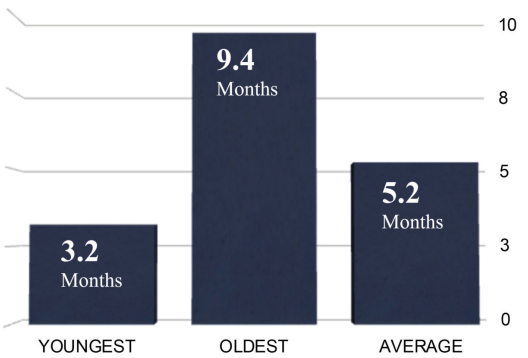

CHART 1. Distribution of age (months) at the time of diagnosis.

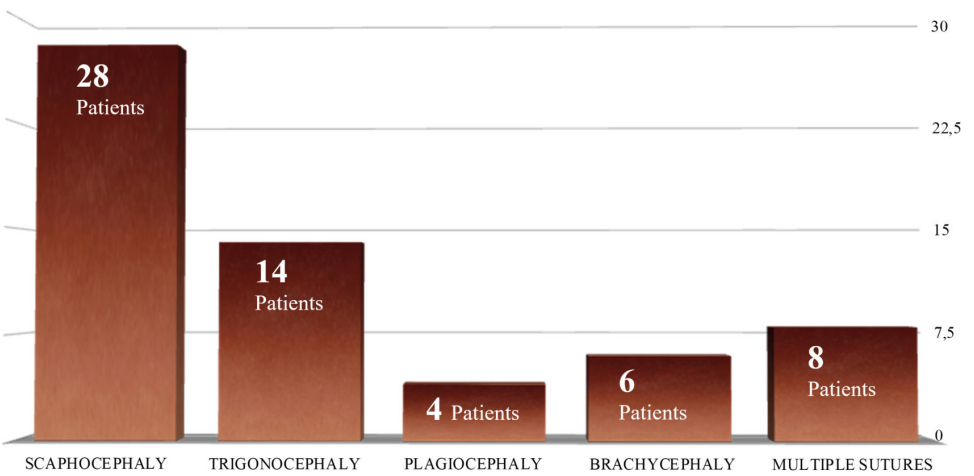

CHART 2. Distribution of patients with head shape deformity as a result of craniosynostosis.

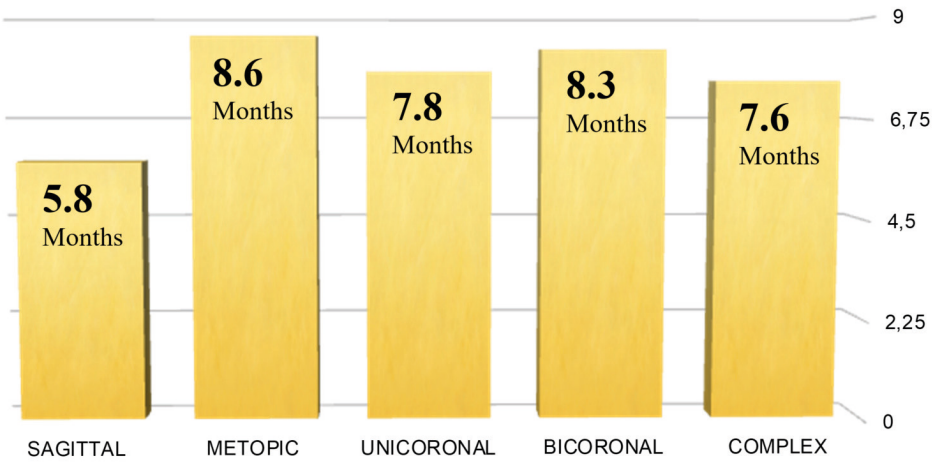

CHART 3. Average age (months) at the time of diagnosis in relation to the synostotic suture.

Results

Sagittal synostosis was the most common synostosis and included approximately 50 percent of our cases (Chart 2). The mean age at the time of first presentation was 5.8 months (Chart 3). Fusion of the sagittal suture restricts growth in the transverse dimension (perpendicular to the suture axis), with compensatory overgrowth in the anteroposterior dimension (along the suture axis). This resulted in a narrow elongated skull with increased AP dimension and decreased transverse dimension (Fig 1A-D). Prominent frontal and occipital protuberances as well as ridging at the suture were seen. The term dolichocephaly describes the skull's shape after the early synostosis of the sagittal suture. Scaphocephaly is a subgroup of dolichocephaly, including evident ridging of the sagittal suture, alike to the boat's keel.

Fourteen children demonstrated a premature closure of the metopic suture at a mean age of 8.6 months at the time of first consultation. Premature fusion of the metopic suture results in symmetrical bone growth at the sagittal suture and asymmetric bone growth at the coronal sutures. This produced a characteristic triangular or pear-shaped frontal deformity called trigonocephaly (Fig 2A-D). Trigonocephaly corresponds to the resulting deformity from synostosis of either the metopic suture (anterior trigonocephaly), or the posterior third of the sagittal suture and both the lambdoid sutures (posterior trigonocephaly). Associated findings included hypotelorism, parietooccipital bossing, narrow anterior cranial fossa, lateral orbital hypoplasia, characteristic metopic notch noted on the inner side along the suture line, metopic ridge on the outer side of the suture, hypoplastic ethmoid sinuses, deficient supraorbital ridges, and a medial upward slanting of the orbital roofs.

The 4 children enrolled in the study with premature unilateral coronal synostosis had a median age of 7.8 months at the time of first meeting. Unilateral coronal synostosis caused restricted growth in the AP dimension and compensatory overgrowth in the transverse dimension, which resulted in anterior plagiocephally over the fused suture, with ipsilateral temporal expansion and contralateral frontal and parietal expansion (Fig 3A-D). Associated findings included shallow anterior cranial fossa, shallow orbits, depression of the petrous bone, and the "harlequin eye deformity" (upward slanting of the orbital roof laterally).

Six children with premature bilateral coronal suture synostosis were included in our series with a mean age of 8.3 months at the time of first evaluation. Bilateral coronal synostosis resulted in decreased AP dimension of the calvaria, which is called brachycephaly (Fig 4A-D). An abnormally tall head (turricephaly) results from symmetrical bone growth along the sagittal and metopic sutures. Bicoronal synostosis is often associated with other synostoses and malformation syndromes.

Eight children with multiple sutures` synostosis presented to our department. The average age during first examination was 7.6 months. Four patients demonstrated a fusion of the unilateral coronal suture in association with the sagittal suture (Fig 5A-D). Three patients presented with fusion of the metopic and sagittal sutures and one patient encountered fusion of the metopic suture together with the coronal sutures bilaterally. Complex craniosynostosis usually occurs in syndromic cases. Deformities depend on varying combinations of sutures involved. Nevertheless, in cases of combined synostosis of all major sutures, the skull has a cloverleaf appearance, which is the most impressive craniofacial deformity.

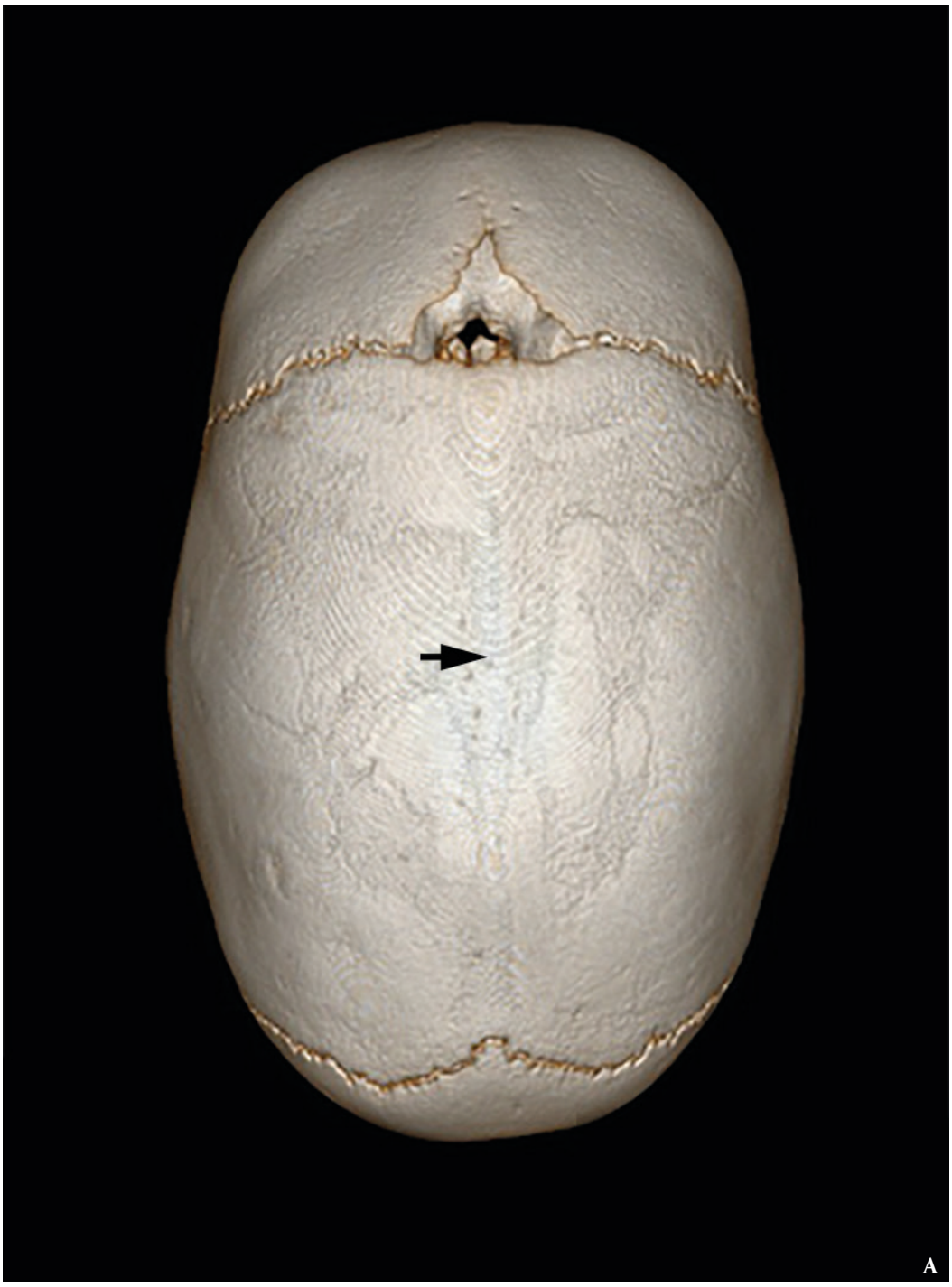

FIGURE 1. Superior view (**A**) of 3D-CT volume-rendered image of a 6-month-old boy with premature, complete fusion (*arrow*) of the sagittal suture. It results in increased anteroposterior diameter, along with bitemporal narrowing due to restriction of biparietal growth. Prominent ridging of the sagittal suture is observed, as well as frontal and occipital bulging. **(Fig 1 continued on next page.)**

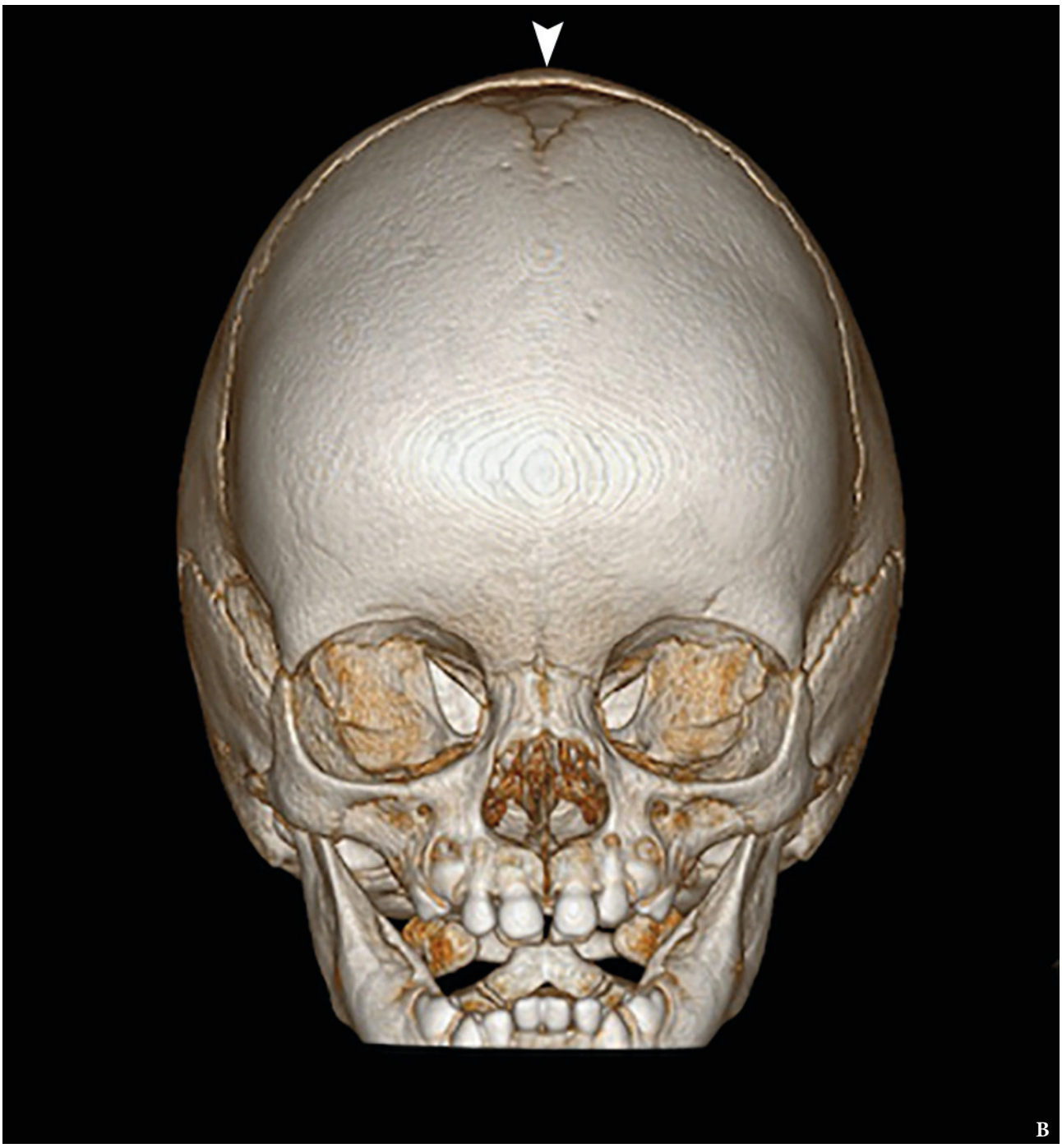

FIGURE 1 (cont'd). Anterior view (**B**) of 3D-CT volume-rendered image of a 6-month-old boy with premature, complete fusion of the sagittal suture. It results in increased anteroposterior diameter, along with bitemporal narrowing due to restriction of biparietal growth. Prominent ridging (*arrowhead*) of the sagittal suture is observed, as well as frontal and occipital bulging. **(Fig 1 continued on next page.)**

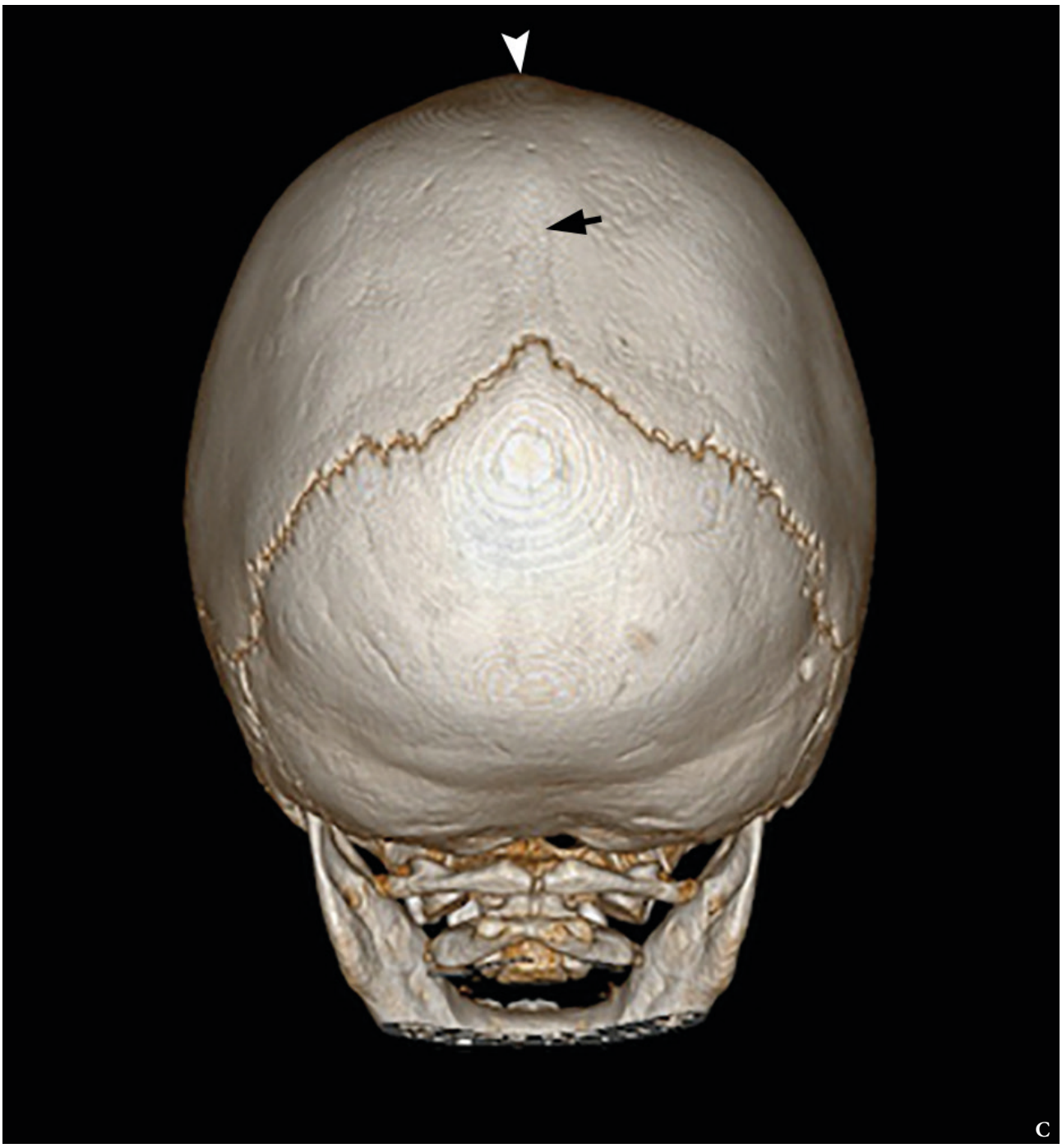

FIGURE 1 (cont'd). Posterior view (**C**) of 3D-CT volume-rendered image of a 6-month-old boy with premature, complete fusion (*arrow*) of the sagittal suture. It results in increased anteroposterior diameter, along with bitemporal narrowing due to restriction of biparietal growth. Prominent ridging (*arrowhead*) of the sagittal suture is observed, as well as frontal and occipital bulging. **(Fig 1 continued on next page.)**

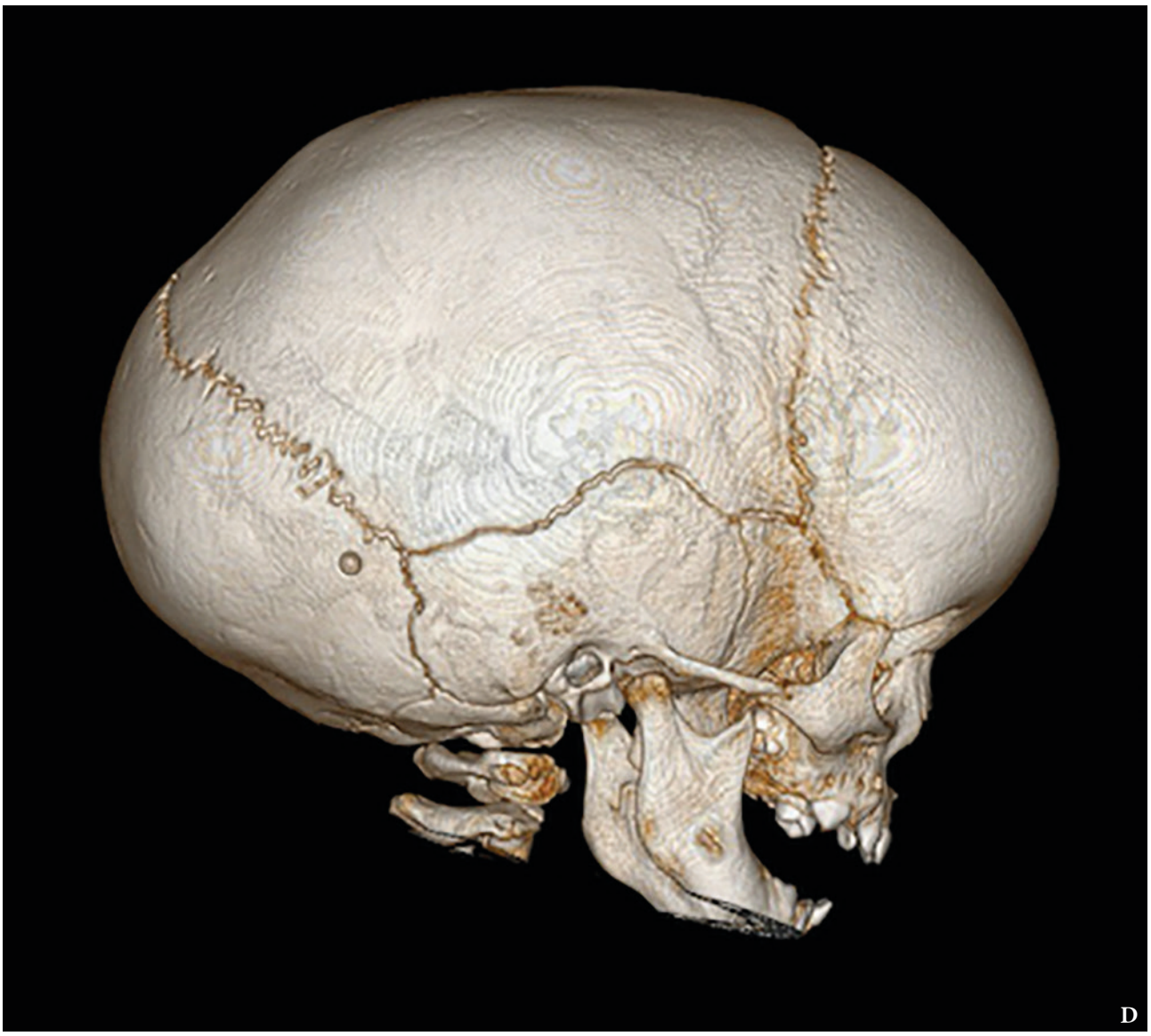

FIGURE 1 (cont'd). Lateral view (**D**) of 3D-CT volume-rendered image of a 6-month-old boy with premature, complete fusion of the sagittal suture. It results in increased anteroposterior diameter, along with bitemporal narrowing due to restriction of biparietal growth. Prominent ridging of the sagittal suture is observed, as well as frontal and occipital bulging.

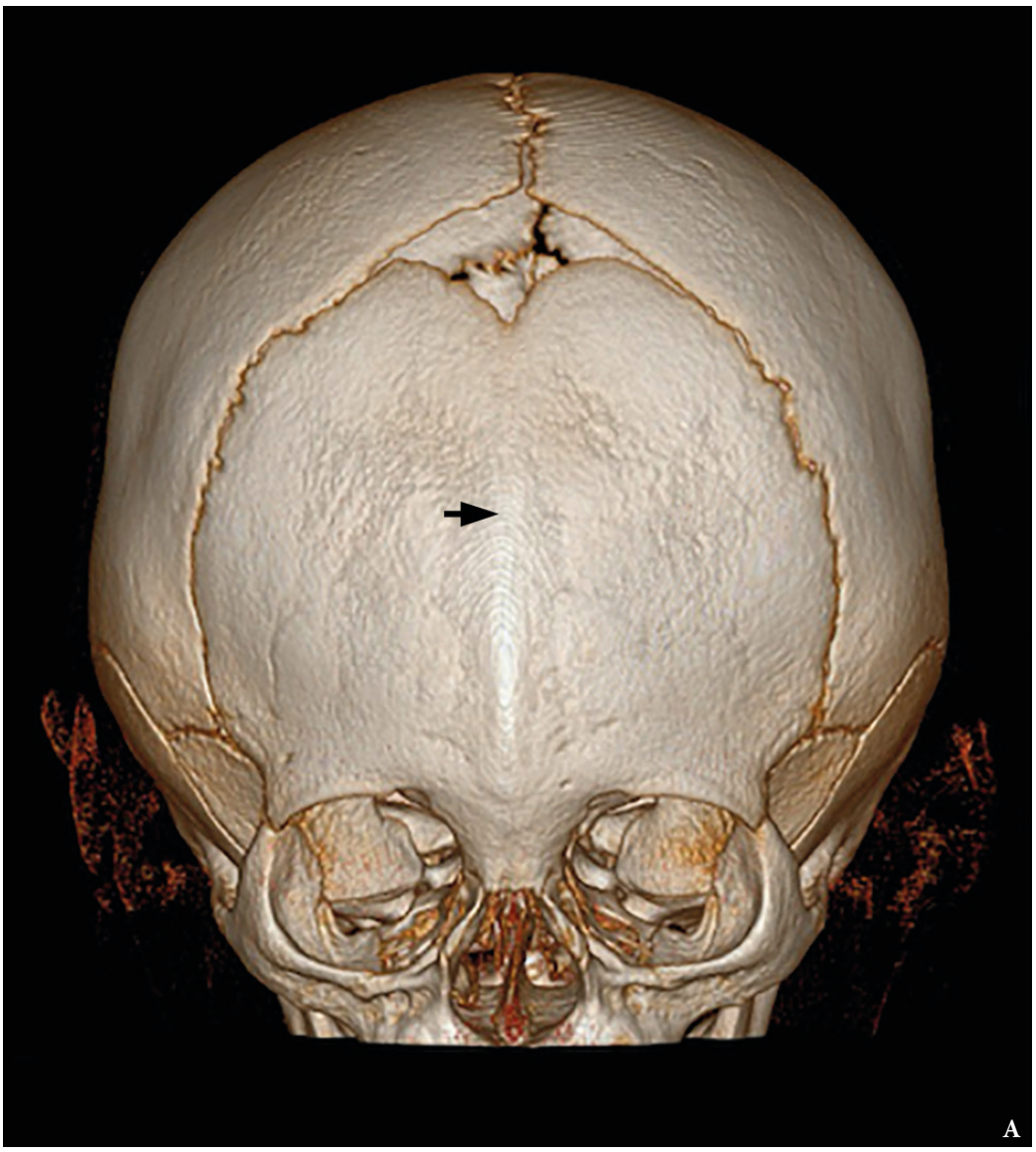

FIGURE 2. Anterior view (**A**) of 3D-CT volume-rendered image of a 4-month-old boy, showing premature fusion of the metopic suture (*arrow)* and the consequent triangular shape of the forehead, together with hypotelorism, flattening of the two frontal bones and bossing of the parieto-occipital regions. A wormian or intrasutural bone is present as well in the lambdoid suture.
(Fig 2 continued on next page.)

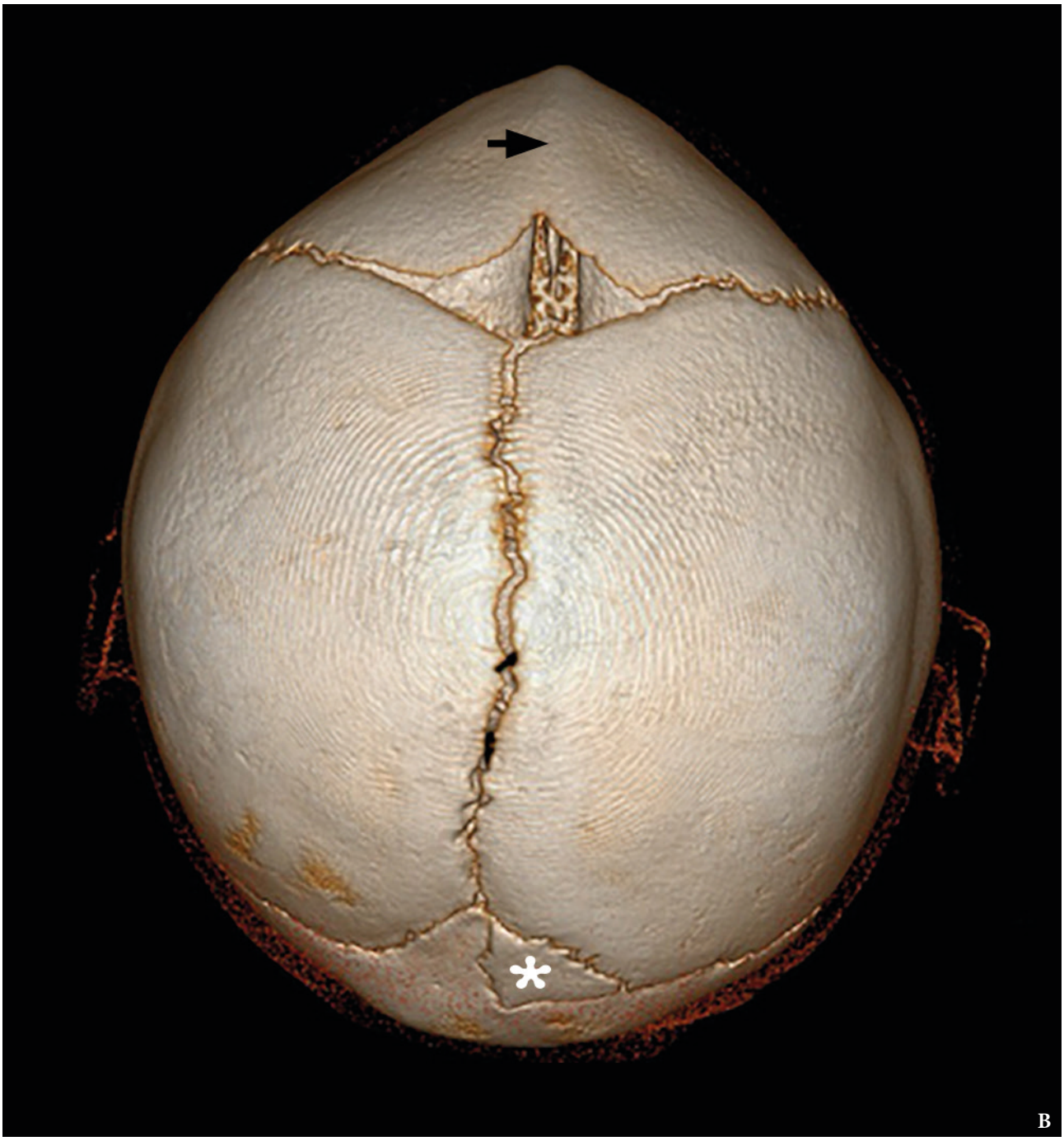

FIGURE 2 (cont'd). Superior view (**B**) of 3D-CT volume-rendered image of a 4-month-old boy, showing premature fusion of the metopic suture and the consequent triangular shape of the forehead, together with hypotelorism, flattening of the two frontal bones and bossing of the parieto-occipital regions. A wormian or intrasutural bone (*asterisk*) is present as well in the lambdoid suture.**(Fig 2 continued on next page.)**

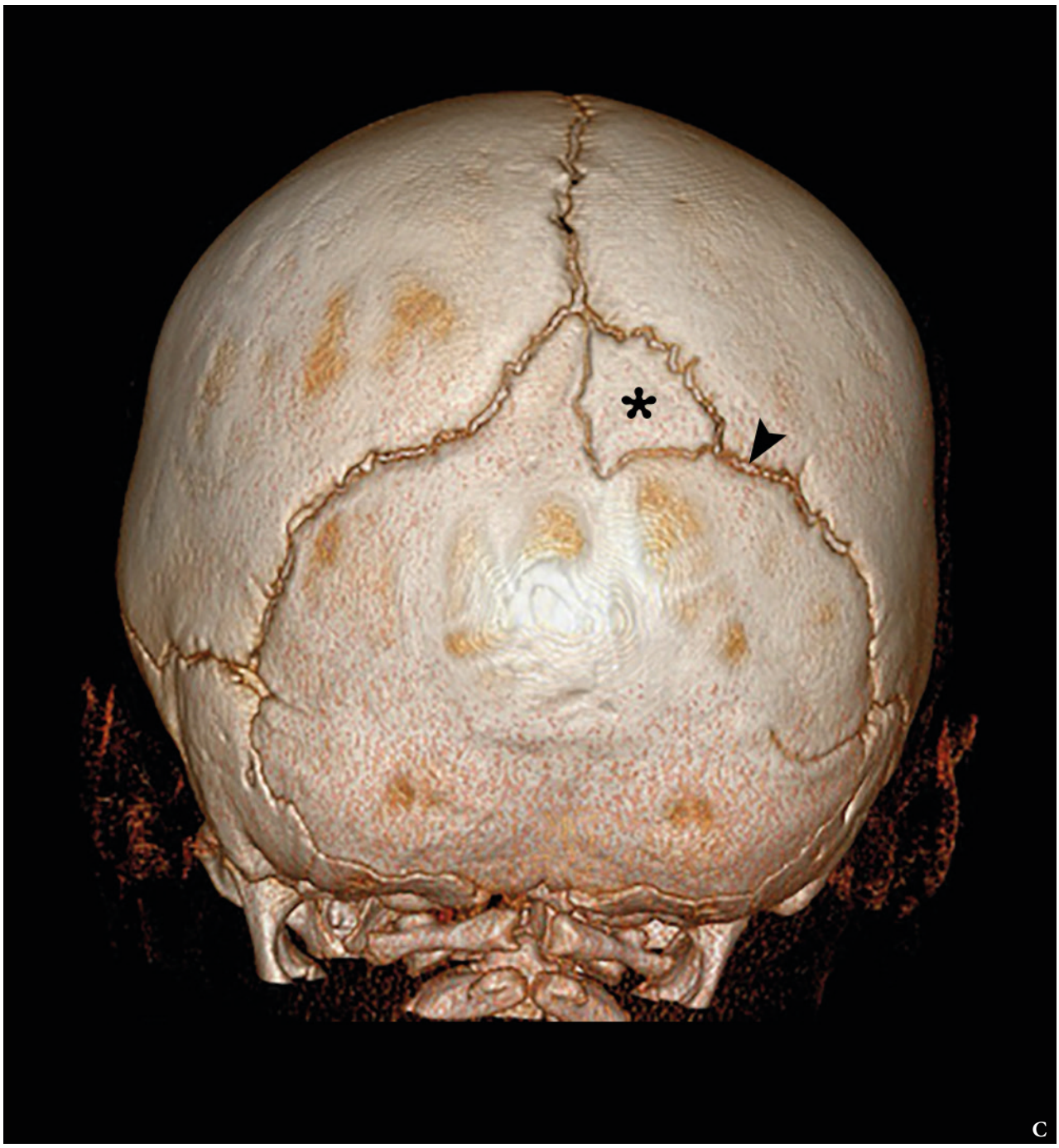

FIGURE 2 (cont'd). Posterior view (**C**) of 3D-CT volume-rendered image of a 4-month-old boy, showing premature fusion of the metopic suture and the consequent triangular shape of the forehead, together with hypotelorism, flattening of the two frontal bones and bossing of the parieto-occipital regions. A wormian or intrasutural bone (*asterisk*) is present as well in the lambdoid suture (*arrowhead*). **(Fig 2 continued on next page.)**

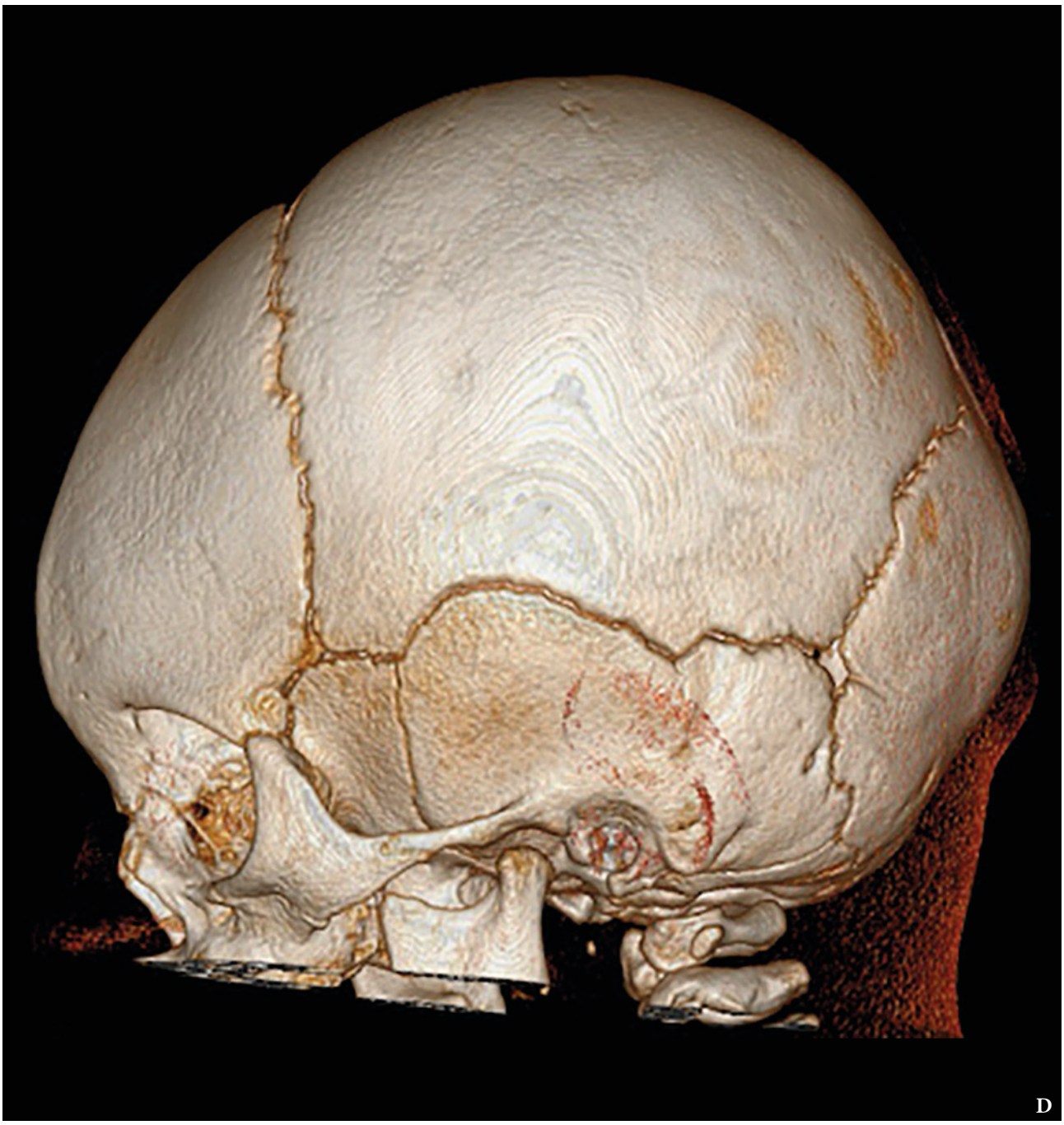

FIGURE 2 (cont'd). Left lateral view (**D**) of 3D-CT volume-rendered image of a 4-month-old boy, showing premature fusion of the metopic suture and the consequent triangular shape of the forehead, together with hypotelorism, flattening of the two frontal bones and bossing of the parieto-occipital regions. A wormian or intrasutural bone is present as well in the lambdoid suture.

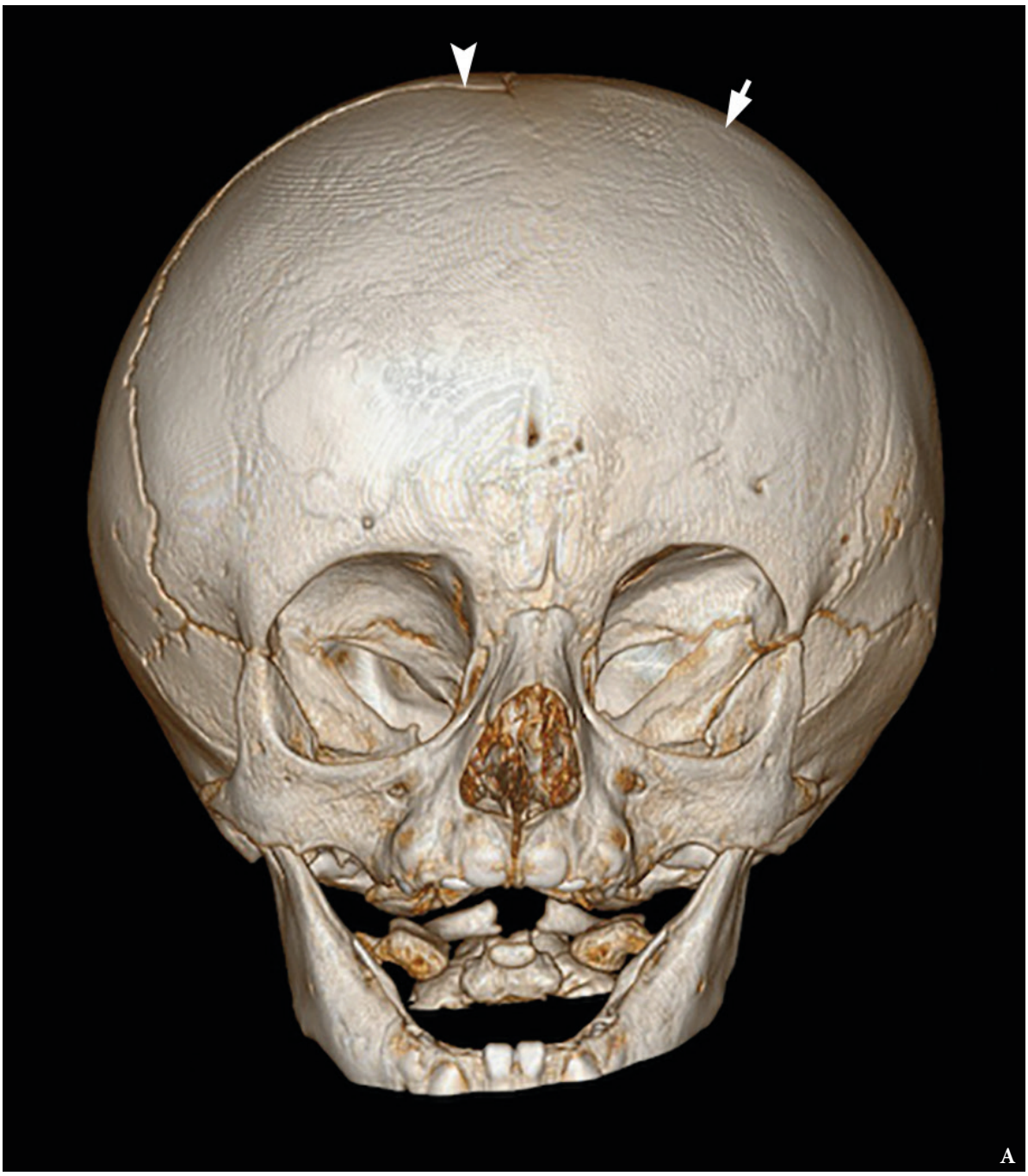

FIGURE 3. Anterior view (**A**) of 3D-CT volume-rendered image of a 7-month-old boy with anterior plagiocephaly as a result of left coronal suture fusion (*arrow*) which leads in flattening of the frontal bone on the affected side, and prominent frontal bossing to the contralateral side. There is also evident orbit asymmetry. The right coronal suture (*arrowhead*) is still open. **(Fig 3 continued on next page.)**

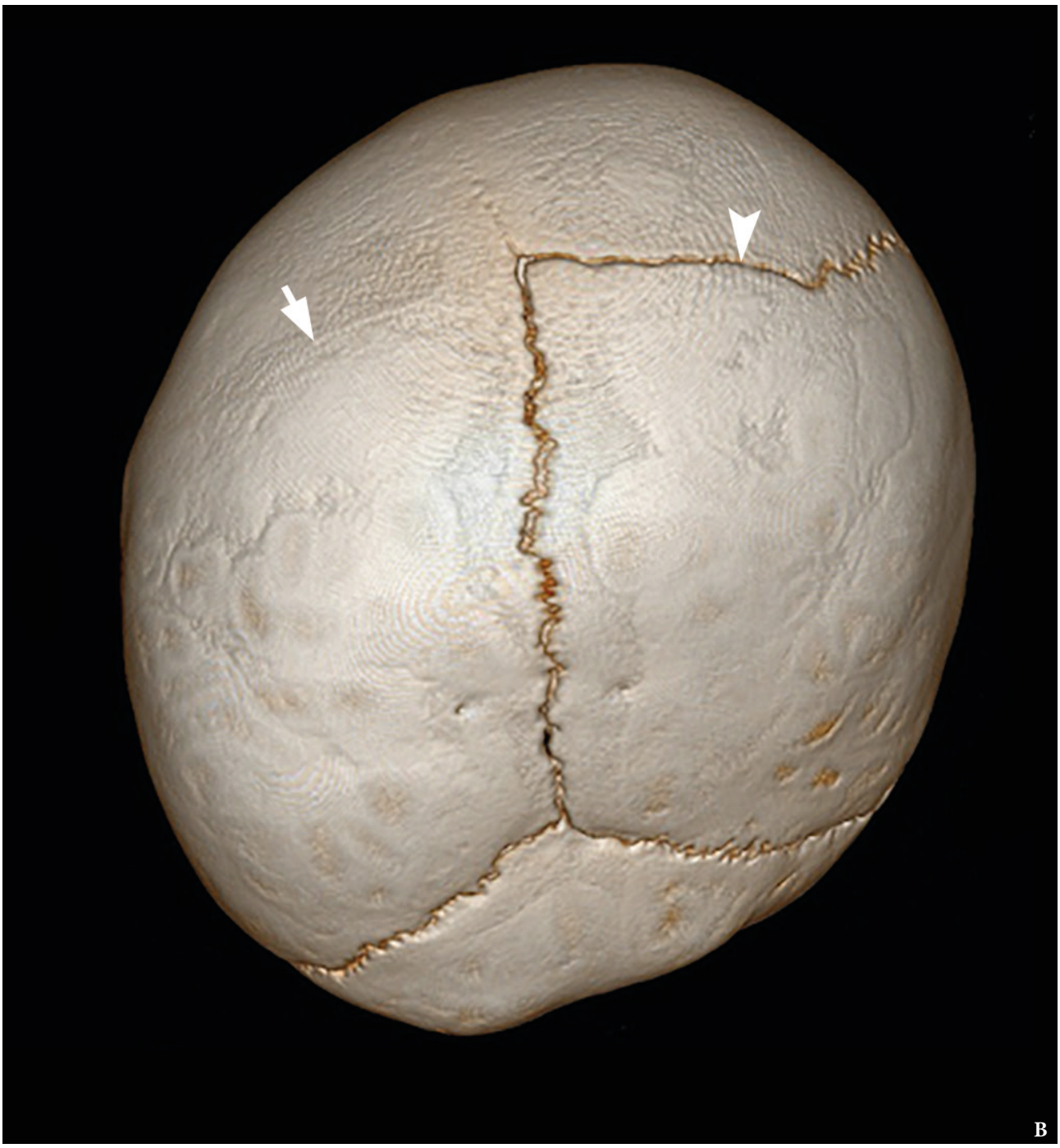

FIGURE 3 (cont'd). Superior view (**B**) of 3D-CT volume-rendered image of a 7-month-old boy with anterior plagiocephaly as a result of left coronal suture fusion (*arrow*) which leads in flattening of the frontal bone on the affected side, and prominent frontal bossing to the contralateral side. There is also evident orbit asymmetry. The right coronal suture is still open (*arrowhead*). **(Fig 3 continued on next page.)**

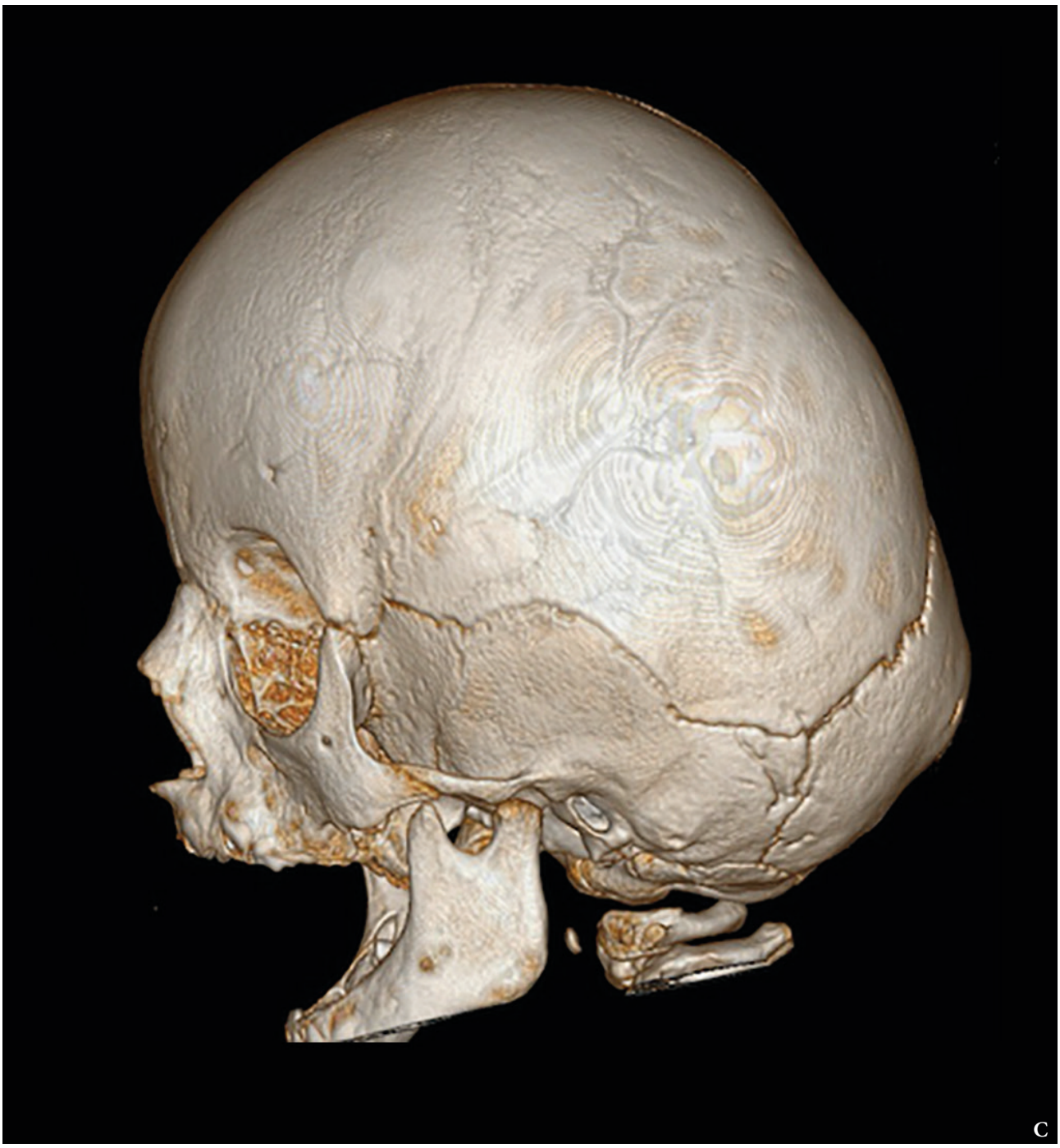

FIGURE 3 (cont'd). Left lateral view (**C**) of 3D-CT volume-rendered image of a 7-month-old boy with anterior plagiocephaly as a result of left coronal suture fusion which leads in flattening of the frontal bone on the affected side, and prominent frontal bossing to the contralateral side. There is also evident orbit asymmetry. The right coronal suture is still open. **(Fig 3 continued on next page.)**

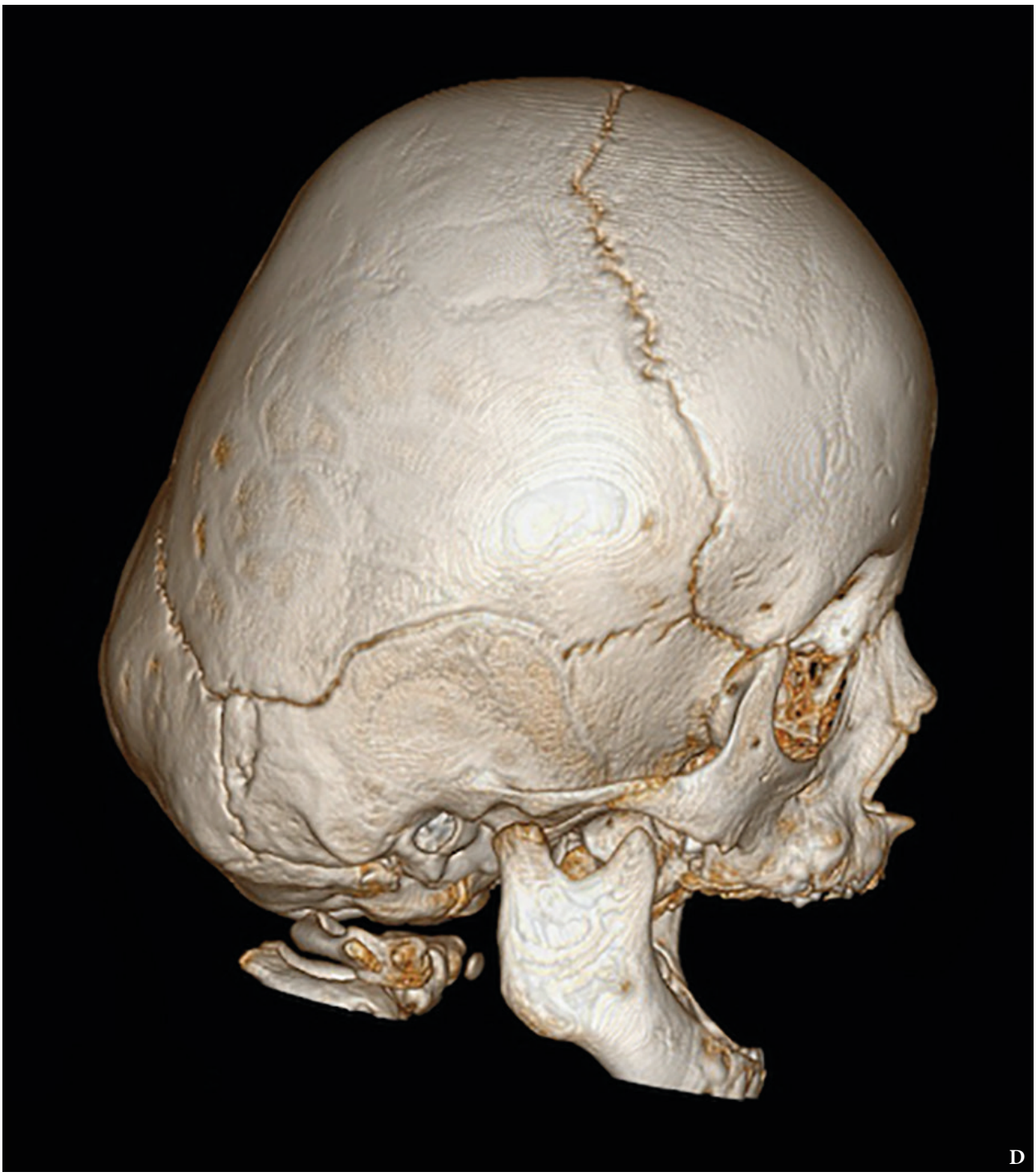

FIGURE 3 (cont'd). Right lateral view (**D**) of 3D-CT volume-rendered image of a 7-month-old boy with anterior plagiocephaly as a result of left coronal suture fusion which leads in flattening of the frontal bone on the affected side, and prominent frontal bossing to the contralateral side. There is also evident orbit asymmetry. The right coronal suture is still open.

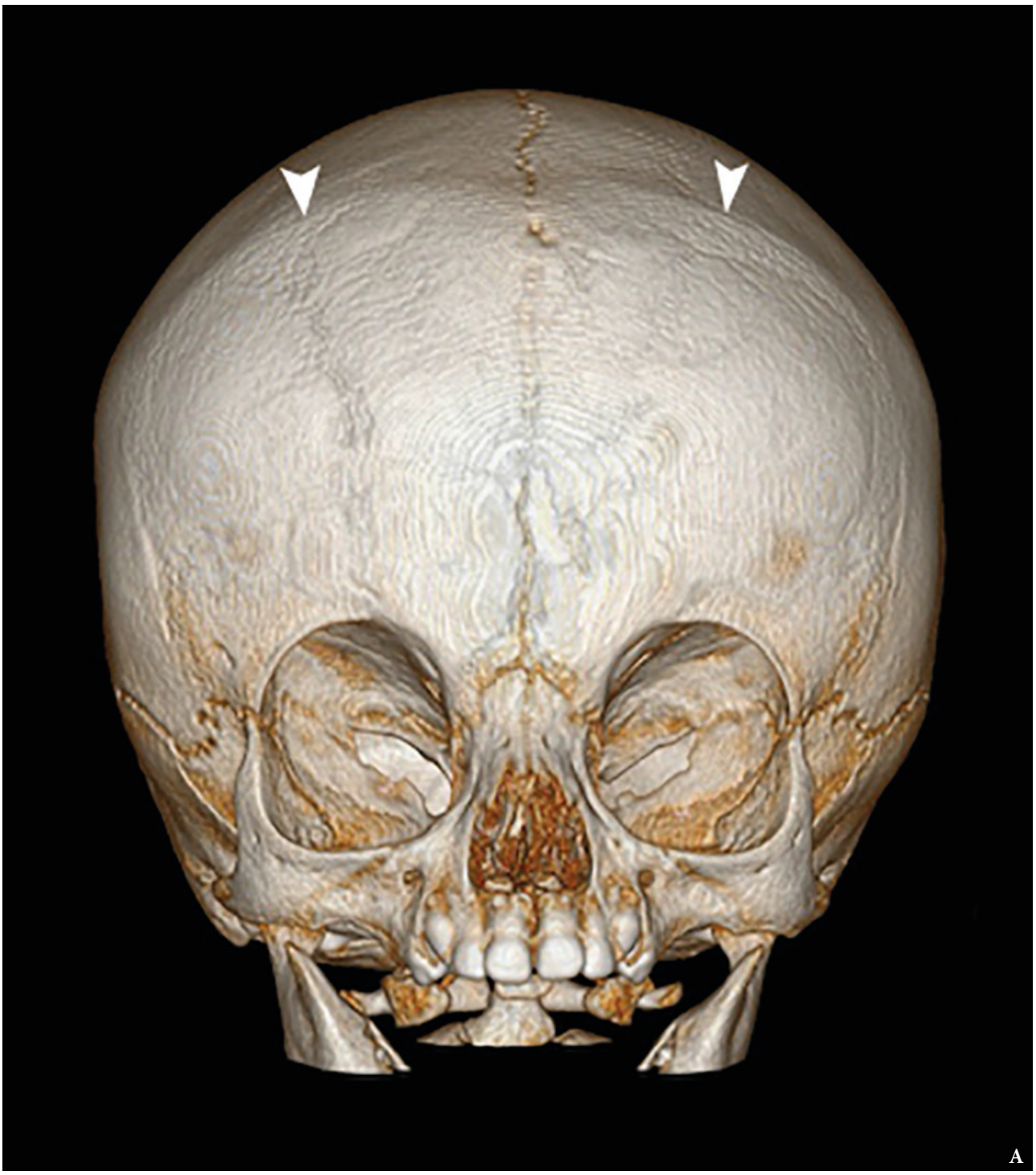

FIGURE 4. Anterior view (**A**) of 3D-CT volume-rendered image of a 6-month-old girl with complete bicoronal suture fusion (*arrowheads*) resulting to restriction of the anteroposterior calvarial growth and pronounced biparietal growth. A consequent prominent frontal bone and an occiput flattening are also evident. **(Fig 4 continued on next page.)**

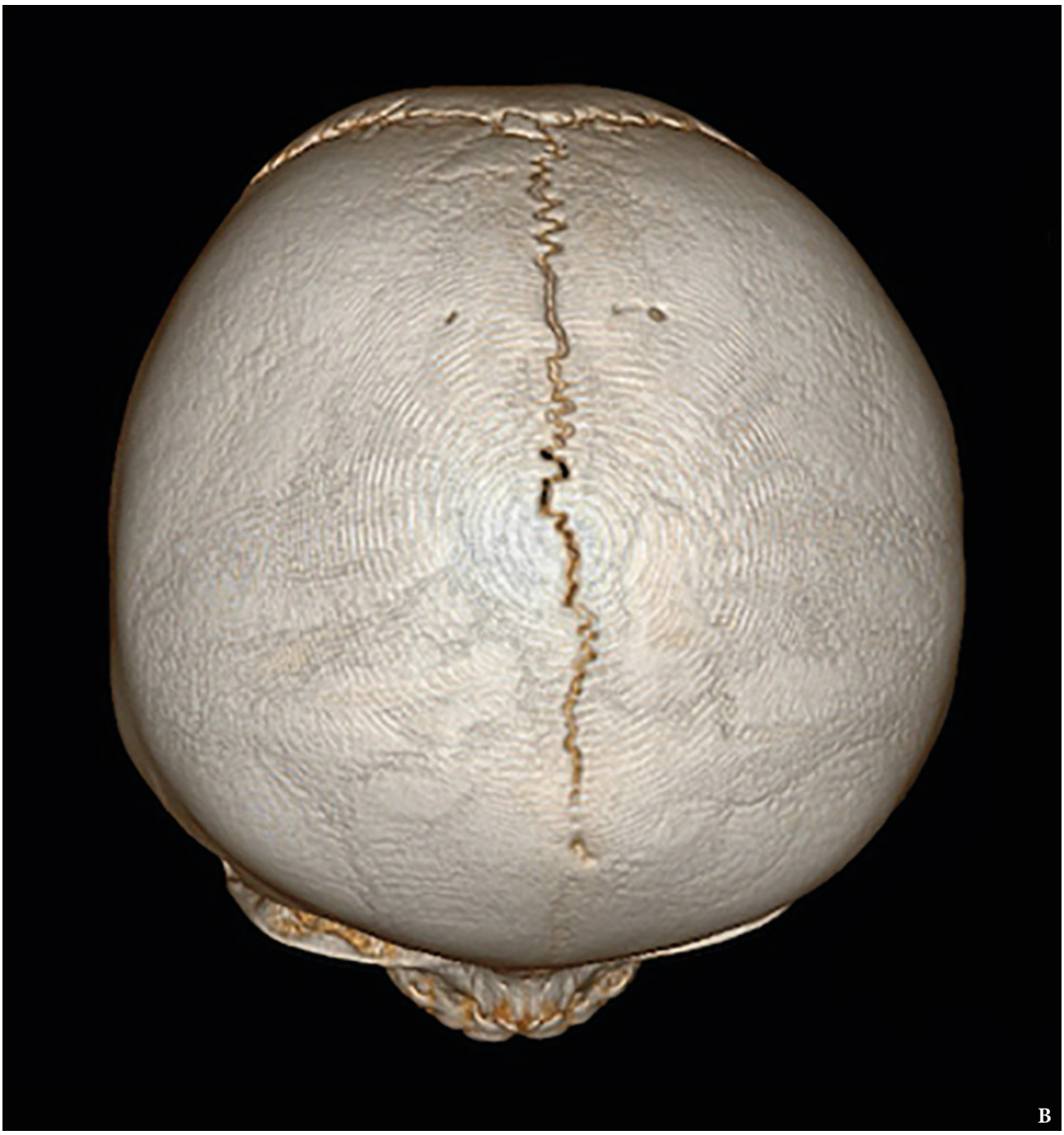

FIGURE 4 (cont'd). Superior view (**B**) of 3D-CT volume-rendered image of a 6-month-old girl with complete bicoronal suture fusion resulting to restriction of the anteroposterior calvarial growth and pronounced biparietal growth. A consequent prominent frontal bone and an occiput flattening are also evident. **(Fig 4 continued on next page.)**

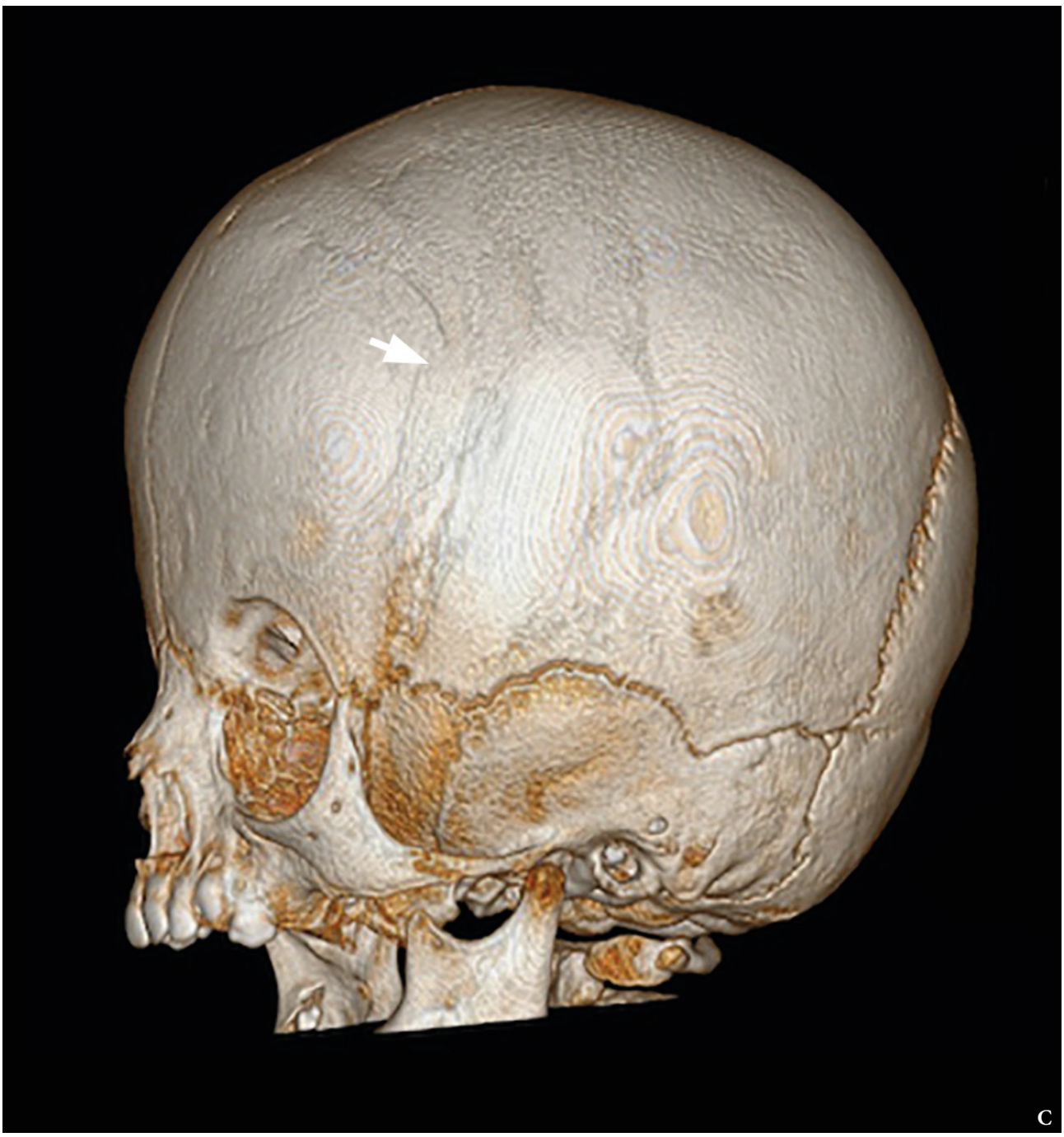

FIGURE 4 (cont'd). Lateral view (**C**) of 3D-CT volume-rendered image of a 6-month-old girl with complete bicoronal suture fusion (*arrow indicated left coronal suture fusion*) resulting to restriction of the anteroposterior calvarial growth and pronounced biparietal growth. A consequent prominent frontal bone and an occiput flattening are also evident. **(Fig 4 continued on next page.)**

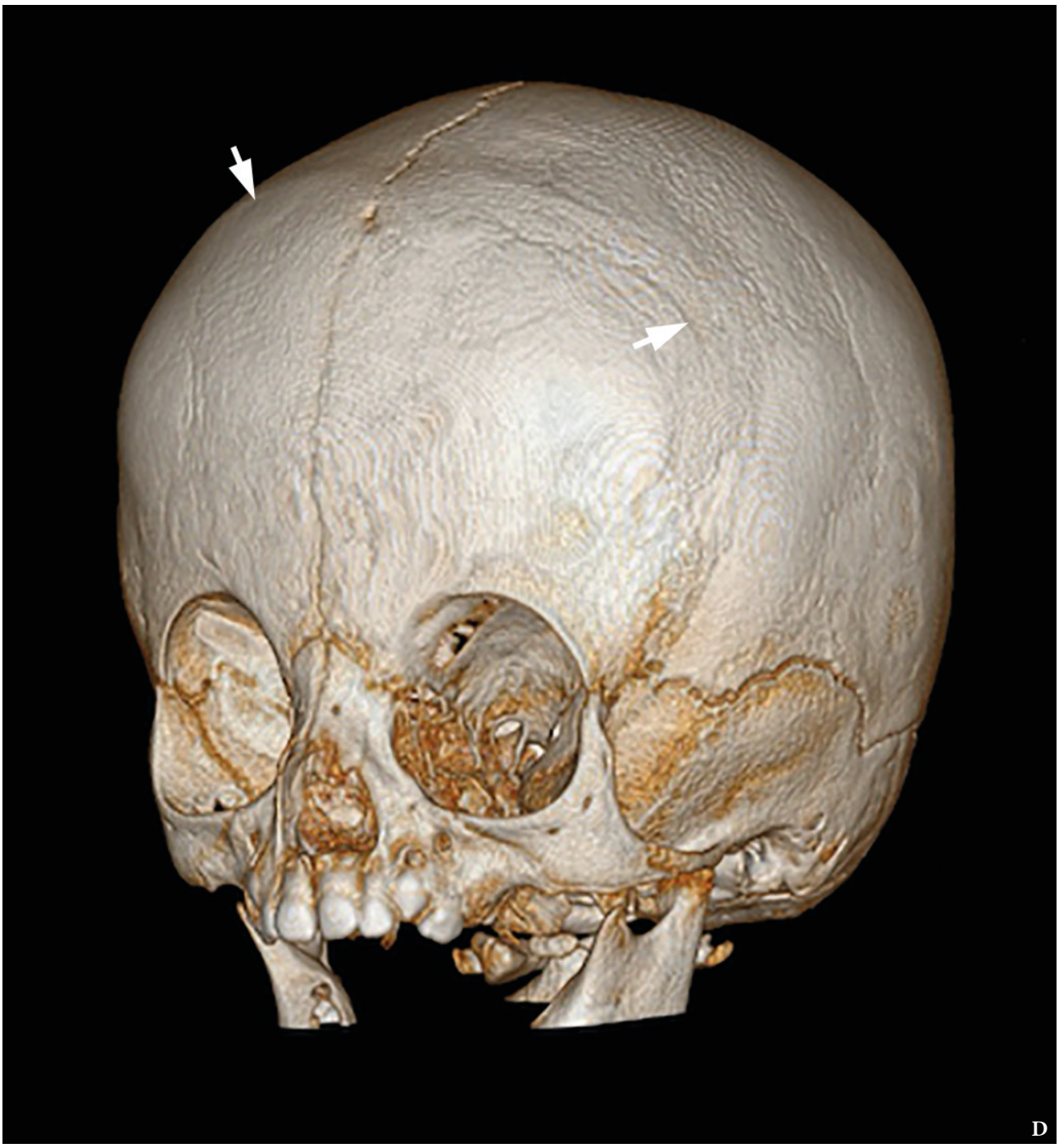

FIGURE 4 (cont'd). Anterolateral view (**D**) of 3D-CT volume-rendered image of a 6-month-old girl with complete bicoronal suture fusion (*arrows*) resulting to restriction of the anteroposterior calvarial growth and pronounced biparietal growth. A consequent prominent frontal bone and an occiput flattening are also evident.

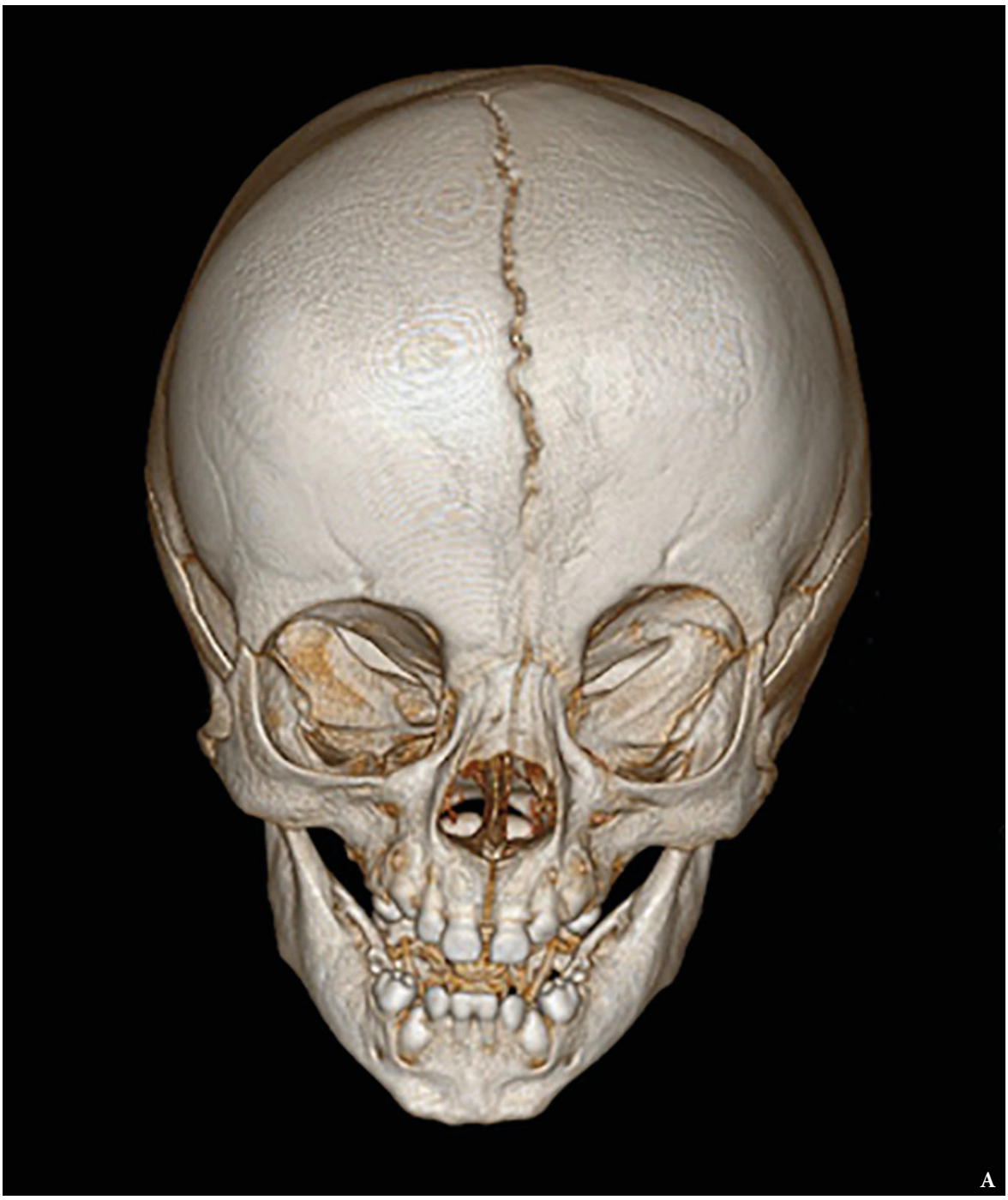

FIGURE 5. Anterior view (**A**) of the 3D-CT volume-rendered image of a 5-month-old girl with premature fusion of the sagittal and left coronal suture ending up with an increased AP dimension, prominent ridging of the sagittal suture, frontal and occipital bulging, flattening of the frontal bone on the affected side and prominent frontal bossing to the contralateral side together with orbit asymmetry. **(Fig 5 continued on next page.)**

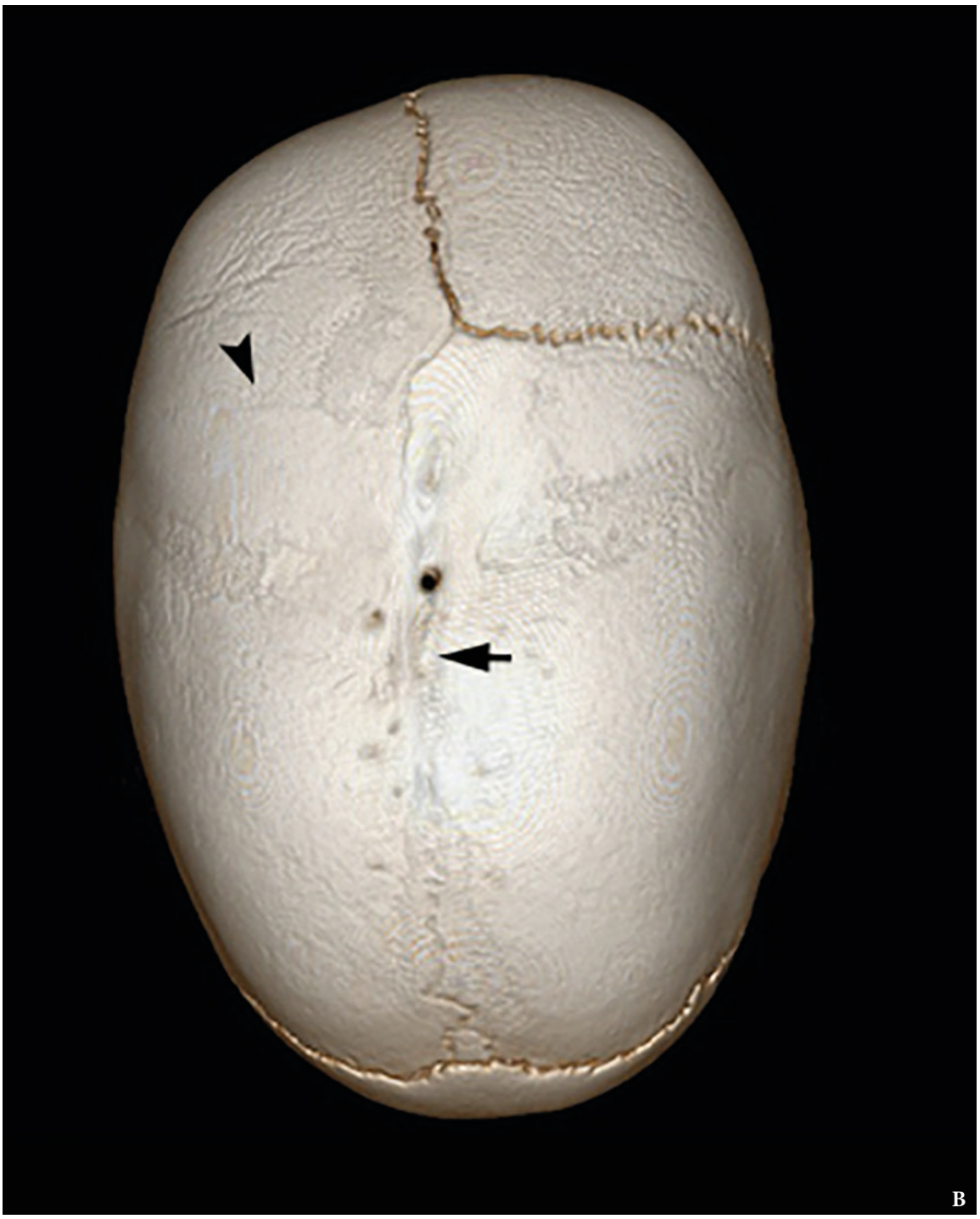

FIGURE 5 (cont'd). Superior view (**B**) of 3D-CT volume-rendered image of a 5-month-old girl with premature fusion of the sagittal (*arrow*) and left coronal (*arrowhead*) suture ending up with an increased AP dimension, prominent ridging of the sagittal suture, frontal and occipital bulging, flattening of the frontal bone on the affected side and prominent frontal bossing to the contralateral side together with orbit asymmetry. **(Fig 5 continued on next page.)**

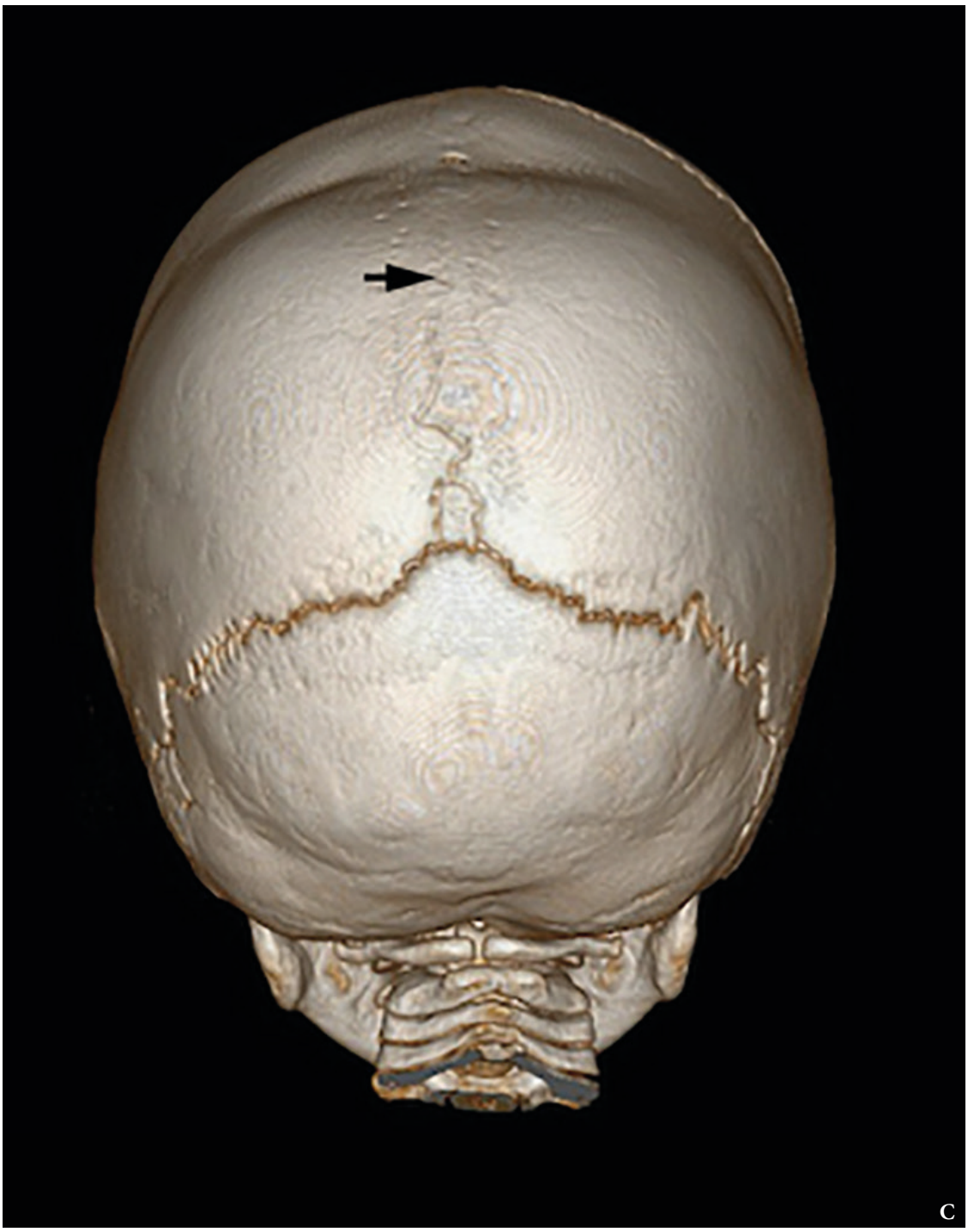

FIGURE 5 (cont'd). Posterior view (**C**) of 3D-CT volume-rendered image of a 5-month-old girl with premature fusion of the sagittal (*arrow*) and left coronal suture ending up with an increased AP dimension, prominent ridging of the sagittal suture, frontal and occipital bulging, flattening of the frontal bone on the affected side and prominent frontal bossing to the contralateral side together with orbit asymmetry. **(Fig 5 continued on next page.)**

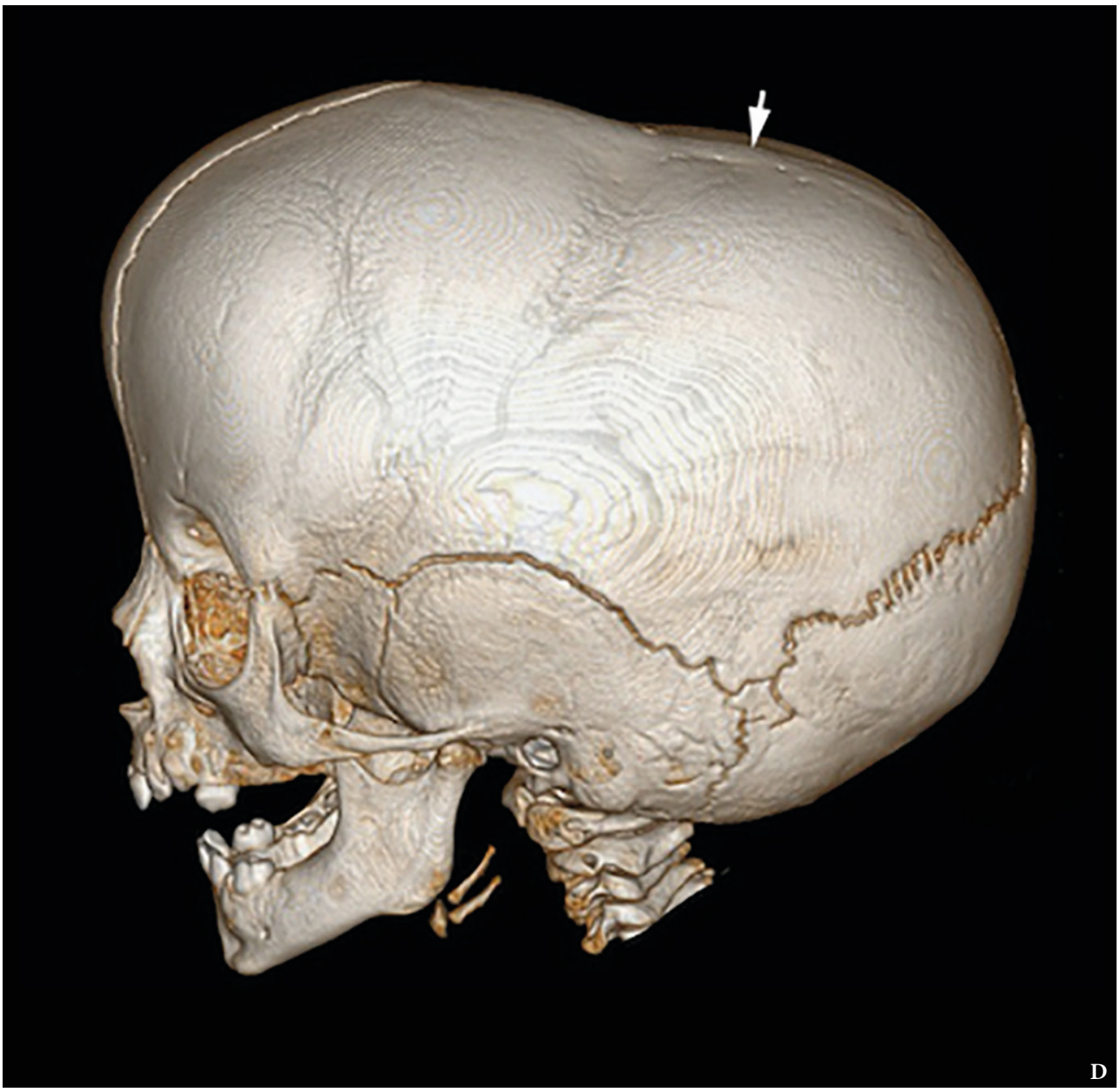

FIGURE 5 (cont'd). Left lateral view (**D**) of 3D-CT volume-rendered image of a 5-month-old girl with premature fusion of the sagittal and left coronal suture ending up with an increased AP dimension, prominent ridging (*arrow*) of the sagittal suture, frontal and occipital bulging, flattening of the frontal bone on the affected side and prominent frontal bossing to the contralateral side together with orbit asymmetry.

Conclusion

Even though craniosynostosis is a well-known entity, at the same time remains a quite demanding disorder as it affects infancy. 3D CT appears as the imaging modality with the best diagnostic performance, but there are still several topics for investigation, as new information is coming up with advancing imaging modalities. The challenges for the diagnosis and treatment of this condition are significant and their consequences will follow the patient throughout the entire life. Thus, every diagnostic intervention has to be cautious and evidence based, in order to have optimal outcomes for the infant. On the domain of diagnosis, there are still questions to be answered, specifically on the possibility to effectively replace diagnostic methods with ionizing radiation (plain radiographs and 3D CT), with other more infant-friendly methods, such as cranial ultrasound and MRI. For this reason large, prospective and multicenter studies are needed in order to reliably establish such diagnostic protocols.

Funding

No funding was received for this study.

Conflict of Interests

The authors declare no conflict of interest.

Role of Author and Co-authors

Evangelos G. Kilipiris (concept, design of the paper and writing)
Stefan Pavlik (material collection and writing)
Frantisek Horn (material collection and writing)
Michal Kabat (material collection and writing)

Ethical Approval

Approval was obtained from the Institutional Ethical Committee.

Acknowledgements

None.

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http://dx.doi.org/10.23999/j.dtomp.2019.2.3.

http://dx.doi.org/10.23999/j.dtomp.2019.2.4

Future Events

for 2019-2021

2019

BSCOSO Spring Course 2019
April 14 – 18, 2019
Vilnius, Lithuania
www.bscoso.com

2nd Duesseldorf International Microvascular Flap Course
April 30 – May 04, 2019
Duesseldorf, Germany
Email: *agnes.jedig@med.uni-duesseldorf.de* (Agnes Jedig)

24rd International Conference on Oral and Maxillofacial Surgery (Fig 1)
May 21 – 24, 2019
Rio de Janeiro, Brazil
www.icoms2019.com.br

18th Meeting of the International Society of Craniofacial Surgery
September 16 – 19, 2019
Paris, France
www.iscfs.org

31st World Congress of the International College for Maxillo-Facial-Surgery (ICMFS)
October 29 – November 01, 2019
Tel Aviv, Israel
www.icmfs2019.com

21st International Congress of the Latin American Association of Bucomaxillofacial Surgery and the Mexican Association of Oral and Maxillofacial Surgery
December 01 – December 04, 2019
Cancun, Mexico
www.cialacibu2019.com/en/welcome/

2020

25th Congress of the European Association for Cranio-Maxillo-Facial Surgery
September 15 – 18, 2020
Paris, France
www.eacmfs.org

2021

14th Quadrennial International Facial Nerve Symposium
August, 2021
South Korea
www.internationalfacialnerve.org

FIGURE 1. Screenshot from a website www.icoms2019.com.br.

http://dx.doi.org/10.23999/j.dtomp.2019.2.5.

Submission of Articles

Papers for the Publication

- original papers
- clinical cases (case reports)
- surgical notes
- radiological notes
- reports of new equipment, instruments or technical innovations
- journal or book reviews
- reviews of other journals articles
- letters to the Editor

Article and Abstracts

Article must be written in English.
The authors from the Russian-speaking countries must send an abstract of the article in Russian. The authors from Ukraine must send an abstract of the article in Ukrainian and Russian.
One co-author is denominated as the corresponding author with all contact details:

- Postal address (ZIP code of a country, City, Street, phone and fax number)
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The abstract should include full title of the article, full names and surnames of the co-authors, affiliation, scien¬tific degree, specialty. Also the abstract should include short information about article content: purpose, material and methods, results, conclusions. Example how the Abstract should be looked like the authors can get from the published articles in current issue.

Figures and Tables

Photographs, CT and MRI images, sonograms should be submitted in original with resolution of at least 300 dpi and saved in JPEG or TIFF file format.

Fundings

The authors should indicate the sources of funding that were allocated for the preparation of the article, if such were the case.

Conflicts of Interest

At the end of the article the authors should specify about conflicts of interest (e.g., no conflict of interest).

Role of Co-authors in Writing

After specifying conflicts of interest the role of co-authors in writing of the article (concept and design of the study; material collection, mate¬rial processing, statistical data processing, writing text, editing, etc.) should be designated.

Patient Consent

Written patient consent should be obtained to publish the clinical images of the patients.

Acknowledgments

The authors can acknowledge the persons or institutions which they helped or useful in writing an article.

The Journal is recommended to use that internet source for the articles preparing according to *Vancouver References Style:* http://libguides.murdoch.edu.au/Vancouver/journal

Examples How to Form a Reference List

List all references in numerical order in the text.
Making a list of references from articles, books, internet links, etc.:

Example for the articles:

Fernandes RP, Quimby A, Salman S. Comprehensive reconstruction of mandibular defects with free fibula flaps and endosseous implants. *J Diagn Treat Oral Maxillofac Pathol* **2017**;1(1):6–10.

Example for the articles with more than three authors:

Neto AMR, Monteiro JL, Borba PM, et al. TMJ´s posterolateral dislocation with tympanic plate fracture – case report. *J Diagn Treat Oral Maxillofac Pathol* **2017**;1:59–64.

Example for the articles from the Journal Supplement:
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or

Hammerle CH, Chen ST, Wilson Jr TG. Consensus statements and recommended clinical procedures regarding the placement of implants in extraction sockets. *Int J Oral Maxillofac Implants* **2004**;19:S26–8.

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Example for references in Cyrillic:

Please indicate the language of writing in square brackets [Ukrainian] or [Russian].
Tymofieiev OO. Manual of maxillofacial and oral surgery [Russian]. 5th ed. Kyiv: Chervona Ruta-Turs; **2012.**
Tymofieiev OO. Diseases of the salivary glands [Ukrainian]. 1st ed. Lviv: VNTL-Klasyka; **2007.**

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Seave A. Elsevier CEO using unique data sets and analytic processes to maintain competitive edge. The Forbes. February 25, 2016. Available at: https://www.forbes.com/sites/avaseave/2016/02/25/elsevier-ceo-using-unique-data-sets-and-analytic-processes-to-maintain-competitive-edge/#1d9e4b3979c2/. Accessed February 25, 2016.

Adult improving access to psychological therapies programme. NHS England. Available from URL:
https://www.england.nhs.uk/mental-health/adults/iapt/ (last accessed 3 March **2017**).

McManus S, Meltzer H, Brugha T, et al., editors. Adult psychiatric morbidity in England, 2007: results of a household survey. The NHS Information Centre for health and social care; 2017. Available from URL: http://www.hscic.gov.uk/catalogue/PUB02931/adul-psyc-morb-reshou-sur-eng-2007-rep.pdf (last accessed 3 March **2017**).

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Example for newspaper articles in print:

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Founded in 1996

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We unite, lead, and develop the maxillofacial community to accelerate theoretical and practical movement forward and improve worldwide.

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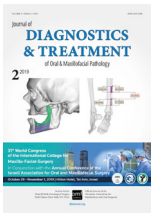

JOURNAL`S
AWARD

Journal`s Award in 2018: Andrii V. Kopchak, ScD, Professor

"Leadership is unlocking people`s potential to become better."
—Bill Bradley
USA senator & former professional basketball player

FIGURE. *Journal`s* Award dedicated to Professor Andrii V. Kopchak. Kyiv, Ukraine; December, 2018.

Andrii V. Kopchak, Doctor of Medical Sciences (ScD), Professor serves in the Bogomolets National Medical University as:

- Professor, Department of Dentistry, Institute of Postgraduate Education.
- Director, Dental Medical Center.

Also Dr. Kopchak does his best as a Director in the Center of Maxillofacial Surgery and Dentistry, Kyiv Regional Clinical Hospital. From 2019 Dr. Kopchak headed a Kyiv Branch of the Association of Dentists of Ukraine.

With a whole editorial staff we are more than grateful for an amazing assistance to the *Journal* that Dr. Kopchak (Fig) does not only with the inspiring articles (co-authors: Romanova and Mykhailenko),[1] (Hresko, Chernohorskyi, and Vereshchagin)[2] but also in his work at a position of Section Editor–Osteosynthesis of Facial Bones from the Issue 3-4, 2017.

So, we feel so humbled when we gave the *Journal`s* honorary plaque to Professor Kopchak. But we find the next words: *"For the unique skills in organization of OMS meetings, uniting and educating the new generations of surgeons sincere thanks and appreciation."*

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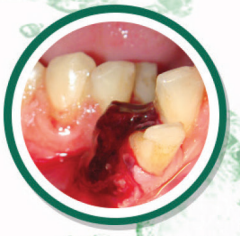

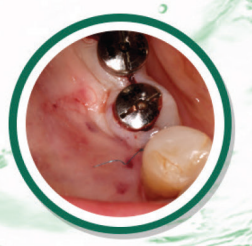

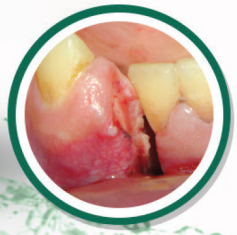

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4. 4,5. Tymofieiev O.O. et al"Prevention of inflammatory complications upon surgeries in maxillofacial region". J Diagn Treat Oral Maxillofac Pathol. 2017;1:105–12.

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