International Journal of Paleopathology 22 (2018) 97–100

Contents lists available at ScienceDirect

International Journal of Paleopathology

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

Brief Communication

On engagement with anthropology: A critical evaluation of skeletal and developmental abnormalities in the Atacama preterm baby and issues of forensic and bioarchaeological research ethics. Response to Bhattacharya et al. "Whole-genome sequencing of Atacama skeleton shows novel mutations linked with dysplasia" in *Genome Research, 2018, 28: 423–431. Doi: 10.1101/gr.223693.117*

Siân E. Halcrow[a,*], Kristina Killgrove[b], Gwen Robbins Schug[c], Michael Knapp[a], Damien Huffer[d], Bernardo Arriaza[e], William Jungers[f], Jennifer Gunter[g]

[a] *Department of Anatomy, Otago School of Biomedical Sciences, University of Otago, New Zealand*
[b] *Department of Anthropology, University of North Carolina at Chapel Hill, United States*
[c] *Department of Anthropology, Appalachian State University, United States*
[d] *Department of Archaeology and Classical Studies, Stockholm University, Sweden*
[e] *Instituto de Alta Investigación, Universidad de Tarapacá, Arica, Chile*
[f] *Department of Anatomical Sciences, Stony Brook School of Medicine, United States*
[g] *Department of Obstetrics and Gynecology, Kaiser San Francisco, United States*

ARTICLE INFO

Keywords:
Ata
Genomic analyses
Foetal skeletal development
Skeletal dysplasia
Research ethics
Chile

ABSTRACT

Here we evaluate Bhattacharya et al.'s (2018) recent paper "Whole-genome sequencing of Atacama skeleton shows novel mutations linked with dysplasia" published in *Genome Research*. In this short report, we examine the hypothesis that the so-called "Atacama skeleton" has skeletal abnormalities indicative of dysplasia, critique the validity of the interpretations of disease based on genomic analyses, and comment on the ethics of research on this partially mummified human foetus. The current paper acts as a case study of the importance of using an anthropological approach for aDNA research on human remains. A critical evaluation of the ethically controversial paper by Bhattacharya et al. highlights how an understanding of skeletal biological processes, including normal and abnormal growth and development, taphonomic processes, environmental context, and close attention to ethical issues of dealing with human remains, is vital to scientific interpretations. To this end, close collaboration with palaeopathologists and local archaeologists through appropriate peer-reviewed journals will add to the rigour of scientific interpretation and circumvent misinterpretation.

1. Introduction

Judging by the sheer amount of press that human skeletons have received in recent years, it is clear that skeletal analysis speaks to many people, easily capturing the public's attention with its potential to help us understand individual lives in the past. Although educating the public about ancient life courses is a goal that we share, the media blitz in early 2018 following the publication of Bhattacharya et al.'s article in *Genome Research* is a prime example of how research that is not rigourous, analytically sound, or performed by appropriately trained researchers can spread misinformation. Further, studies such as these that do not address ethical considerations of the deceased and their descendant communities threaten to undo the decades of work anthropologists and others have put in to correct past colonialist tendencies. When human skeletal studies that flout standard conventions of science are published, it is imperative for us to demonstrate how collaborative efforts in the analysis and interpretation of remains can counteract incorrect and problematic scientific narratives.

In this brief commentary, we use the Bhattacharaya et al. article as an example of the kind of problematic research from which we can learn the importance of taking a holistic perspective in science. Drawing on scientific analytical techniques using human

* Corresponding author at: Department of Anatomy, School of Biomedical Sciences University of Otago, Great King Street, Dunedin 9054, New Zealand.
E-mail address: sian.halcrow@otago.ac.nz (S.E. Halcrow).

https://doi.org/10.1016/j.ijpp.2018.06.007
Received 30 March 2018; Received in revised form 28 June 2018; Accepted 28 June 2018

developmental osteology standards, comparative foetal osteological material, and paediatric genetic syndrome literature, we begin by outlining our concerns with the analysis of the age-at-death and 'abnormalities' in Ata's skeletal remains and with the flawed scientific rationale to conduct genomic analysis. We then bring attention to essential ethical concerns and conclude with suggestions for how to engage in rigorous scientific research using human remains.

2. Critical commentary

2.1. Ata's skeletal morphology

Bhattacharya and colleagues (2018: 1) state in their abstract that the Atacama "specimen carried a strange phenotype – 6-in[ch] stature, fewer than expected ribs, elongated cranium, and accelerated bone age." The original assessment of the skeleton, however, was never published in a peer-reviewed journal, finding a public audience in *Science Magazine* (Stone, 2013). In their Supplemental Note to their 2018 article, Bhattacharya and colleagues say that the "morphologic features include that the specimen has only 10 ribs, mild mid-face hypoplasia, and shows abnormalities of the skull. […] As represented by a specialist in pediatric human bone and growth disorders, the 6-inch specimen is a human that was likely 6–8 years of age at the time of death (age based on epiphyseal plate X-ray density standards). […] The specimen was concluded by the medical specialist to be a human child with an apparently severe form of dwarfism and other anomalies."

As experts in human anatomy and skeletal development, we find no evidence for any of the skeletal anomalies claimed by the authors. Their observations of 'anomalies' represent normal skeletal development in the foetus, cranial moulding from delivery, and potential post-mortem taphonomic effects. Specifically:

1 Bhattacharya et al. claim the skeleton demonstrates "precocious epiphyseal ossification" (2018: 1) and "was possibly 6–8 yr at the time of demise" (2018: 6). They provide no evidence in the paper to support this claim. Based on the long bone (diaphyseal) lengths published in Gabilondo (2007) of a femur (20 mm) and clavicle (15 mm), we can estimate that this baby died at approximately 15 weeks gestational age (Cunningham et al., 2016). Further, if we accept the 6-inch crown-heel length reported for the Ata specimen as accurate, this also allows us to estimate gestational age at 15 weeks (Archie et al., 2006); however, there may be some reduction of length of the skeleton from desiccation.
2 Oblique reference is also made to the *Science Magazine* article (Stone, 2013) in which Nolan noted that Ata was 6–8 years of age-at-death based on an epiphyseal plate density test, a claim repeated in Bhattacharya and colleagues' (2018) Supplemental Note. The actual methods for reaching this conclusion are not specified, nor is the applicability of the method on desiccated tissue explained. Based on Bhattacharya and colleagues' (2018) Figure 1, there is no evidence for phenotypic abnormalities in any of the long bones (Baker et al., 2005).
3 The authors note (2018: 1) that "after examining the X-ray images, it is concluded that Ata had only 10 pairs of ribs instead of the normal 12 in humans." The 11th and 12th ribs may not be observable as they are smaller, shorter, 'floating' ribs that do not articulate anteriorly at the sternum and are not as robust. There is little information about the formation of ribs *in utero*, but Scheuer and Black (2000: 238) state that "by the eleventh and twelfth weeks of intrauterine life, each rib (often with the exception of the twelfth)" has started to form, which implies that the lower ribs are later forming. All ribs that are visible in the Ata specimen have normal morphology. Interestingly, the clinical literature (e.g., Calder and Offiah, 2015: 539) acknowledges the potential for misdiagnosis of skeletal dysplasia due to normal lack of ossification in early gestation foetuses. This misdiagnosis seems to be the case in the paper in question.
4 Bhattacharya et al. (2018: 1) also argue that the baby has an "elongated cranium." Although the cranium does appear to be longer than it is wide, this can be better explained in terms of both taphonomic and birth processes. It is common for a process called plastic deformation to alter the shape of cranial remains that have been interred in the ground, where heat and pressure can slowly affect their shape (McPherson and Kriewall, 1980). Additionally, a foetus of this age does not have the same cranial proportions of a full-term foetus (Calder and Offiah, 2015; Campbell and Newman, 1971). Furthermore, during delivery, the relationships between the cranial bones may be altered from compression of the bones in the cervix in a process referred to as moulding. Such moulding can reduce the skull diameter, resulting in an elongated appearance; this has been shown to be more severe in preterm foetuses (McPherson and Kriewall, 1980). Based on the photos provided, the frontal and parietal bones of the Atacama baby indeed show significant moulding; the parietals are compressed, and the superior part of the left parietal bone is passing over the right parietal at the midsagittal suture. Lifting of the parietal bones is often reported in obstetric and paediatric literature (McPherson and Kriewall, 1980; Lapeer and Prager, 2001). The "elongated cranium" of Ata is therefore phenotypically normal for a preterm foetus that has been delivered.
5 The authors state that they have identified known mutations in genes associated with cranioectodermal dysplasia and Greenberg skeletal dysplasia (Bhattacharya et al., 2018: 5), both of which they assert may have produced Ata's supposed phenotype: the inferred cranial dysplasia, the claim that the foetus demonstrates "accelerated bone age" (2018: 1), a "premature ossification phenotype" (2018: 6), and "was possibly 6–8 yr at the time of demise" (2018:1). Cranioectodermal dysplasia (Sensenbrenner syndrome) is a rare multiple anomaly syndrome with distinctive skeletal changes including craniofacial findings (e.g., forehead bossing, dolichocephaly), and metaphyseal dysplasia (e.g., short limbs, small thorax) (Lin et al., 2013), and Greenberg skeletal dysplasia causes punctate calcification of cartilage and asymmetrical shortening of long bones (Offiah et al., 2003). Given that there is no skeletal evidence for any of these conditions in the Atacama foetus, the basis for this conclusion is questionable.

Taken together, none of the methods or findings regarding Ata's skeletal age presented by Bhattacharya and colleagues meet the accepted standards for age estimation using bioarchaeological, forensic, or paediatric/obstetric techniques. One of us (WJ) raised these concerns some years ago, saying that "genetic anomalies aren't evident, probably because there aren't any" (quoted in Stone, 2013).

2.2. Genomic data interpretation

We also want to comment on the genomic results in the Bhattacharya paper, as we are sceptical that the genomic results support morphological anomalies that are not actually present. Although we concede that only one of us (MK) is a specialist in human genomics, we have serious misgivings about the interpretation of the genomic analysis. Specifically:

1 According to the authors (2018: 6), the specific variants they have identified are "associated with scoliosis (COL1A1, FLNB, COL2A1, PMP22), Ehlers-Danlos syndrome (COL1A1, FLNB, COL2A1, PMP22), and musculoskeletal abnormalities (COL2A1, WDR65, ASPM, PMP22, FLNB)." We question why the authors have used missense variants in the COL1A1 and COL2A1 genes (rs575285203 and rs768451951) as evidence of a predisposition to dysplasia. These genes provide instructions for making type I collagen; the specific variant found in the COL1A1 gene could possibly influence the development of Ehlers-Danlos syndrome, Caffey's disease