Revista Argentina de Antropología Biológica

BRIEF COMMUNICATION

Imaging diagnosis of probable osteomyelitis in a 9-month-old infant from prehistoric Brazil: a brief history of healthcare in ancient times

Diagnóstico por imágenes de probable osteomielitis en un infante de 9 meses del Brasil prehistórico: una breve historia sobre cuidados de salud antiguos

Diagnóstico imagiológico de um caso provável de osteomielite em uma criança de 9 meses do Brasil pré-histórico: uma breve história sobre cuidados de saúde na antiguidade

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Abstract

Individual 9, a 9 ± 3-month-old infant from the Middle-Holocene (6,650-6,170 years BP) found in Toca do Enoque rock-shelter in Piauí, Brazil, showed significant pathological bone changes and received exceptional mortuary treatment. Previous studies indicated administration of normative parental care and non-normative healthcare, although the differential diagnosis remained vague. This study reexamines the pa-

leopathological diagnosis using X-rays, CT scans, and 3D reconstructions of 10 long bones. Pathological changes included endocranial bone growths and polyostotic, bilateral, and asymmetrical periosteal new bone formation (PNBF) affecting long bones and ribs. The right tibia was the most affected, showing an anteromedial deformity and inside out-perforations with burred, jagged edges. Imaging revealed Harris lines in the left humerus, endosteal bone proliferation in the tibiae, humeri, and right radius, and loss of cortical density in the right tibia. A direct connection between the medullary, subperiosteal, and external spaces suggested characteristics of *cloacae* or subperiosteal abscesses. Tibial changes suggest an involucrum formation without signs of *sequestra*, consistent with acute, hematogenous neonatal/infantile osteomyelitis (OM). Although extremely rare, *cloacae* can arise at early ages under specific circumstances, such as chronic neonatal/infant OM. Delayed pus evacuation, coupled with breastfeeding, resilience, and healthcare may have extended Individual 9's lifespan and the duration of the infection. This possible case of neonatal/infantile OM is rare and valuable, potentially the youngest documented in Paleopathology and the first in the Americas. However, nonspecific costal and endocranial lesions do not rule out the presence of comorbidities. Expanding the corpus of case studies is essential for refining diagnoses in bioarcheological and paleopathological research. Rev Arg Antrop Biol 27(1), 099, 2025. https://doi.org/10.24215/18536387e099

Keywords: periosteal new bone formation; infectious disease; non-adult paleopathology

Resumen

El Individuo 9 (9 ± 3 meses) del sitio Toca do Enoque, Holoceno medio (6650-6170 años AP), en Piauí, Brasil, mostró cambios óseos patológicos significativos y recibió un tratamiento mortuorio excepcional. Estudios previos infirieron cuidados de salud especiales, aunque el diagnóstico diferencial fue indefinido. Este estudio reexamina el diagnóstico patológico utilizando radiografías, tomografías y reconstrucciones 3D de 10 huesos largos. Los cambios patológicos incluyeron crecimientos óseos endocraneales y formación de hueso nuevo perióstico poliostótico, bilateral y asimétrico que afectó a huesos largos y costillas. La tibia derecha mostró deformidad anteromedial y perforaciones de adentro hacia afuera con bordes dentados y rebabas. Las imágenes revelaron líneas de Harris en el húmero izquierdo, proliferación ósea endóstica en tibias, húmeros y radio derecho, y pérdida de densidad cortical en la tibia derecha. Una conexión entre los espacios medular, subperióstico y externo sugirió características de cloacas o abscesos. Los cambios en la tibia sugieren involucro sin signos de *secuestros*, consistente con osteomielitis neonatal/infantil aguda hematógena. Aunque extremadamente rara, la cloaca puede surgir a edades tempranas en circunstancias específicas. Los retrasos en la evacuación de pus, la lactancia materna, la resiliencia y los cuidados de salud, pueden haber prolongado la vida del Individuo 9 y agravado la duración de la infección. Este posible caso de osteomielitis neonatal/infantil es raro y valioso, potencialmente el más joven documentado en Paleopatología y el primero en América. Sin embargo, las lesiones costales y endocraneales inespecíficas no descartan comorbilidades. Ampliar el corpus de estudios de casos es esencial para refinar los diagnósticos en bioarqueología y paleopatología. Rev Arg Antrop Biol 27(1), 099, 2025. https://doi.org/10.24215/18536387e099

Palabras Clave: formación de hueso nuevo perióstico; enfermedad infecciosa; paleo-patología de no-adultos

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Resumo

O Indivíduo 9 (9 ± 3 meses) do sítio Toca do Enoque, Holoceno médio (6650-6170 anos AP), Piauí (Brasil), mostrou mudanças ósseas patológicas significativas e recebeu um tratamento mortuário excecional. Estudos prévios inferiram cuidados de saúde especiais, embora o diagnóstico diferencial manteve-se indefinido. Este estudo reexamina esse diagnóstico patológico utilizando radiografias, tomografias e reconstruções 3D de 10 ossos longos. As mudanças patológicas incluíram crescimentos ósseos endocranianos e formações bilaterais e assimétricas de osso novo subperiosteal, que afetaram os ossos longos e as costelas. A tíbia direita mostrou deformidade ântero-medial e perfurações centrífugas com rebordos dentados e rebarbas. A imagiologia revelou Linhas de Harris no úmero esquerdo, proliferação óssea endosteal nas tíbias, úmeros e rádio direito, assim como perda de densidade cortical na tíbia direita. Conexões entre os espaços medular, subperiosteal e externo sugerem caraterísticas de cloaca ou abscessos. As manifestações tibiais sugerem a formação de involucrum sem sinais de *sequestra*, sendo consistente com uma osteomielite (OM) neonatal/infantil aguda hematogênica. Embora seja extremamente raro, as cloacas podem surgir em idades precoces sob circunstâncias específicas, tais como a OM crônica neonatal/infantil. Atrasos na evacuação do pus, aliados à amamentação, resiliência e cuidados de saúde, podem ter prolongado tanto a vida do Indivíduo 9, quanto a duração da infeção. Este possível caso de OM neonatal/infantil é raro e valioso, podendo ser o mais jovem documentado em Paleopatologia e o primeiro no continente americano. No entanto, lesões inespecíficas nas costelas e na superfície endocraniana não excluem a presença de comorbilidades. A ampliação do conjunto de estudos de caso é essencial para aprimorar os diagnósticos na investigação bioarqueológica e paleopatológica.
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Palavras-chave: formação de osso novo periosteal; doença infecciosa; paleopatologia de não-adultos

In 2020, Solari and colleagues published the excavation results from the Middle Holocene (6,220 ± 50 to 6,610 ± 40 years BP) funerary rock-shelter located at *Toca do Enoque* site in *Serra das Confusões* National Park, in the state of Piauí (PI), northeastern Brazil (Fig. 1). In the collective Burial 2 (Fig. 2A), Individual 9 (Ind. 9) was discovered, and their age-at-death was estimated through dental development to be 9 ± 3-month-old (Ubelaker, 1978). Additionally, this individual warranted evaluation using Tilley (2015)'s Bioarchaeology of Care (BoC) model, not only due to the exuberant and extensive pathological porous lesions observed (Solari *et al*., 2020), but also because of the distinctive funerary treatment (Figs. 2B-D). The mortuary context of Ind. 9 involved the deliberate rearrangement of previously interred remains to accommodate the burial, along with the presence of the most elaborate grave goods among all individuals, consisting of body relics and offerings made from cervids, canids, felines, birds, turtles, large gastropods, dasypodid or tayassuid remains, among other species. It was therefore suggested that Ind. 9 received both normative parental care and non-normative special healthcare due to a systemic condition, with a range of possible etiologies, including comorbidities (see Solari *et al*., 2020). However, no additional methodologies have yet been applied to investigate this further, and more detailed differential diagnoses have not been explored.

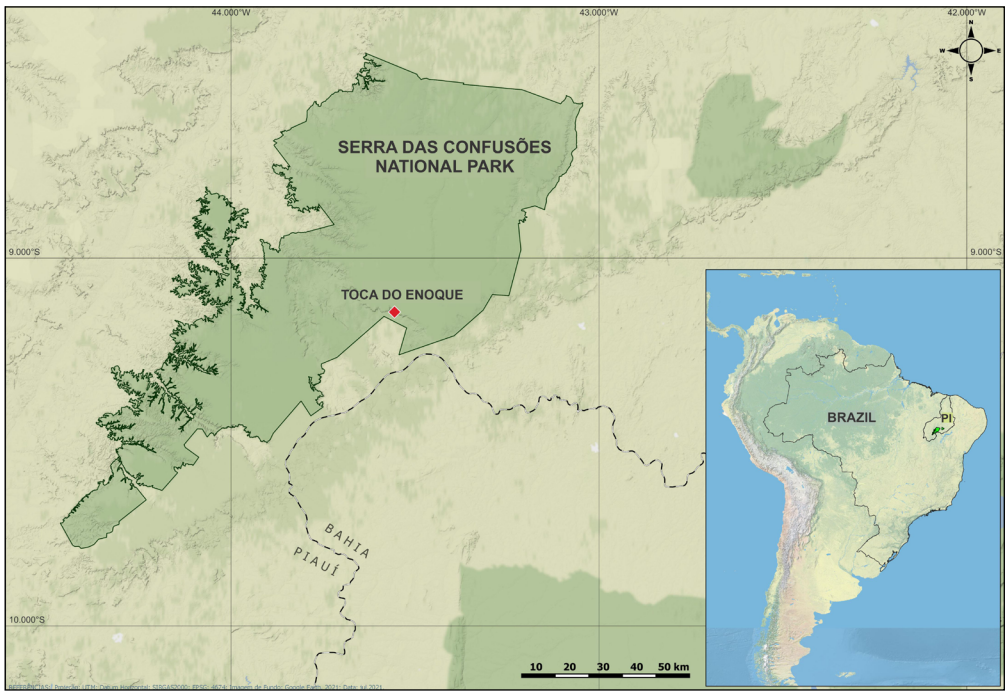

FIGURE 1. Geographic location of the archaeological site (*Toca do Enoque*, Piauí, Brazil).

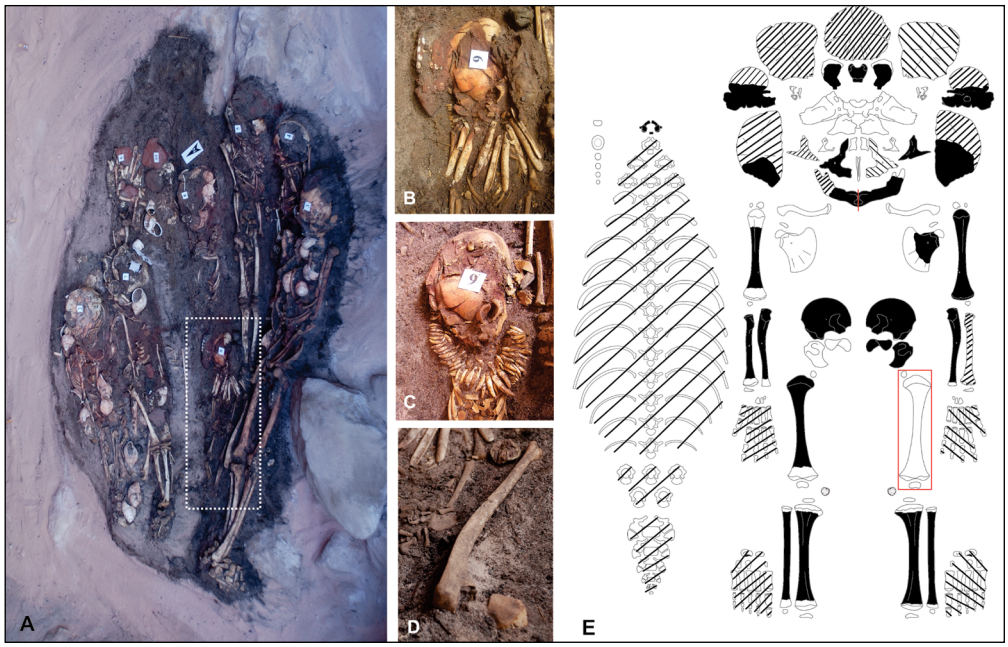

FIGURE 2. A) Burial 2 showing the central position of Individual 9 (Ind. 9) in the collective grave. **B-D)** Different views of Ind. 9's funerary treatment and mortuary context, highlighting offerings that include animal bone collars and human bone relics. **E)** Preservation of Ind. 9's skeleton (in black preserved bones, in hatched very fragmented or incomplete bones, in white destroyed bone tissue or missing bones like right femur extracted for DNA). Scheme modified from Hodson (2022).

Instead of reiterating the information published by Solari *et al.* (2020), this paper focuses on delving into the paleopathological diagnosis of this rare case. This brief report re-examines the bone lesions identified on the infant's skeleton (Fig. 3) to more precisely circumscribe the differential diagnosis, integrating additional pathological characterization of inner bone structures using radiographs and CT scans. In doing so, this work aims to strengthen the current understanding of the special treatment given, before and after death, to this infant individual from *Toca do Enoque*.

FIGURE 3. Pathological bone changes observed in Individual 9. **A)** Reactive bone on the entire endocranial surface of a parietal bone fragment. **B)** Costal periosteal new bone formation (PNBF). **C-G)** Alterations along the diaphysis of humeri, right radius, ulnae, right femur, and fibulae.

MATERIAL AND METHODS

The skeleton of Ind. 9 was reanalyzed macroscopically to reconsider the pathophysiology of the identified lesions. Since non-adult individuals may exhibit periosteal new bone formation (PNBF) and increased bone porosity due to both normal growth and disease, the distribution and appearance of the PNBF were examined using Monge Calleja's

(2022) benchmarks. The previously noted expanded vertebral *foramina* were now associated with variants of basivertebral blood vessels (Barnes, 2012, p.103), while particular care was taken in in considering post-depositional taphonomic destruction affecting the metaphysis of long bones and the extreme fragmentation of other bones. Based on this reassessment, it was concluded that only the endocranial surfaces, ribs, and long bones displayed pathological bone changes, which were attributed to a systemic disease.

Imaging techniques were applied to 10 out of the 12 long bones. No images were taken of the left radius due to extreme fragmentation, and the left femur had previously been destroyed during an unsuccessful aDNA attempt. Conventional X-rays were performed using a GE Healthcare XR6000 radiograph (in both projections), and CT scans were acquired using a Philips Ingenuity 128-channel CT scanner. CT slices (width and height: 0.45 mm, thickness: 0.9 mm), and 3D reconstructions were analyzed using TIVMI software (Dutailly *et al.*, 2009).

RESULTS

All pathological bone changes identified on Ind. 9 are depicted in Figure 3. The inner tables of the preserved cranial fragments showed active new bone growth covering the entire surface, without any involvement of the ectocranial table. The ribs displayed diaphyseal thickening. However, the most striking changes were found on the long bones, where a polyostotic (i.e., involving multiple bones), bilateral, and asymmetrical PNBF was observed, with variation in both location and severity along the diaphysis. The humeri, right radius, left tibia, and both fibulae showed mild, diffuse porous PNBF, while in the right femur and ulnae, only the anterolateral aspect was affected.

The right tibia displays the most exuberant changes, with a profuse shell of PNBF sheathing both its anteromedial aspect and the proximal half of its lateroposterior surface, creating a double-layered, bone-within-bone appearance. The thickness of this hyperplastic bone deposit shows a monolayered, perpendicular, palisade structure, resulting in a deformity characterized by a more pronounced curvature along its longitudinal axis. Cortical perforations penetrated the bone, extending from the internal to the external bone surface, with burred, jagged edges located slightly above the midshaft on the lateral cortex, which is not covered by PNBF (Fig. 4). The tibial metaphysis were not preserved, so their involvement is uncertain. In fact, only the left humerus and the right femur preserved their ends, though neither showed any morphological or structural changes.

Conventional radiography confirmed that all long bones exhibited similar alterations (Fig. 5), with the most substantial pathological lesions affecting both humeri and tibiae, in the form of circumferential thickening along the diaphyses due to the deposition of less dense, porous, newly formed bone around the original cortex. X-rays of the distal end of the left humerus revealed Harris lines. The right tibia showed unusual variations in its radiopacity, with low-density structures surrounding the cortical bone. In fact, CT scans (Fig. 6) confirmed that the cortical bone of both tibiae and humeri contained hypodense areas of heterogeneous thickness. At least in the right tibia, this pattern is due to the set of cortical perforations interconnecting the medullary cavity, cortical bone, and subperiosteal space, resembling subperiosteal abscesses or *cloacae* (see Multimedia File, Monge Calleja *et al*., 2025). Finally, significant endosteal new bone proliferation is visible on the surfaces of the cortical bone in the tibiae, humeri, and, to a lesser extent, the right radius. These alterations show variations in density and form irregular compartments between the cortical bone and the endosteal new bone proliferation, particularly in the left humerus and right tibia.

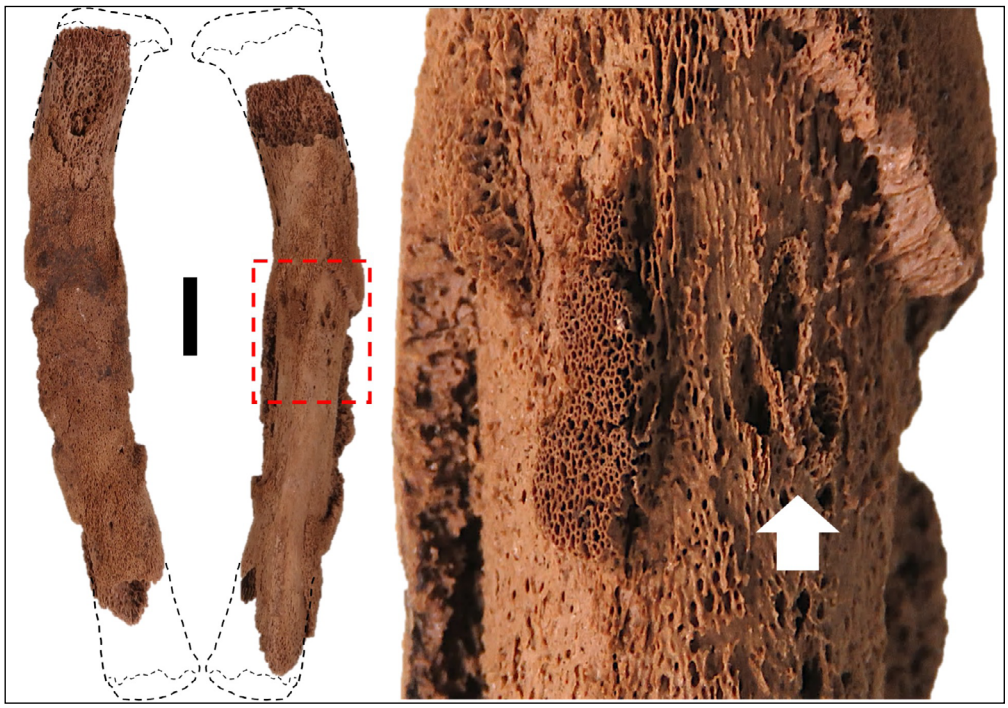

FIGURE 4. Changes observed in the right tibia of Individual 9 with a close-up of the burr, jagged perforations located on its lateral surface and connecting the medullary cavity to the outside.

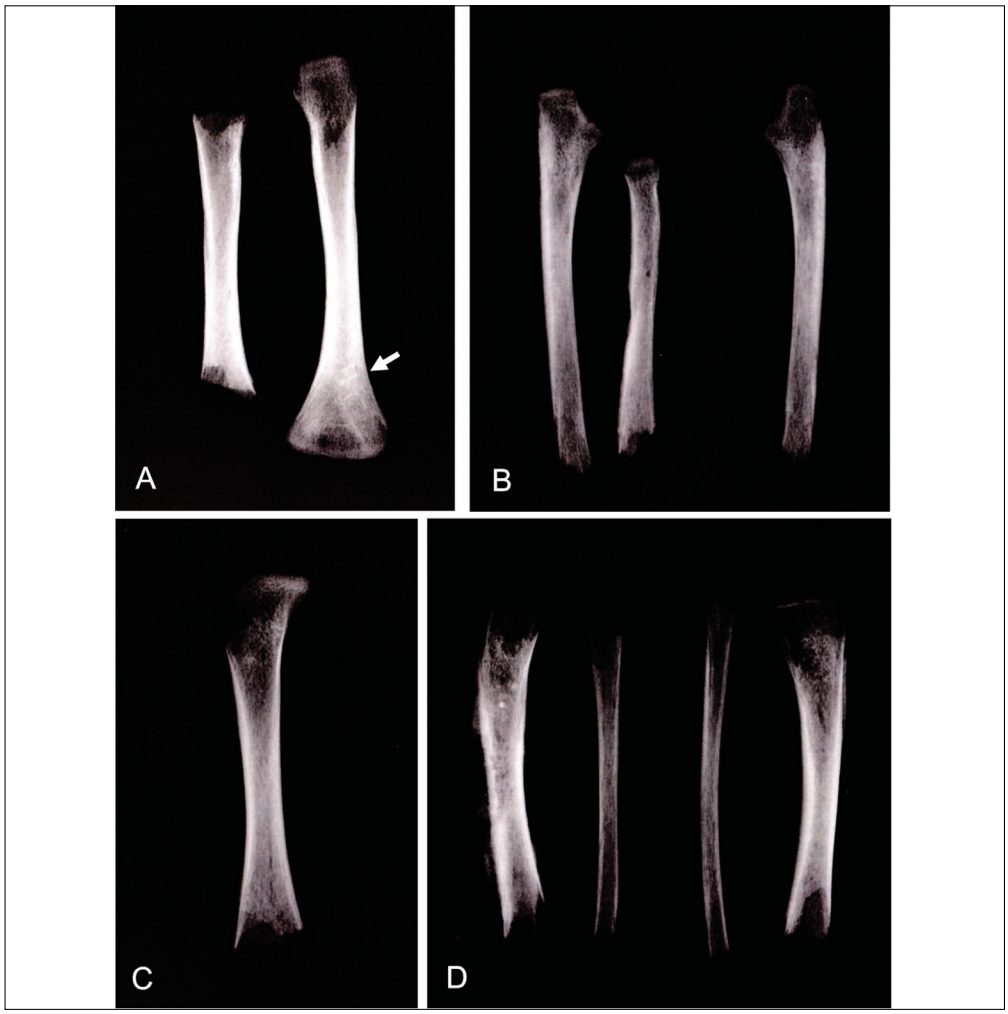

FIGURE 5. Conventional radiography of the long bones. **A)** Humeri with Harris Lines (white arrow). **B)** Forearm bones. **C)** Right femur. **D)** Tibiae and fibulae.

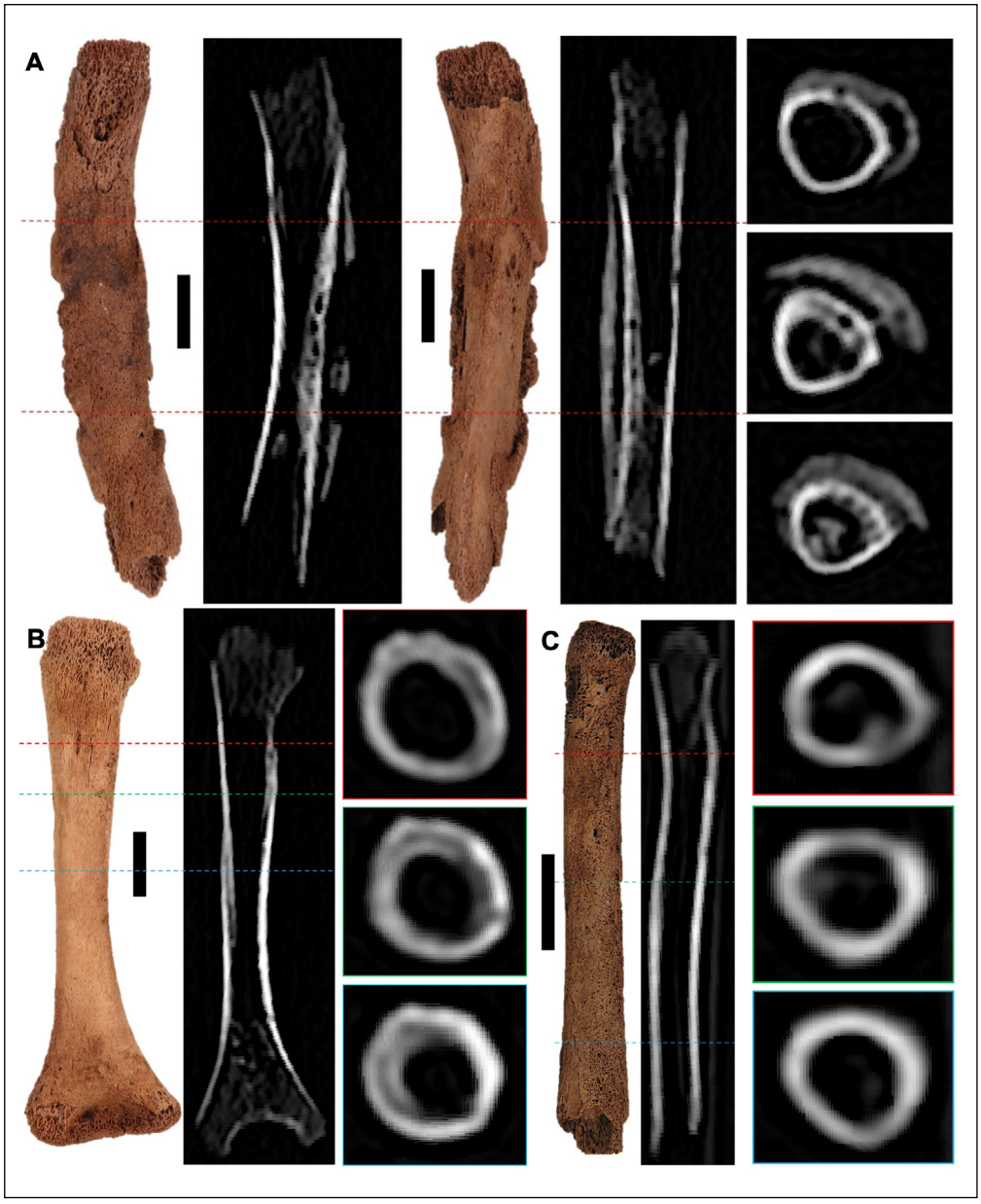

FIGURE 6. Coronal (longitudinal) and axial (transverse) tomographic image of the right tibia **(A)** left humerus **(B)** and the right radius **(C)** of Individual 9. Note the growth of new endosteal bone, the variation of the cortical density and bone compartments between the original cortical bone and the newly formed bone. White asterisks indicate the irregular compartments between the cortical bone and the newly proliferated endosteal bone.

DISCUSSION AND CONCLUSION

Table 1 outlines a differential diagnosis based on Ind. 9's skeletal lesions. Conditions such as yaws, bejel, and Caffey's disease can be ruled out due to the individual's early age-at-death. Additionally, the unilateral tibial deformity with subperiosteal (cloaca-like) abscesses helps exclude scurvy, rickets, hypervitaminosis A, and hypertrophic osteoarthropathy (HOA), while the polyostotic, bilateral distribution of the lesions and the tibial PNBF causing the deformity, further narrow the diagnosis, ruling out infant abuse. Consequently, this case study focuses on two specific diseases for closer examination: Early Congenital Syphilis and Osteomyelitis.

Early Congenital Syphilis (ECS) refers to transplacental or vaginal mother-to-child infections caused by the *Treponemal pallidum pallidum,* bacteria manifested before 2 years

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TABLE 1. Summary of the conditions considered in the differential diagnosis of Individual 9 (Ind. 9).

		Metabolic diseases				Infectious diseases				Others		
	Ind. 9	Scurvy[a]	Infantile rickets[b]	Infantile hypophosphatasia[b,c]	Chronic hypervitaminosis A[c]	Early congenital syphilis[d]	Yaws[e]	Bejel[f]	Infantile osteomyelitis[g]	Infant abuse[h]	Caffey's disease[b,i]	Hypertrophic osteoarthropathy (HOA)[ij]
Age of onset	9±3m	Any	<6m		1-3y.o	<2y.o	>2y.o	>2y.o	<1y.o	<3y.o	≥9m	Adults <non-adults
Endocranial growths	+	+	-		-	Ectocranial porous aspect and diploic irregularities	-	-	+	+	-	-
Polyostotic, bilateral, and asymmetrical distribution on the long bones	+	+	+		By calcification of the soft tissues	+	+	+	+	+	Mainly clavicles, ulnae, and mandibular rami	+
Thick subperiosteal growth sheathing the tibia	+	+	Undermineralized, porous new bone over fast-growing endochondral and appositional bone portions		-	+	+	+	+	+	+	Distal ends of the long bones
Multilayered, palisade hyperplastic subperiosteal bone deposit	+	Rare	-		-	+	+	+	+	Rare	-	+
Subperiosteal growths loosely attached to the original cortex	+	+	+		-	+	+	+	+	+	+	+
Unilateral saber-shin deformity	+	-	Bending	Bending, shortening and fractures	-	+	+	+	+	-	Spindle-shaped deformity	-
Cloacae	+	-	-	-	-	-	-	-	+	-	-	-
Endosteal new bone proliferation	+	-	-	-	-	-	+	+	+	-	-	-
Metaphyseal involvement	-/N.O	+	+	+	+	+	+	+	+	+	-	+

m: months; **y.o:** years old; **N.O:** not observable; **+:** presence; **-:** absence

[a]Snoddy *et al.* (2018), [b]Brickley *et al.* (2020), [c]Blalock *et al.* (1995), [d]Malgosa *et al.* (1996), [e]Antal *et al.* (2002), [f]Powell & Cook (2005), [g]Trueta (1959), [h,i]Gresky & Schultz (2023), [i]Cavanaugh & Holman (1965).

of age (Sankaran *et al*., 2023). Without treatment, a significant proportion of fetuses result in stillbirth or spontaneous abortion due to impaired organogenesis (Rodríguez-Cerdeira & Silami-Lopes, 2012). Among survivors, ECS primarily affects the skin and can progress to neurological issues (e.g., meningitis, choroiditis, hydrocephalus or seizures) and multiple skeletal alterations (Medoro & Sánchez, 2021), with a wide range of interindividual incidence and severity (Cremin & Fischer, 1970; Rathbun, 1983). These include osteochondritis, metaphysitis, diaphyseal osteitic dystrophy, and periostitis of the long bones and ribs (Brion *et al*., 1991; McLean, 1931; Rasool & Govender, 1989).

In the case of Ind. 9, although the distal ends of the left humerus and the right femur are normal, the absence of the remaining metaphyses and any epiphyses limits both macroscopic and radiological evaluation, including assessment for Wegner's and Wimberger's signs (Baker *et al*., 2019). Nevertheless, this case did not show diaphyseal sclerosis (osteitis) due to inflammation. Additionally, medical records indicate that the presence of syphilitic saber-shin deformity requires the formation of gummatous ulcers, which symmetrically soften the leg bones (Rathbun, 1983), typically occurring after the second year of age, in other words, in late congenital syphilis (Cooper & Sánchez, 2018; Rodríguez-Cerdeira & Silami-Lopes, 2012). Based on these discrepancies in age and skeletal manifestations in Ind. 9, ECS is excluded from the differential diagnosis.

During the pre-antibiotic era, osteomyelitis (OM) was a more fatal condition the younger and more immunocompromised the individual (McPherson, 2002; Mok *et al*., 1982). Osteomyelitis is known to exploit the characteristics of early immature bone biology, producing a distinct pathogenetic, pathochronic, and nosologic bone infection compared to that seen in older children and adults (Fisher, 2011; Fraser, 1934; Ogden, 1979; Starr, 1922; Trueta, 1959). Non-bacterial OM–and its more severe, chronic, recurrent, and multifocal form (CRMO)–are extremely rare autoimmune conditions, seldom occurring in non-adult cases, and typically affecting long bones symmetrically (Buch *et al*., 2019). In contrast, neonatal/infant OM is predominantly acute and hematogenous (Stone *et al*., 2016), usually triggered by respiratory infections (Green, 1935; Green & Shannon, 1936) or infected open wounds (Dirschl & Almekinders, 1993).

Overall, OM infections are typically mono-focal, but in neonates and infants, the most common pathogen causing these infections, *Staphylococcus aureus*, is frequently associated with systemic symptoms and multifocal infections (Asmar, 1992; Weissberg *et al*., 1974). However, the list of microorganisms that can potentially cause neonatal/infantile OM is extensive, each with species-specific pathogenicity and age dependence (Paizano Vanega *et al*., 2021). The metaphyseal-epiphyseal ends of long bones are especially vulnerable, particularly in the tibia, where blood flow is the slowest (Stone *et al*., 2016).

This susceptibility stems from the pathogenic preference for colonizing the slow-flowing loop vessels that interconnect both bone ends, a condition that can persist up to 18 months postnatally (Jaramillo *et al*., 2017; Trueta, 1959). However, according to the pathogenetic explanation proposed by Labbé *et al*. (2010), *involucrum* formation occurs before the septic spread to the metaphysis.

In the non-adult paleopathological record, only 20 OM cases have been described to date (Anderson & Carter, 1995; Böni & Ultich-Bochsler, 2014; Kołodziej *et al*., 2015; Lieverse *et al*., 2022; Santos & Suby, 2015; also see the cases summarized by Tavares *et al*., 2017). This scarcity of documented cases is largely attributable to the sudden, high septic mortality triggered by proinflammatory cytokines in the past (Roberts, 2019). Diagnoses in these cases are consistently based on the presence of other typical, chronic indicators in older children, such as *sequestra* (necrotic/dead isolated bone) and *cloacae* (pus

discharge gap). Clinical literature indicates that, just as *sequestra* often go undetected in neonates and infants due to rapid enzymatic digestion (Green & Shannon, 1936), *cloacae* should also be absent, since the high bone porosity of infant bone provides natural conduits for purulent drainage (Ogden, 1979; Trueta, 1959). Individual 9 meets the first premise but not the second, as the cloaca-like abscesses were observed connecting the lateral cortex of the right tibial medullary and subperiosteal cavities, with burred, jagged edges oriented from the interior to the exterior.

Medical and paleopathological cases involving less common, severe forms of OM have shown that cloaca formation can occur at an early age (Lee *et al*., 2016; Waters-Rist, 2012), while turn-of-the 20th century medical texts report the progression of the infection (and individual survival) even over periods of up to 15 years (see Böni & Ultich-Bochsler, 2014). Dich *et al*. (1975) endorses that delays in pus evacuation may increase the risk of chronicity. However, in clinical contexts, the rapid surgical interventions performed to halt the progression of infection have often precluded comparative cases like Ind. 9, even during penicillin-resistant relapses (Gilmour, 1962). The distinction between acute and chronic clinical stages remains artificial, minimalistic, and arbitrary, terms that oversimplify both the multifactorial nature of this infection and the external factors influencing its course (Waters-Rist, 2012; Zimmerli, 2021).

In 2014, Böni and Ultich-Bochsler reported that neonatal/infant OM could feasibly become chronic when host defenses are limited. Neonates and infants have an immature immune system (Lewis, 2018), though it can be enhanced by breastfeeding, a possibility already proposed by Waters-Rist (2012), who published the first case of mandibular OM with cloaca in a ~1.75-year-old individual from Early Neolithic Lake Baikal (6890 ± 40 cal BP, Siberia). Unfortunately, both isotopic and genetic studies were not possible in the present study due to the degradation of Ind. 9's bone collagen, limiting insights into the potential suboptimal nutritional values and preventing paleogenomic identification of the pathogen responsible for the observed bone alterations. Based on the interpretations by Solari *et al*. (2020), it is proposed that the specialized care provided to Ind. 9, both normative and non-normative, as evidenced by the privileged funerary treatment and offerings, may have significantly contributed to prolonged survival and influenced the progression of OM. Additionally, the presence of Harris lines on the distal end of the left humerus (Fig. 5) suggests some degree of individual resilience, indicating recovery from a morbid episode that temporarily arrested growth.

The paucity of analogous cases documented in literature underscores the significance of this individual as a valuable contribution to the expanding paleopathological knowledge concerning infant remains. However, labeling Ind. 9 as the youngest case of neonatal/infant OM diagnosed to date in the global paleopathological record, and the first one reported in the Americas has its limitations. After all, "*Osteomyelitis is known as the "great pretender" because of the difficulties encountered in diagnosis*" (Calhoun *et al*., 2006: 62). Diagenetic damage hampered a more thorough assessment of the entire skeleton, as well as the use of complementary studies to support the diagnosis or identify the specific pathogen responsible. Within the differential diagnostic framework, the initial focus of neonatal/infant OM remains unknown: while involvement of the ribs could suggest a respiratory infection, the hypertrophy of the right tibia could also point to an infected open wound.

Furthermore, there is no evidence linking this condition to the appearance of endocranial new bone formation. Consequently, it remains possible that the changes identified in Ind. 9 resulted from a comorbidity between OM and other pathological condi-

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tions, such as metabolic diseases (see Buckley *et al*., 2014). The large number of faunal ornaments accompanying the individuals recovered from Burial 2 (MNI = 73 cervids and 150 canids), used in elaborate necklaces, along with remains of various species of felines, birds, turtles, large gastropods, dasypodids, tayassuids, among others (Faure *et al*., 2011), may offer clues about a diet richer in game meats than in vegetables, possibly for cultural reasons. This also reflects a lavish burial and the care and value placed on the infant, evidence that is rare in bioarchaeology, but which lends greater significance to this case.

Expanding the corpus of case studies in Paleopathology is, thus, essential for advancing and refining diagnostic criteria and interpretations, enhancing our understanding of complex conditions, and addressing the challenges posed by rare and potentially comorbid diseases. This is particularly crucial for studying more exacerbated conditions that may not be observed in clinical settings, where immediate treatments or surgical interventions often halt disease progression.

ETHICAL CONSIDERATIONS

We declare that the procedures developed in this research involving human skeletal remains comply with Brazilian legislation and follow international ethical recommendations. Consent was not required for this study, as no local communities or families have expressed any connection to the remains under study.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Álvaro M. Monge Calleja: Conceptualization, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing - Original Draft, Writing - Review & Editing. Dany Coutinho Nogueira: Data curation, Formal analysis, Methodology, Software, Validation, Writing - Review & Editing. Anne Marie Pessis: Funding acquisition, Resources, Writing - Review & Editing. Ana Solari: Conceptualization, Investigation, Project administration, Supervision, Validation, Visualization, Writing - Review & Editing.

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