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Case study

Overlapping genetic pathways in the skeletal dysplasias of a middle woodland individual: A case study

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ABSTRACT

Studies of interacting/overlapping genetic skeletal disorders are rare for populations today, but even more so for archaeological contexts. The skeletal remains of an adult female (EZ 3-7-1) were excavated in the 1980s from the Middle Woodland (50BC–AD400) context of the Elizabeth site (11PK512) in the lower Illinois Valley (LIV), USA. Reported here are the standard score (z-score) comparisons of the measured skeletal differences of EZ 3-7-1 with a reference sample and a re-analysis of the individual's pathological changes, with special consideration placed on refining the disease diagnosis. The impressive preservation and meticulous recovery of these skeletal remains have provided the opportunity to identify the first and earliest archaeological example of an individual (EZ 3-7-1) with a combined genetic skeletal dysplasia, Leri-Weill dyschondrosteosis and achondroplasia.

1. Introduction

This paper re-evaluates skeleton EZ 3-7-1, excavated from the Middle Woodland (50 BC-AD 400) context of the Elizabeth site (11PK512) in Pike County, Illinois (Fig. 1), at the northern limits of the lower Illinois River Valley. EZ 3-7-1 was an adult female who probably died in childbirth, as fetal remains (EZ 3-7-2) were found partially disturbed and "lodged in the birth canal of Skeleton 1 [EZ 3-7-1]… [with the] upper-body elements rested on [the] sacrum of Skeleton 1" (Charles et al., 1988, p. 256). EZ 3-7-1 was originally described and diagnosed as a "textbook case" of achondroplasia, with bone changes including woven bone and sclerotic periostosis co-morbidity (Charles et al., 1988, p. 286). Over the approximately 35 years since excavation, advances in clinical, genetic, and osteological observations and interpretations of genetic skeletal dysplasias have stimulated this reassessment (Cohen, 1998; Foldynova-Trantirkova et al., 2012; Munns and Glass, 2008; Ross et al., 2003; Wei et al., 2001; Xue et al., 2014). We present here our re-examination of EZ 3-7-1's atypical morphology, with special consideration of recent information about combined skeletal dysplasias.

Skeletal dysplasias refer to disturbances in bone modeling and development mostly associated with a genetic etiology (Beighton et al., 1992; Brook and de Vries, 1998; Butler, 1977; , p. 481; Warman et al., 2011). Further, dysplasias differ from dysostoses in that dysplasias are the result of "defects in structural proteins, metabolic processes, or in growth plate regulation," while dysostoses "arise from embryonic morphogenic defects" (Warman et al., 2011, p. 967). The term *combined skeletal dysplasia* refers to the presentation of a combination of skeletal dysplasias within an individual where the phenotype appears to be less than additive, meaning the genes involved interact at least in part within "overlapping pathways of bone growth and development" (Ross et al., 2003, p. 61).

Artistic and archaeological evidence indicate that individuals with skeletal dysplasia existed within ancient populations throughout the world (Fowke, 1902; Frayer et al., 1987; Kozma, 2008; Rodríguez et al., 2012; Snow, 1943), most notably from the Old Kingdom, Middle Kingdoms, and the Greco-Roman Period of Ancient Egypt (Kozma, 2008). Very few examples of skeletal dysplasias have been archaeologically-recovered from prehistoric North American contexts (Curry, 1999; DiGangi et al., 2010; Fowke, 1902; Langdon et al., 1993; Snow, 1943). EZ 3-7-1 serves as the sole example of skeletal dysplasia excavated from contexts dating to the Middle Woodland Period.

2. Materials and methods

Skeleton EZ 3-7-1 (Fig. 2) was excavated from the Elizabeth site (11PK512) in Pike County, Illinois, by the Center for American Archeology (CAA) Contract Archeology Program and the Northwestern University Archeological Field Schools during 1980 (Douglas K. Charles personal communication, 2015). The Elizabeth site was located on the

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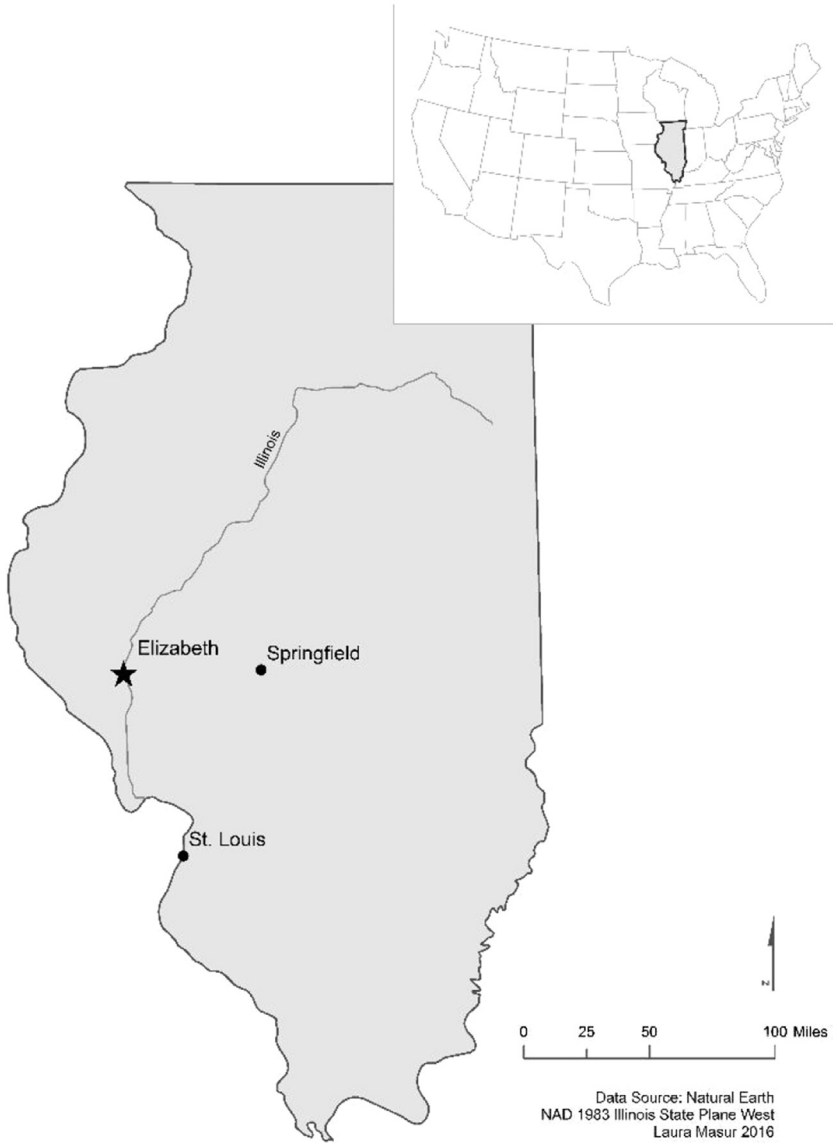

Fig. 1. Location of the Elizabeth site, Illinois. The Elizabeth site is located in the Midwestern state of Illinois, approximately 60 miles (95 kilometers) north on the Illinois River.

western bluff overlooking the Illinois River, with the mound group situated on the northern bluffs (Charles et al., 1988). EZ 3-7-1 was excavated from a burial feature (No. 7) intrusive into Mound 3. A 1998 radiocarbon analysis of bone from this individual (Lab # GX-18529-AMS) yielded a calibrated range of AD 132-388, with a median date of AD 268, associating it with this Middle Woodland context (King et al., 2011). Middle Woodland (50 BC to c. AD 500) populations were clustered into mostly sedentary communities with residential stability (Buikstra et al., 1986; King et al., 2011). In west-central Illinois, the Middle Woodland was a period of hunting, gathering, and minor cultivation, followed by the intensive collecting and cultivation of plants during the Late Woodland (c. AD 500 to AD1000) (Buikstra et al., 1986).

Following inventory, estimations of age, sex, and pathology were made through macroscopic analysis. The estimation of the sex of EZ 3-7-1 used the methods of Phenice (1969) and Buikstra and Ubelaker (1994, p. 15), while age-at-death estimation was attempted considering Lovejoy (1985) patterns of occlusal attrition. Because dental wear patterns are related to cultural subsistence practices, Lovejoy (1985) phases of functional attrition were selected for comparison due to their development in skeletons from a similar cultural context, the Libben population of Late Woodland Ohio. Due to the abnormal bone development evident in EZ 3-7-1, other standard age and sex estimation methods may not yield accurate results and therefore were not used (Bertrand et al., 2016). Further, due to the abnormal morphology and incomplete cranium, few methods for calculating living stature would be appropriate. The metric proportional comparisons of the long bones serve to understand the stature of EZ 3-7-1. For the pathological evaluation of EZ 3-7-1, the recording of the location, distribution, and quality of bone formation and destruction followed the method of Ortner (2003, pp. 45–57).

Following a preliminary metric study by students from Northwestern University supervised by the second author, the long bone measurements of EZ-3-7-1 were further analyzed in comparison to a reference population consisting of 62 Middle and Late Woodland adult females from the Elizabeth Site (Burgess, 1989; Osterholtz et al., 2001). This reference sample was chosen to provide a comparison with individuals of the same sex and from the same location. Using Mitutoyo digital calipers, Osterholtz measured the complete long bones of EZ 3-7-1 and those from the reference population multiple times to ensure that intraobserver error was negligible. Each measurement included in the analysis had less than 2 mm of difference between long bone lengths and less than 1 mm for shape measurements such as diameters.

In order to quantify the extent of EZ 3-7-1's short stature, standard score (z-score) analysis compared EZ 3-7-1's long bone lengths and the mean measurements from the same bones from the reference