



Case study

An 8000-year-old case of thalassemia from the Windover, Florida skeletal population

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ABSTRACT

Thalassemia is a congenital blood disorder which destroys red blood cells at a faster rate than can be produced, resulting in anemia. Historically, this disease is found more often in Old World populations, such as Middle Eastern and Southeast Asian. The earliest reported skeletal evidence of thalassemia comes from the eastern Mediterranean (Atlit-Yam) and is correlated with early agriculturalists' exposure to malarial parasites. While there have been virtually no skeletal reports of thalassemia in prehistoric Native American populations, among the individuals from the 8000-year-old hunter-gatherer site of Windover, Florida there is a single potential case of the disease. A female in her early 20's exhibits bilateral foreshortening of the humeri with indications of premature epiphyseal fusion. Both proximal humeri are medio-laterally compressed, the gleno-humeral joint surfaces exhibit medial deformation, and bones show expansion of the medullary cavity with increased cancellous bone growth. These characteristics have been reported as indicators of thalassemia in both clinical and archaeological contexts. Alternate diagnoses such as congenital dislocation or injuries during child birth are considered but fail to account for the full set of characteristics shown. Individual #76 may, therefore, represent the oldest reported case of thalassemia from a native North American skeletal population.

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1. Introduction

The thalassemias are a group of inherited blood disorders that affect the way the body makes hemoglobin, a protein found in red blood cells that is responsible for carrying oxygen throughout the body. While there are multiple types of thalassemia, the two main groups are alpha thalassemia and beta thalassemia (referring to the globin subunits affected). In both cases red blood cells are destroyed at a rate faster than normal, causing anemia and resulting in skeletal pathologies associated with varying degrees of anemic response. Prehistoric cases of thalassemia have primarily been found among Mediterranean populations and date back as far as 6000 BCE at Atlit-Yam, Israel (Hershkovit and Edelson, 1991) and have been linked to incidence of malaria. Today the range of expression of thalassemia spans from the Mediterranean basin into East Asia. The majority of thalassemia cases have been diagnosed through the presence of cribra orbitalia or porotic hyperostosis (giving a hair-on-end appearance in x-rays) and additional anemic responses such as expanded medullary cavities in conjunction with regions known for having heavy malarial infection rates. Thalassemia has also been

tied to a deformation of the shoulder known as humerus varus (Hershkovit and Edelson 1991; Hershkovitz et al., 1991). The severities of bone deformation also vary based on the type of thalassemia an individual inherits genotypically. Major and minor versions of the disorder illustrate drastic differences in the amount of skeletal involvement and the overall life expectancy of the affected individual. Homozygous individuals generally express a greater degree of skeletal malformation compared to heterozygote counterparts (who can sometimes be asymptomatic). In addition, the heterozygote carriers of thalassemia express a level of resistance to malarial infection.

To date, there have been no recorded cases of thalassemia in the prehistoric (pre-contact) North or South American skeletal record. Theoretically, without the presence of malaria in the pre-contact New World, the primary selective factor of protection against malaria is nonexistent within those populations. This scenario has resulted in the a general lack of consideration for this disorder when differential diagnoses are being developed to explain the presence of severe anemic responses of New World skeletal material. Development of additional skeletal symptoms correlated with thalassemia will allow for the diagnosis to be applied to remains expressing these specific bony alterations regardless of geographic location or time period. This broader application may result in the reassessment of New World cases and may show that although

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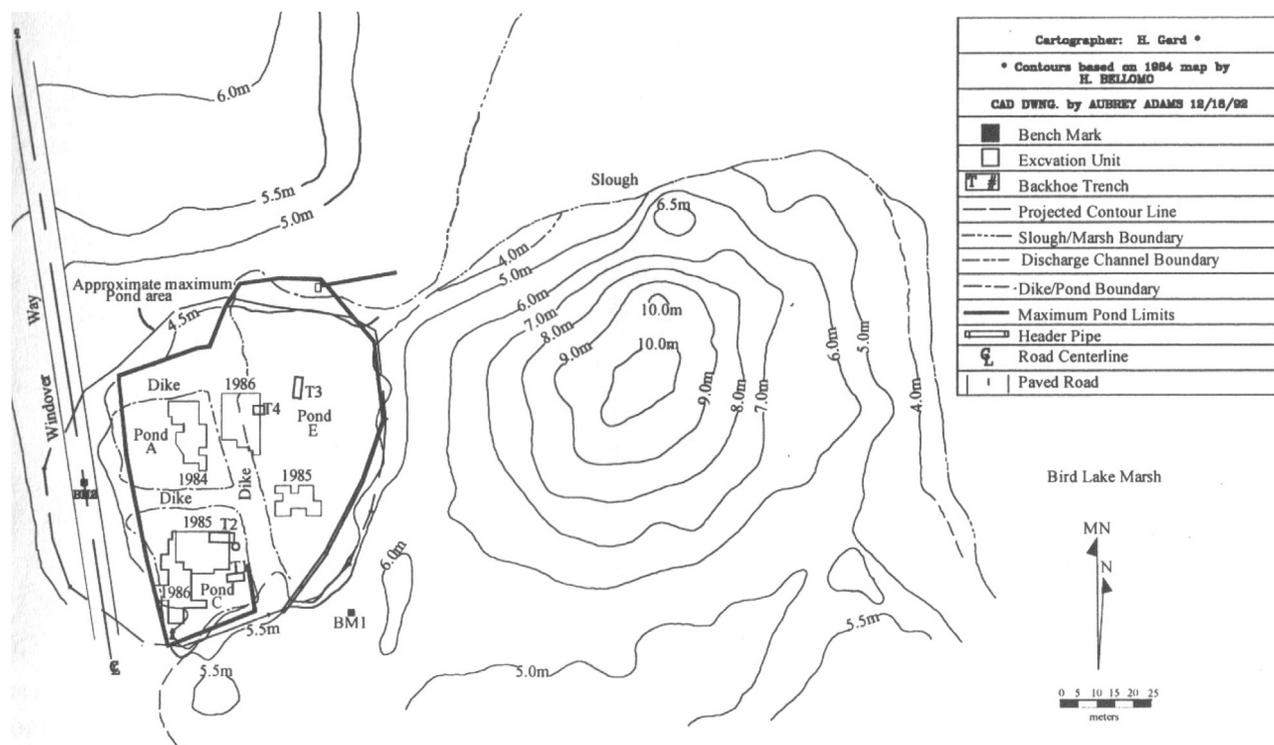


Fig. 1. Windover site map (Doran, 2002).

thalassemia is largely related to the degree of malaria in the environment, it is not the only cause for the disease. It may be rarely seen as a purely genetic disorder, but if the symptoms are present among pre-Columbian Native American remains, thalassemia should not be ruled out as a potential diagnosis purely based on time and location.

2. Materials and methods

2.1. Windover site

North American skeletal collections older than 5000 years are relatively rare, and of these, 60% of the individuals (N=194) are from Florida and date to before 7000 years BP. The Windover site yielded a minimum of 168 adult and subadult individuals and dates to the Early Archaic period (8522–7421 BP calibrated) (Doran, 2002). The site, near present day Titusville, was discovered in 1982 during the cleaning of a small pond for road construction in the Windover Farms housing development. During the process a backhoe operator discovered human remains and artifacts in the black peat spoil banks coming from the bottom of the pond. After several excavation seasons (1984–1986) it was discovered that the wet site was a charnel (mortuary) pond containing peat sediments in which burials were placed (Fig. 1). The skeletal preservation was greatly enhanced through the combination of water chemistry, rapid burial, and physical stability maintained by the peat sediments (Doran, 2002). Through the examination of the burials and associated materials it was found that after death the bodies were placed in shallow graves in flexed positions on their sides around the margin of what was a small pond (Doran, 2002). The burials were deep enough to create anaerobic conditions and the context of the preserved textiles indicates that the bodies were possibly wrapped in matting or fabric and marked by protruding wooden stakes driven into the pond floor to delineate individual burials or groups (Dickel, 2002).

There seems to be very little compelling evidence of a significantly marine orientated diet in Florida's early Archaic period (Dickel and Doran, 2002). Through the analysis of stomach contents and bone isotopes (Tuross et al., 1994), the Windover population was found to have a hunter-gatherer subsistence strategy focused on inland riverine, pond, and marsh resources. The primary sources of food included duck, turtle, and catfish as well as large and small terrestrial resources such as deer and rabbit (Dickel and Doran, 2002). In addition, floral remains indicate the use of a wide array of fresh fruits (grapes, prickly pear, and elderberry), nuts, greens, seeds, and tubers (Newsom, 2002).

Due to road construction leading to the discovery of the site, an estimated 58 individuals were recovered as disarticulated scatter. Of the remaining in situ burials now curated at Florida State University, 63 adults (36 males, 27 females) and 30 subadults (under the age of 18) were found in varying degrees of preservation and completeness. Age and sex estimates were calculated based on traditional non-metric pelvic and cranial assessments, as well as subadult dental eruption (Doran, 2002). Antler tools, deer ulna awls, and atlatls were found to be associated with male burials, while antler punches, modified shell, and simple bone pins were associated with females (Doran, 2002). Subadults were found with a mixture of artifacts including awls, a single atlatl handle, ulna scrapers, drilled fish vertebra beads, modified shell, and lithics (Dickel, 2002). Among the individuals from the 8000-year-old hunter-gatherer site of Windover, Florida there is a single individual that expresses bilateral humerus varus deformity.

2.2. Individual 76

2.2.1. Age and sex

The biological sex of this individual was estimated to be female based on the degree of sexual dimorphism present in this population and the gracility of the skull and long bones in comparison to other members of the Windover population. She died in her early-



Fig. 2. Wormian bones located along the lambdoidal suture of Individual 76.

mid 20's based on the degree of epiphyseal fusion exhibited in the proximal radius, the proximal ulna, and the left distal humerus.

2.2.2. Calvaria

The calvaria is extremely fragmentary and approximately 85% of it has been reconstructed. Superior sections of the right parietal as well as infero-anterior sections of the left and right parietal/temporal are still missing. Approximately 60% of the occipital is intact, with the basicranial sections including the foramen magnum missing. What remains of the face includes a largely intact frontal bone with the superior margins of the orbits and the superior aspect of the nasal bones. The zygomatics, maxilla, mandible, and all of the internal structures (except for the internal auditory meatus) are missing.

Overall, the calvaria is small compared to other females in this population. In terms of the shape of the cranium, no obvious indications of a pathological condition are present. There is a moderate degree of fusion along the sagittal and lambdoidal sutures indicative of a young individual. There are also two wormian bones along the left lambdoidal suture with a possible missing wormian bone along the right lambdoidal suture (Fig. 2). These bones are associated with various diseases including chronic anemia (Ortner, 2003). The frontal bone (unattached from the rest of the cranium) is small with no obvious indications of a severe pathology, such as Down's syndrome, Turner's syndrome, microcephaly, and hydrocephaly. Along the superior orbit there are subtle markers of cribra orbitalia, an indication of anemia.

Examination of the calvarial x-ray (Fig. 3) reveals no obvious indication of pathology. The ectocranial table appears to be missing, which suggests expansion of the diploe in association with anemia.

2.2.3. Thorax and vertebrae

2.2.3.1. *Ribs.* The ribs of this individual are extremely fragmentary with the largest single piece measuring approximately 7 cm in length. There are no apparent pathologies associated with the rib fragments of this individual. The articular surfaces (head and neck) do not appear to be expanded when compared to members of the population with the same age and sex. Upon radiographic examination of the largest fragments, remodeling is apparent, but there is no sign of the rib-within-a-rib appearance (Fig. 4) commonly associated with anemia.

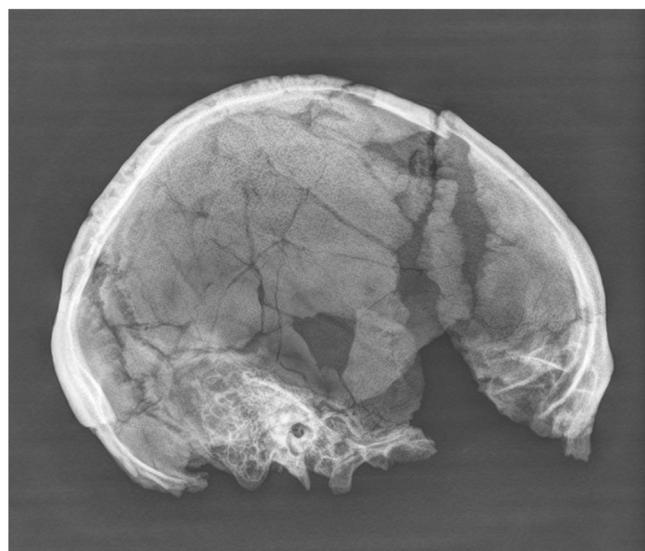


Fig. 3. Lateral cranial radiograph. No definitive signs of hair-on-end striations seen with many thalassemia patients (particularly major forms of the disease).

2.2.4. Scapulae and clavicles

This individual's scapulae are fragmentary. The left and right costal surfaces are virtually missing. The left scapula includes the glenoid fossa, the acromion process and most of the axillary border, while the right scapula includes 90% of the glenoid fossa and attached coracoid as well as the separated acromion process. This individual exhibits bilateral deformation of the glenoid fossae. Both right and left glenoid fossae exhibit malformations including pitting and lipping with a rough shape and uneven contour. Along the superior surface of both fossae there is a deep cavity that is not the result of postmortem preservation (Fig. 5).

The right and left clavicles are 90% and 85% complete, respectively. There are no obvious indications of pathology in either the right or left clavicle. Both size and shape are in line with other members of the population, though they are slightly small compared to another female of the same age.

2.2.5. Humeri

The right humerus is complete except for the distal articulation and an unattached proximal articulation. The overall curvature of the bone is pathological in nature. The bicipital groove has rotated and expanded medially, while the proximal aspect of the bone has been compressed medially. This compression results in a narrower medio-lateral and expanded anterior-posterior orientation of the proximal epiphysis. Along the medial margin of the proximal epiphysis there is also an overgrowth of bony material possibly due to misaligned skeletal muscle attachment points. The right humeral head is malformed along the same directions with a medio-lateral and inferior orientation compared to normal individuals. The articular surface is rough and oddly oval. In addition to this, the overall length of the bone is greatly reduced compared to same sex and aged individuals at Windover (Fig. 6). The same can be said for the left humerus. It is also far shorter than a non-pathological individual of the same age and sex. The proximal epiphysis has rotated medially and inferiorly creating a protrusion of the articular surface. What appears to be the left humeral head exhibits a greater amount of deformity compared to the right side. The left head is also oval, but there is a large cavity through the center of the articulation. The distal articulation is present on the left humerus and does not show any obvious signs of pathology (Fig. 7). The x-rays of both right and left humeri show an expansion of the medullary cavity and a thinning of the cortical areas in both the mediolat-

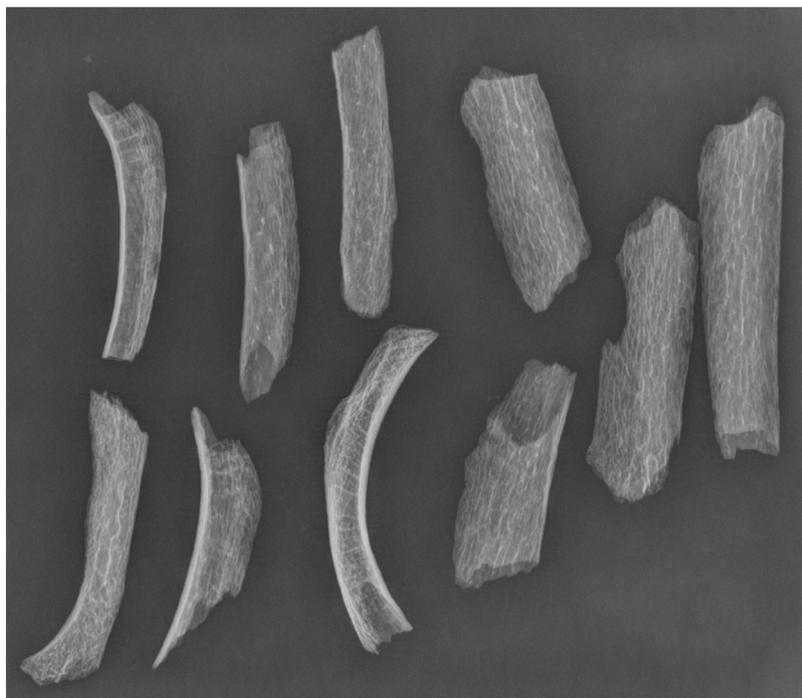


Fig. 4. Radiograph of the largest rib fragments. No indication of the rib-within-a-rib seen in many severe cases of anemia and thalassemia.

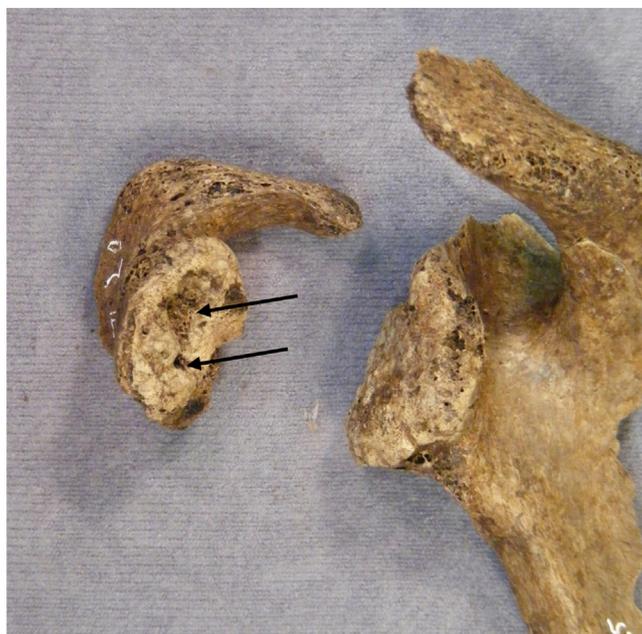


Fig. 5. Deformation of the right and left glenoid fossa of the scapulae. Arrows indicate deep cavities that are not the result of postmortem preservation.

eral and anteroposterior views. This increase in cancellous bone is an indication of red blood cell production in response to anemia (Fig. 8).

2.2.6. *Radii and ulnae*

This individual's right and left radii are nearly complete, although the distal articulation is missing from both. The left radius is also missing the proximal articulation. There are no observable pathologies in either radius. The right radial head appears normal in size and contour with a subtle remnant of the growth plate visible. The overall lengths of the radii are normal in comparison to

others of the same age and sex, and their lengths are comparable to that of the humeri.

The ulnae are also very complete for this individual. Only the distal articulations are missing for both the right and left side. There are no visible pathologies present for either the right or left. Their lengths match that of the radii and are also comparable (slightly longer) to the lengths of the humeri (Fig. 9).

Radiographic images indicate a slight increase in the medullary areas for both radii and ulnae compared to others in this population. The left side exhibits a subtle difference with slightly more expansion of the medullary cavity.



Fig. 6. Right proximal humerus medial and anterior views. Notice the downward rotation of the humeral head along the medial aspect.



Fig. 7. Left proximal humerus medial and anterior view. Similar to the right humerus, note the rotation of the proximal metaphysis in a downward and medial direction.

3. Differential diagnosis

Trauma to the skeleton can be caused by any number of disorders, diseases, and injuries. Assessments of the resulting pathologies seen within skeletal populations are then left to the researcher's diagnosis of each individual's expression of specific symptoms. Through the accumulation of medical knowledge in

both clinical and archaeological contexts, many pathologies, such as degenerative joint disease, are easily diagnosed and generally well understood amongst bioanthropologists. Yet, there are a multitude of skeletal anomalies that are less well known, particularly if they are infrequently found in the archaeological record. Such is the case with varus deformity of the long bones, particularly the humerus. The deformity can be described as a, "disto-medial



Fig. 8. Right and left humeri – antero-posterior and medio-lateral views. Note the relative thinness of the cortical areas and overall expansion of the medullary cavity, particularly at the proximal end of the bones.

displacement of the proximal epiphysis of a long bone from the longitudinal axis, with concomitant shortening of the anatomical neck” (Kacki et al., 2011: 119). This deformity has been attributed to trauma and infection (Ellefsen et al., 1994), genetic disorders such as mucopolysaccharidosis and thalassemia (Ogden et al., 1976), and metabolic disorders like rickets and osteomalacia (Ogden et al., 1976). Although each of the explanations for the expression of varus deformities is possible, each individual case is not the result of a combination of the disorders listed above. Herein lies the problem. With so many pathways that lead to this distinctive pathology, which one is the most likely candidate for a given individual? There are few examples that illustrate this deformity in the archaeological record and those that do, tend to result from a single catalyst for its expression in a combination of traits.

3.1. Mucopolysaccharidosis

Mucopolysaccharidoses are a group of genetic disorders characterized by abnormalities in the fibroblasts and chondrocytes of affected individuals. They are autosomal recessive disorders that have been classified into eight distinct types (McAlister and Herman, 1995; Ortner, 2003). The most well-known and discussed types in the paleopathological record are Hurler’s syndrome (Type I), Hunter’s syndrome (Type II), and Morquio-Brailsford’s syndrome (Type IV). Regardless of type, this group of disorders manifest through various skeletal deformations that affect multiple structures. Type I is diagnosed through a combination of macrocephaly, craniostenosis, expansion of the anterior rib ends, malformation of the vertebral bodies, and shortening of the upper and lower long bones (McAlister and Herman, 1995; Ortner 2003). This type begins skeletal expression early in childhood development and often results in a shortened life span for the affected individual (few live beyond age 10). The skeletal manifestation of Type II is virtually identical to that of Type I. The greatest difference is

the link to biological sex (only males) and degree of expression. Individuals that have a minor version of the disorder survive into adulthood, whereas, the major form of the disorder greatly shortens life expectancy (early 20s). Type IV is not apparent at birth and begins its expression in early childhood. This type also results in severe kyphosis of the spine due to anterior wedging of the vertebral bodies, as well as enlargement of the thorax along the antero-posterior plane. Unlike Types I and II, the skull is relatively normal in shape, while the upper and lower long bones are severely shortened, resulting in dwarfism for the individual. Tarsal deformation (Jaffe 1972) and abnormally shaped permanent teeth (Aegerter and Kirkpatrick 1968) have also been noted with this type. All three types discussed here also exhibit the humerus varus deformity. The long bones commonly exhibit expanded medullary cavities, periosteal deposition, and thinning metaphyseal cortical bone, along with premature fusion of the humeral head (McAlister and Herman 1995; Ortner and Putschar 1981; Ortner 2003). The diagnosis of mucopolysaccharidosis can primarily be ruled out as the cause of Individual 76s’ humeral deformities based on the general lack of diagnostic features associated with this disorder. The individual does not express the cranial, vertebral, and lower limb deformities commonly seen with mucopolysaccharidoses types.

3.2. Trauma and infection

Other possible causes for the humerus varus deformity found in Individual 76, include congenital dysplasia, infection, or acute trauma (particularly to the growth plate). As noted by Johnson and Davies (2004) congenital gleno-humeral dysplasia is relatively rare in isolation and is often a symptom of larger genetic disorders including fucosidosis (Lee et al., 1977), Grant syndrome (Maclean et al., 1986), TAR syndrome (Hall, 1987), and Holt-Oram syndrome (Poznanski et al., 1970). In addition, this congenital deformity often involves not only the gleno-humeral joint surfaces, but also



Fig. 9. Right and left humeri, ulnae, and radii of Individual 76. Note the severe reduction in the overall length of both humeri compared to their paired radii and ulnae.

the acromion process, coracoid process, and clavicular deformities (Johnson and Davies, 2004). It is due to these inconsistencies that congenital dysplasia can be ruled out as a cause for the deformative symptoms found with Individual 76.

Clinical data shows that the varus deformity can also be caused by adjacent infections (Peters et al., 1992; Kacki et al., 2011). However, Individual 76 does not show signs of osteomyelitic or periostitic bony reactions near or around the affected areas. In addition, this individual shows no signs of infection throughout her remains. In the absence of infectious origins, acute trauma becomes the next likely candidate for the varus deformity. Damage (even moderate damage) to the proximal humeral growth plates has been shown to cause disturbances in growth and an overall shortening of the bone (Makela et al., 1988; Kacki et al., 2011). Depending on the nature of the injury, the joint may be affected differentially. For instance, an injury during delivery could cause damage unilaterally or bilaterally, and functionality of the arms would not necessarily be visibly impaired, until the child begins to grow. As long bone length increases the damage caused to the growth plate injuries should become more visible, especially compared to other (non-injured) children. The more difficult aspect of assessing injury timing comes into play when examining the difference between birthing injury and damage to the growth plates during early infancy/childhood. Both can cause severe stunting of growth as well as the varus deformity of the humeral head (Molto, 2000; Kacki et al., 2011).

The complication with this diagnosis surfaces when examining the additional symptoms of Individual 76. Trauma alone does not account for the numerous expressions of long-term anemia and the humerus varus deformity. That being said, there is a possibility

that the individual suffered from both chronic anemia (manifested through thinning cortical areas, expansion of the cranial diploe, and mild cribra orbitalia) along with gleno-humeral trauma during birth or in early childhood.

3.3. *Thalassemia*

There are multiple levels of thalassemia (major and minor) each expressing different levels of skeletal malformations. Beta thalassemia is a quantitative defect in the production of normal β -globin, and in homozygous patients (Cooley's anemia) it results in very high rates of mortality in infants and children. In addition, the homozygous form is characterized by severe anemia, delayed growth, extensive skeletal malformations, and iron overload. Heterozygous β -thalassemia is a less severe form of the disease where individuals often survive to adulthood and most often express microcytosis (smaller than normal red blood cells), as well as little to no anemia (Hershkovitz et al., 1991; Embury and Steinberg, 1994). Alpha thalassemia occurs when the gene controlling the production of α -globin is absent or defective. This also can be found in both homozygous and heterozygous forms, resulting in a gradation of skeletal and physical abnormalities from mild anemia to mild bone deformations and eventually death (Embury and Steinberg, 1994). The easiest way in which to determine the presence of either α or β thalassemia is through DNA testing and observation of the α and β globin genes. However, in the temporal and contextual framework of anthropological study and paleopathology, this may not be a viable option. Therefore, examination of the skeletal

remains must be used to determine the presence or absence of this disease in a given individual.

The major and intermediate forms of thalassemia normally manifest skeletal indicators, while the more minor cases do not (Ortner and Putschar, 1981). Clinical examinations of patients with thalassemia (most often β -thalassemia) have mainly focused on the skeletal deformities found in the shoulder, specifically premature fusion of the proximal humeral epiphyses (Currarino and Erlandson, 1964). This premature fusion most commonly occurs along the medial aspect of the proximal humerus, leading to a shortening of the humerus, expansion of the medullary cavity, thinning of the cortex, and a narrowing of the trabeculae primarily due to marrow hyperplasia. This deformation is also referred to as varus deformity (De Roeck et al., 2003; Lawson et al., 1983).

In the archaeological record, multiple studies have claimed the presence of thalassemia based on descriptions of the skeletal remains. The oldest potential case comes from Atlit-Yam site in Israel and is 8100 years old (Hershkovitz et al., 1991; Hershkovitz and Edelson, 1991). The authors describe the left humerus of a 16–17 year old male as,

“The affected humerus was considerably shorter than the right (by 43 mm). This length difference was caused by premature fusion of the proximal growth plate. Irregularity of epiphyseal fusion, with the medial portion of the epiphyseal plate closing prematurely, caused the head to be tilted medially and inferiorly into varus. The humeral head, usually spherical in contour, has collapsed into a flat, rugged shape, with a deep cavity in its center. It is inclined steeply downward and rotated to such an extent that it faces the same direction as the medial epicondyle; i.e. the bone completely lacks the normal 30° of humeral head retroversion. The anatomical neck is not noticeable. Below the surgical neck, a longitudinal furrow and a rounded fossa with a porotic surface adjacent to it are noted. X-ray of the entire humerus shows porotic changes in the cancellous bony elements together with hyperostotic changes in the cortex.” (Hershkovitz and Edelson, 1991:52)

According to the authors, this combination of skeletal traits including (unilateral or bilateral) premature fusion of the proximal humeral epiphysis, arrestment of the medial growth plate, shortening of the bone, varus head deformity, and lytic cortical defects are not seen in virtually any other disease (Hershkovitz et al., 1991; Post, 1988).

One of the potential indicators of thalassemia can be seen through radiographic images of the patient's skull. The cranial bones of many, but not all, thalassemia patients exhibit a hair-on-end appearance when x-rayed, characterized by vertical striations through the bone. Although this distinct pathology is more often found in extreme cases of anemia and more frequently with thalassemia, recent studies have found no direct correlation between the anemic diagnosis and the expression of this characteristic (Lagia et al., 2007; Caffey 1937). Individual 76 appears to lack any definitive signs of hair-on-end striations upon examination of her cranial x-rays (see Fig. 3).

This Windover female's humeri express the same qualities as the Atlit-Yam individual described by Hershkovitz et al. (1991), only bilaterally. She exhibits bilateral foreshortening of the left and right humeri, with the proximal aspects of both humeri compressed medio-laterally and rotated inward, and with gleno-humeral joint surfaces that are deformed medially. Further similarities are apparent from radiographic images of the humeri. The internal distribution of bone shows expansion of the medullary cavity (in antero-posterior and medio-lateral views) with increased cancellous bone growth (see Fig. 8). This again is an indication of chronic

anemia and the need for the production of red blood cells with the expansion of the marrow.

The ribs of thalassemia patients have been known to exhibit multiple pathologies including a rib-within-a-rib appearance when radiographed. Other characteristics include expansion of the neck and head at the articulations with the vertebrae and marrow space expansion, which leads to erosion of the inner cortex of the rib. Similar to the radiographic evidence seen in the skull, the rib-within-a-rib appearance is found most often among severe (major) thalassemia cases (Tunaci et al., 1999; Tyler et al., 2006). Similar to the absence of hair-on-end striations of the skull, the absence of this symptom does not rule out the diagnosis of thalassemia, although the presence would have greatly strengthened the case (as seen in Fig. 7).

4. Discussion

Based on the presence and absence of specific symptoms associated with a particular pathological disorder, it is relatively simple to narrow down the possible origins of the skeletal malformations in an archaeological context. Thanks to both clinical and archaeological research on the skeletal manifestation of disorders like thalassemia, the diagnosis of new cases is relatively reliable. Nevertheless, skeletal malformations can be caused by multiple disorders and it can be difficult to pinpoint a single diagnosis amongst several possibilities. Such is the case for this female from the Windover population, who exhibits various signs that may be associated with thalassemia, such as foreshortened humeri (bilaterally), medial rotation of the humeral heads (varus deformity), and multiple signs of anemia (expansion of the medullary cavity and cribra orbitalia). However, signs often seen in the more serious cases of thalassemia are lacking in this female (clear hair-on-end and rib-within-a-rib).

Based on the clinical and archaeological literature, thalassemia is not the only potential cause for each of these traits when viewed separately. There are multiple potential causes for anemia including sickle cell disease, vitamin deficiencies, malnutrition, hypothyroidism, and other hereditary disorders. Individual 76, however, shows no obvious pathological markers to indicate any of these disorders with the exception of possible malnutrition. Meanwhile, the varus deformity along with the foreshortened humerus has been known to occur in patients with infections and trauma (often during childbirth or infancy – congenital dislocation) that result in damage to the proximal humeral growth plates. Several studies have reported humerus varus deformities in the archaeological record that are likely due to injuries sustained early in life (Kacki et al., 2011; Molto, 2000). The descriptions of the humeral malformations are identical to those found in studies claiming thalassemia as the culprit for the deformity. The greatest difference is seen in the presence of anemia. This lack of any clear signs of injury to the bone or joint surfaces and the lack of an indicator of infection along with the presence of anemia for Individual 76, results in a diagnosis of thalassemia as being the most likely cause for the deformities.

The largest hurdle to this diagnosis is the relationship thalassemia has with malaria. There have been many historical studies linking the heterozygous thalassemia gene frequency to areas of the world with heavy concentrations of malaria (Cepellini 1955; Dunn, 1965). Heterozygote resistance to *plasmodium* appears to be a lacking factor for pre-Columbian New World populations (Cormier, 2010). Evidence for the recent introduction of malaria to the Americas includes the lack of wide spread diversification amongst infected animal species and the genetic similarities of new world strains as compared to those found in the Old World (Cormier, 2010). According to Joralemon (1992) early explorers to South America describe an absence of malaria in areas where

today it is commonly found. It is believed in the 17th century, multiple species of *plasmodium* were introduced to the Americas by the English and by African slaves (Russell, 1968). This scenario has then allowed many researchers to disregard the possibility of thalassemia as a potential diagnosis in the Americas prior to contact time periods. This notion however, is in direct conflict with the findings of this paper. In regards to the overall potential for the spread of recessive disorders, there needs to generally be an evolutionary or selective pressure for the selection of that condition or set of alleles. It is then relatively easy to link the high gene frequency of conditions like thalassemia or sickle cell anemia to regions heavy with malarial loads (Cormier, 2010). The heterozygote expression of both these hereditary anemias gives the carrier resistance to malaria (cannot contract it) and non-expression of the recessive disorder. This balanced polymorphism then proliferates throughout a population because the only individuals that are surviving to reproductive age and reproducing are the carriers. Those individuals unfortunate enough to inherit homozygous alleles for the disorder or non-carriers of the recessive allele will then be susceptible to the disorder or contract malaria. How then does an individual inherit thalassemia without the strong selective pressure that is present/correlated with malarial presence and resistance? Thalassemia is caused by a mutation in the genes responsible for the production of hemoglobin in red blood cells. The origin or actual mechanism for a genetic mutation is most often unknown. Thalassemia is not caused by malaria. In areas heavy with malarial loads, individuals that carry the mutated gene for thalassemia are more resistant to the disease. Therefore, the requirement for diagnosing thalassemia in the paleopathological record should not depend on location and time period. The chances of observing the skeletal malformations caused by thalassemia – particularly in the New World – dramatically increase after the introduction of *plasmodium* in the environment due to their introduction by explorers from the Old World, but it is likely that the condition existed (just with less frequency) prior to contact.

5. Conclusion

The only way to be 100% accurate in this diagnosis would be to extract and test this individual's DNA. Without a DNA test of this individual's α and β globin genes, the diagnosis of thalassemia presented here must be viewed as tentative. If future DNA results show non-mutated globin genes, then the malformations seen in the Windover female may be due to a combination of bilateral humerus varus (trauma) and independently contracted anemia. Amongst the individuals at Windover, approximately 25/168 individuals show varying degrees of cribra orbitalia (anemia), so this possibility must be considered. In addition to the DNA evidence, location is also a factor working against the thalassemia diagnosis. The Windover population is from Titusville, Florida and dates to approximately 8000 years ago, whereas thalassemia primarily occurs, at least amongst archaeological specimens, along the Mediterranean where malaria is heavily involved. Because modern Asian populations are known to express certain types of thalassemia, it is not impossible that a case would appear spontaneously within a prehistoric Native American population, but this has yet to be documented in the archaeological record. If this individual had been found in the Old World, the diagnosis would be more consistent with the regional archaeological record. If that is the case, then Individual 76 is the oldest documented case in the New World with this disease. Samples from other Windover individuals have been sent for testing to Eske Willerslev (University of Copenhagen), but unfortunately, have not resulted in a significant portion of usable DNA (less than 0.05%) (Glen H. Doran, personal communication). As it stands now, this specimen is the earliest potential individual in

the New World with thalassemia. And this is a call for paleopathologists/human osteologists/archaeologists to not rule out thalassemia as a diagnosis in Pre-Columbian New World individuals.

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