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Presence of Diffuse Idiopathic Skeletal Hyperostosis in an Avinganya Rural Population (Lleida, Iberian Peninsula)

Daniel Fuentes-Sánchez[1], Diego López-Onaindia[1], Rosa Dinarès[2], Maria Eulàlia Subirà[1]
1 Universitat Autònoma de Barcelona
2 Hospital General de Catalunya, Barcelona Spain

Diffuse idiopathic skeletal hyperostosis (DISH) has largely been associated with high socioeconomic status rather than lower social status in paleopathological studies. In the clinical literature, this association is explained as a consequence of a diet high in fat intake as well as a sedentary lifestyle, leading to metabolic syndrome and other obesity-associated risk factors that can in turn cause DISH. In this work, we present a case of DISH in a male individual exhumed from a civil burial site of the necropolis of the Trinitarian Monastery of Avinganya, in the North-East of the Iberian Peninsula. In this case, DISH coexists with evidence of occupational stress markers (spinal lesions and trauma) that suggest a non-sedentary lifestyle. Therefore, mechanical stress is proposed as another risk factor for DISH, which provides a more convincing explanation in this case.

Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a common skeletal disease in paleontological and archaeological remains (Aufderheide & Rodríguez-Martín, 1998; Rothschild, 1987; Rothschild & Martin, 2006). It was first clinically described as a senile ankylosing hyperostosis of the spine in 1950 (Forestier & Rotes-Querol, 1950), and has been observed in dinosaurs and ancient mammals (Rothschild, 1987). It has been described in Neanderthals (Crubézy & Trinkaus, 1992; Trinkaus, Maley, & Buzhilova, 2008), and in human remains across a broad range of periods: including in pre-Columbian societies (e.g., Arriaza, 1993; Ostendorf Smith, Dorsz, & Betsinger, 2013), and especially in the medieval and modern ages (Fornaciari and Giuffra, 2013; Rogers, Watt, & Dieppe, 1985; van der Merwe, Maat, & Watt, 2012; Vidal, 2000; Waldron, 1985). Although it is widely described in the paleopathological and clinical literature, the definitions and diagnostic criteria for DISH differ. We present a historical case of DISH in an individual exhumed from a civil burial from the Trinitarian Monastery of Avinganya (Spain, 8th-14th centuries AD).

DISH is commonly described in clinical cases as an ossification of the anterior and lateral aspects of the vertebral column (Forestier & Rotes-Querol, 1950; Resnick, Shaul, & Robins, 1975) as a result of the ossification of the anterior longitudinal ligament (ALL) (Aufderheide & Rodríguez-Martín, 1998; Resnick & Niwayama, 1976; Waldron, 2008). In some cases, other spinal ligaments are also involved (Bombak, 2012; Ohishi et al., 2003; Resnick & Niwayama, 1976;

Author correspondence should be directed to *Eulalia.Subira@uab.cat* (GRAPAC (Grup de Recerca Aplicada al Patrimoni Cultural). Unitat d'Antropologia Biològica, Departament de Biologia Animal, Biologia Vegetal i Ecologia. Facultat de Biociències, Edifici C. Universitat Autònoma de Barcelona. 08193, Bellaterra (Cerdanyola del Vallès, Barcelona, Spain)

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Rothschild & Martin, 2006). However, some bioarchaeologists consider ALL ossification to be pathognomonic evidence of DISH (Bombak, 2012). This manifestation creates a tortuous hyperostosis, called ‘candle wax dripping’, and ankylosis of contiguous vertebrae. For a valid clinical and archaeological diagnosis, at least four contiguous vertebrae need to be affected (Aufderheide & Rodríguez-Martín, 1998; Resnick & Niwayama, 1976; Utsinger, 1985). Nevertheless, archaeological cases in which three or fewer vertebrae are affected may indicate an intermediate state of the disease, and may represent possible cases of DISH (Arlet & Maziéres, 1985; Bombak, 2012; Rogers & Waldron, 2001).

Resnick and colleagues (1975) were the first to report extra-spinal enthesophytes in modern cases of DISH. Enthesopathies are characterized by a bony outgrowth on entheses, or points at which tendons and ligaments insert into bone (François, Eulderink, & Bywaters, 1995; Waldron, 2008). For this reason, DISH has recently been redefined as a calcification and ossification of ligaments and entheses (e.g., Mazières, 2013; Sarzi-Puttini & Atzeni, 2004; Waldron, 2008) with a marked predilection for the axial skeleton and its associated ligaments, particularly the ALL.

DISH is generally asymptomatic, and mainly affects men at advanced ages (Holton et al., 2011; Resnick et al., 1975; Vidal, 2000). Some cases present with low-mild radiating pain and stiffness (Cammisa, DeSerio, & Guglielmi, 1998; Forestier & Rotes-Querol, 1950; Mazières, 2013; Resnick et al., 1975). In rare or severe cases, this condition may cause complications such as dysphagia, myelopathy, spinal fractures, or spinal cord injuries (Cammisa et al., 1998; Hughes, Wiles, Lawrie, & Smith, 1994; Sarzi-Puttini & Atzeni, 2004). Despite its association with genetic, metabolic, anatomical, and environmental factors, the aetiology of DISH is unknown. Three different risk factors have been related to DISH that are observable in human remains: metabolic disorders (obesity, diabetes mellitus type II, hyperuricaemia, dyslipidaemia, hypertension, and coronary arterial disease), age, and the use of retinoids (Kiss, Szilágyi, Paksy, & Poór, 2002; Sarzi-Puttini & Atzeni, 2004).

Numerous archaeological studies (e.g., Fornaciari & Giuffra, 2013; Jankauskas, 2003; Rogers & Waldron, 2001; Verlaan, Oner, & Maat, 2007; Waldron, 1985) have suggested that DISH could be a valuable indicator of the socio-economic status of historical populations or individuals, supporting this hypothesis with clinical studies that suggest an association between DISH and the metabolic syndrome (Kiss et al., 2002; Sarzi-Puttini and Atzeni, 2004). The aim of the present study is to provide a detailed description of a new case of DISH (UE-140062) in a rural male, and to outline its possible implications for socioeconomic interpretations.

Archaeological Background

The Trinitarian Monastery of Avinganya is located in the Segrià region of western Catalonia (Figure 1). It represents the first Trinitarian settlement of the Iberian Peninsula, and is situated on the site of an ancient Islamic farm. The necropolis utilized by people who lived in the nearby village (8th-14th centuries AD) is located to the northeast of the monastery, and was excavated between 2009 and 2011. Forty-nine inhumations were found in this area. Preliminary anthropological and paleopathological study (Fuentes-Sánchez et al., 2015) indicates a higher representation of men (38%) than women (17%). For the rest of individuals from the site (45%), sex could not be determined due to the lack of features necessary for sex estimation. Females from this site show a higher prevalence of articular diseases than males, mainly represented by osteoarthritis (OA) (71.4%). The frequency of this condition is also high in males (42.1%). In both males and females, articular disease is associated with individual age and probably with occupational stress, based on musculoskeletal evidence (Fuentes-Sánchez et al., 2015). The average age at death is quite similar for men (31-39 years) and women (30-38 years) at this site.

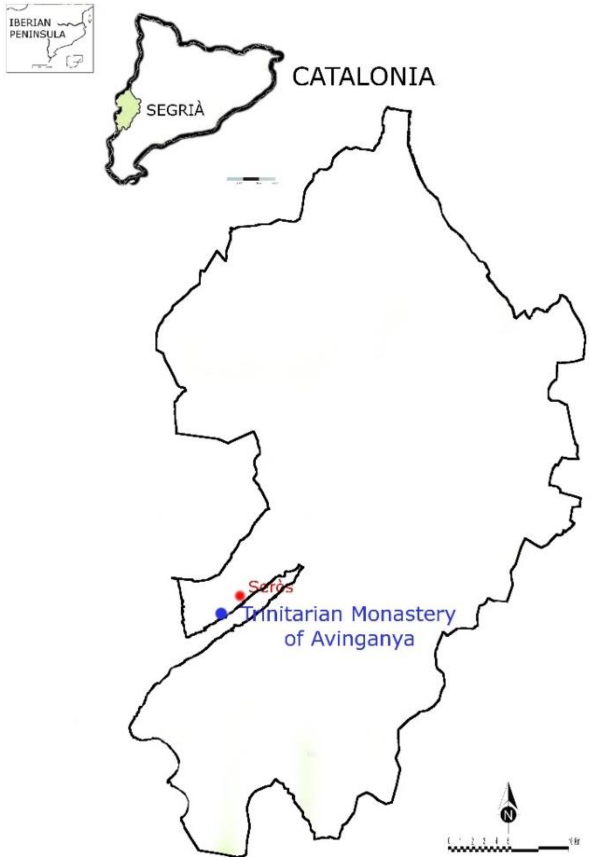

Figure 1. Geographic location of the Trinitarian Monastery of Avinganya (Segrià, Iberian Peninsula).

Materials and Methods

Individual UE-140062 was excavated from tomb 104 in the zone surrounding the monastery, which has been identified as the lay cemetery. In this collection, individual sex was estimated using standard sex estimation criteria (Ferembach, Schwidetzky, & Stloukal, 1980; Krogman & Iscan, 1986). Age at death was estimated using multiple standard aging criteria (Krogman & Iscan, 1986; Lovejoy, Meindl, Pryzbeck, & Mensforth, 1985; Masset, 1982; Meindl & Lovejoy, 1985), varying according to the skeletal elements preserved for each individual. Of all methods applied, the most accurate at this necropolis are changes to the auricular surface of the ilium (Lovejoy et al., 1985). However, due to pathological alterations, this criterion could not be applied to individual UE-140062.

Accurate macroscopic observation allowed us to determine an initial diagnosis and differential diagnosis. In order to obtain more evidence, elements key to the diagnosis were analysed by X-ray and X-ray Computed Tomography (CT) at the Hospital General de Catalunya. To determine the origin and state of spinal and pelvic fusion, X-ray images of the spine and pelvis were taken at 4.5kV/2.5 mAs. To study healed rib fractures and enthesopathies, X-ray images of the four ribs exhibiting lesions and the upper limb were taken at 4,5kV/2.5 mAs. For further study, CT images of the spine were taken at 120 kV/200mAs.

Results

Osteological Analysis

Individual UE-140062 is represented by a well preserved and almost complete skeleton (Figure 2). The only elements missing are the sternum and a few carpals, metacarpals, and phalanges from both hands. Osteological indicators in the pelvis (Ferembach et al., 1980; Krogman & Iscan, 1986) indicate that this individual is male, and the fully fused epiphyses and fully erupted permanent dentition indicate that they are an adult. Analysis of the ectocranial sutures suggests that age at death is probably between 45 and 55 years

Figure 2. Individual UE-140062 inside the tomb

(Krogman & Iscan, 1986; Lovejoy et al., 1985; Masset, 1982; Meindl & Lovejoy, 1985).

Pathological Description

Spinal Manifestations

The main spinal lesion observed in individual UE-140062 is the anterolateral ossification of the ALL, leading to ankylosis of four contiguous thoracic vertebrae (T9 to T12) (Figure 3). The intervertebral disk space is preserved between affected vertebrae, except between the third and fourth lumbar vertebrae, which are also fused. Ossification of the ALL presents with a candle-wax morphology, and affects the right side of the spine. The vertebral column also shows other bony outgrowths and hyperostoses along the anterior and lateral margins.

Five bony bridges are present in the anterior margins of the vertebrae along the entire length of the spine (C3 to C4, C5 to C6, T3 to T4, T9 to T10 and L3 to L4). An additional lateral bony bridge is seen between the ninth and tenth thoracic vertebrae. Osteophytes are also present in the vertebral column. In the cervical spine, there is a unique osteophyte platform that affects the anterior margins of the sixth and seventh cervical bodies. Dorsal and lumbar regions of the spine exhibits additional osteophytic evidence. Generally, osteophytes are present on the anterior (T1, T2, T3, T7, T8, T11, T12, L1, L2, L3, L5) or lateral margins (T9, T10, T11 and T12) of the vertebrae. Only the third and fourth lumbar vertebrae display posterior osteophytes, although the posterior margins and apophyseal joints of the rest of the spine are well preserved. Schmorl's nodes are present on the inferior and superior bodies of the tenth and eleventh thoracic vertebrae.

Extra-spinal Manifestations

There is no marked evidence of whiskering (filamentous hypertrophic bone) on the iliac crest, but there is a great presence of osteophytosis in both paracetabular regions. The right sacroiliac joint is partially fused in the anterior and posterior regions. This morphology indicates that the anterior and posterior sacroiliac ligaments have undergone ossification (pelvic enthesopathy), but, as the CT image shows, the auricular facet is not involved (Figure 4). Extraspinal enthesopathies are present, particularly in the lower limbs, and involve the humeri (deltoid and pectoralis major muscles), radii (interossei, biceps, and pronator teres muscles), ulnae (triceps brachii, supinator, and brachialis muscles) and femora (gluteus maximus, vastus medialis, iliopsoas, quadratus femoris, and soleus muscles) (Figures 5). Poor preservation of the foot bones makes it difficult to observe potential enthesopathies in the talus.

Figure 3. Thoracic vertebral column of individual UD-140062 (right anterior view). Osseous ankyloses with anterior longitudinal ligament ossification between T9, T10, T11 and T12.

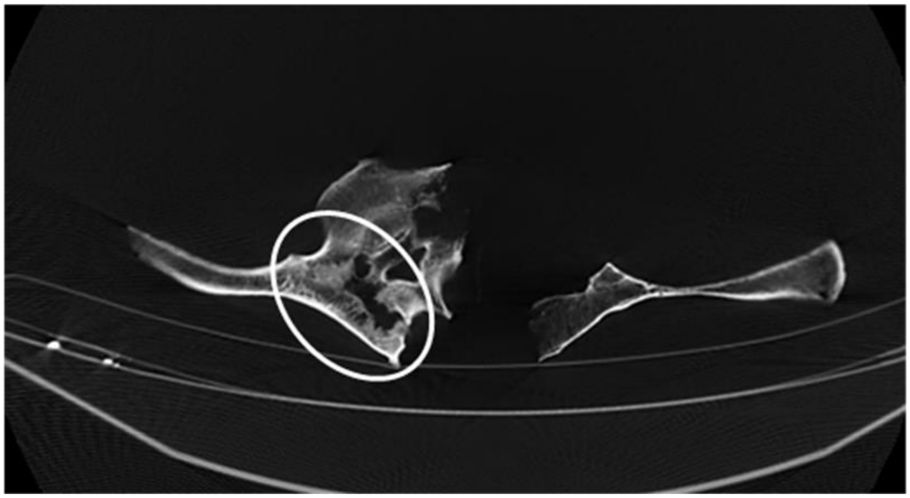

Figure 4. Axial computed tomography (CT) from the pelvis of individual UE-140062. The sacroiliac joint is partially fused, but the auricular facet is not involved.

Figure 5. Enthesopathy on the right femur (arrow) of individual UE-140062.

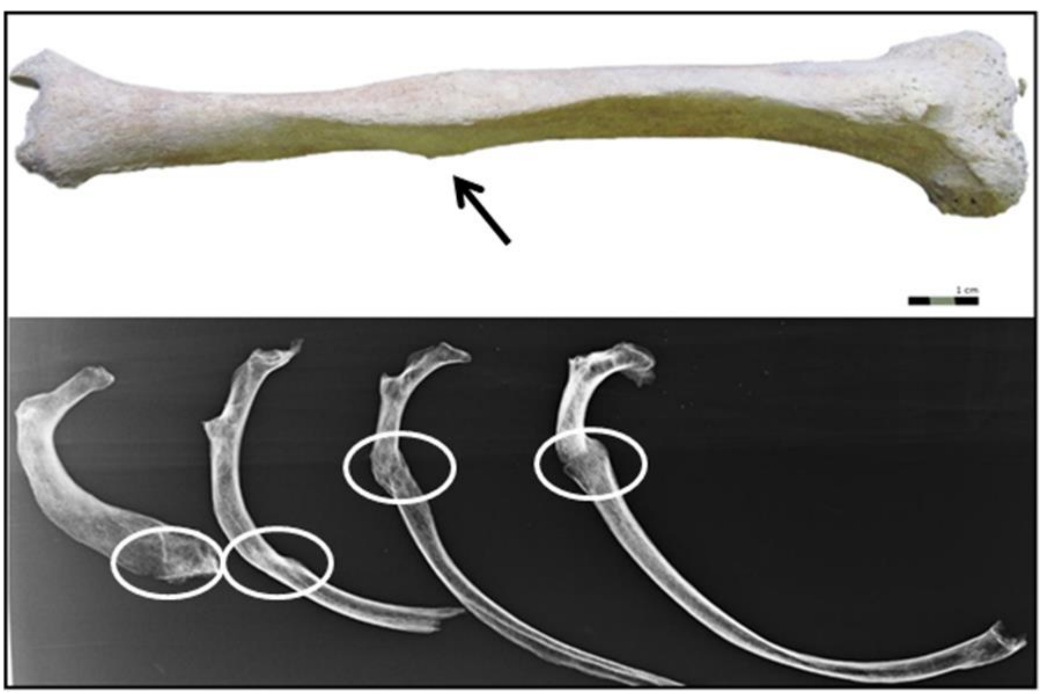

Figure 6. Left tibia of individual UE-140062 (upper), with healed fracture (arrow). X-ray of four right ribs from individual UE-140062 (bottom) with satisfactory healed fractures (circled; parameters in caption: 4.5kV/2.5 m).

Although the enthesopathies observed in this individual are bilateral, they are more pronounced on the right side.

In addition to these lesions, the distal epiphyses of the humeri, ulnae and radii show evidence of OA. The epiphyses of both femora also present marked osteophytes.
Four of the right ribs of this individual, including the first rib, have healed fractures in the dorsal region. The left tibia also shows a well healed transverse fracture at the approximate center of the diaphysis. These five fractures present with osseous calluses, indicating their satisfactory healing (Figure 6).

Discussion

Differential and Definitive Diagnosis

Several pathological conditions can lead to vertebral ankyloses, vertebral bony outgrowth, sacroiliac fusion, and extra-spinal enthesopathies. These skeletal disorders are DISH, ankylosing spondylitis (AS), calcium pyrophosphate deposition disease (CPDD), and Reiter's syndrome (RS), as well as fluorosis. Fluorosis, which causes general enthesopathies, can be discarded as it is not consistent with the observed hyperostosis.

CPDD is a pathological disorder characterized by the deposition of calcium pyrophosphate dihydrate crystals in the articular tissues (Aufderheide & Rodríguez-Martín, 1998; Jordana et al., 2009). This condition often produces calcification of the joints and tends to destroy them, affecting, in rare cases, vertebral bodies. It can also affect sacroiliac joints and some spinal ligaments (Resnick & Pineda, 1984). This diagnosis can be rejected because of the overall well-preserved apophyseal and extra-spinal joints. Moreover, CPDD leads to disc calcification, which is not seen in individual UE-140062.

RS is an articular pathology of infectious aetiology (Aufderheide & Rodríguez-Martín, 1998; Waldron, 2008) characterized by a triad of evidence: urethritis, conjunctivitis, and polyarthritis. In skeletal remains, only polyarthritis would be observable; it occurs in knee, ankle and foot joints. In addition, RS can affect apophyseal and costovertebral joints and can lead to sacroiliac fusion. In individual UE-1400062, there is no sign of involvement in the knee, ankle, and foot joints. Moreover, except for the third and fourth lumbar vertebrae, no vertebral joints are affected. Therefore, Reiter's syndrome can be ruled out as a diagnosis for this individual.

AS and DISH are probably the most suitable candidate diagnoses for individual UE-140062. AS is a systematic and progressive disorder of the connective tissue that leads to spinal, sacroiliac, and peripheral calcification. In the spine, this calcification tends to form bony bridges, but it usually involves apophyseal and costovertebral joints. (Aufderheide & Rodríguez-Martín, 1998; Ortner, 2003; Resnick et al., 1975; Waldron, 2008). Sacroiliac fusion is also observable where there is trabecular continuity between the sacrum and the ilium, so that the joint is completely destroyed (Ortner, 2003). This diagnosis can be rejected because apophyseal and costovertebral joints in this individual are well-preserved. Moreover, individual UE-140062 does not present with trabecular continuity in the fusion of the sacroiliac joint (Figure 4), ruling out AS as a diagnosis.

Therefore, DISH seems to be the most accurate diagnosis for the pathological lesions observed in individual UE-140062. The main evidence of DISH –ALL ossification- is seen in the spine, leading to ankylosis of four thoracic vertebrae (T9-T12) with a 'candle wax' morphology. Moreover, extensive bony outgrowth is present in the spine. Generally, proliferative lesions appear around anterior and lateral margins and do not affect apophyseal and costovertebral joints, except in the third and fourth lumbar vertebrae. This feature is characteristic of DISH, jointly with the disk space preservation that is also seen in the cervical and thoracic vertebrae of individual UE-140062. Most authors agree that sacroiliac joint fusion is not a feature of DISH (Arlet & Maziéres, 1985; Bombak, 2012; Forestier & Rotes-Querol, 1950; Resnick & Niwayama, 1976; Utsinger, 1985), but some studies show that it can occur when ankylosis does not affect the joint, as in individual UE-140062 (Aufderheide & Rodríguez-Martín, 1998; Mazières, 2013; Ortner, 2003). Sacroiliac joint fusion is present in 25% of modern patients with clinical features of DISH (Dar, Peleg, Masharawi, & Steinberg, 2007). In addition, peripheral enthesopathies are a typical feature of DISH established by Resnick et al. (1975; Aufderheide and Rodríguez-Martín, 1998; Mazières, 2013; Rogers & Waldron, 2001; Utsinger, 1985), appearing most often on the patella, femur, calcaneus, pubic symphysis, ischial tuberosity, and iliac crest (whiskering). In individual UE-140062, peripheral enthesopathies are present in the humerus, radius, ulna, femur, and pelvis.

These data indicate that individual UE-140062 is likely to represent a case of DISH. However, this individual shows other pathological features or skeletal alterations. The presence of Schmörl nodes in the tenth and eleventh thoracic vertebrae, and bony outgrowth in the apophyseal joint, along with contacting fusion, in the third and fourth lumbar vertebrae, can also indicate degenerative spinal spondylosis (DSS). DDS, or deforming spondylosis, is a disturbance produced by intervertebral disk degeneration, osteophytosis, spinal OA, and spinal ligament disturbances (Aufderheide & Rodríguez-Martín, 1998). Repetitive activity affecting the back is a major causal factor in the onset of DSS (Ortner, 2003). OA can be rejected as a general diagnosis for individual UE-140062 because this condition affects apophyseal joints, while in the present case the alteration is local. OA is also present in peripheral elements of the skeleton, mainly represented by the marked osteophytes in the femora and along the upper limbs. Unfortunately, we cannot know if these lesions developed before or after the onset of DISH. For this reason, it is not possible to identify them as DISH-related alterations or alternatively as independent degenerative processes. In fact, some clinical and paleopathological studies show that OA, spinal osteophytosis, and DISH frequently coexist (Sarzi-Puttini & Atzeni, 2004; Verlaan et al., 2007).

Individual UE-140062 also shows traumatic lesions in the tibia and the ribs. Some authors describe vertebral trauma as a consequence of vertebral ankyloses, including DISH (Callahan & Aguilera, 1993; Mazières, 2013), but these lesions do not usually occur in the peripheral skeleton. Only Veerlaan and colleagues (2007) describe a case of DISH associated with two healed rib fractures. Trauma is usually the consequence of an extrinsic cause, so it can be influenced by social aspects (Aufderheide & Rodríguez-Martín, 1998; Ortner, 2003). For this reason, the aetiology of trauma is very diverse, including factors such as warfare and occupational stress (Roberts, 2000). According to Roberts (2000), warfare or domestic accidents are most likely to result in traumatic lesions of the head, neck and/or forearm. In the case of occupation-related trauma, Lovell (1997) and Waldron (2008) suggest that a prolonged activity such as carrying heavy objects can produce rib fractures. In the same way, tibiae, metatarsals, and calcanei are the elements most frequently affected by stress fractures (Lovell, 1997). Therefore, it is possible that the traumatic and spinal lesions not related to DISH are related to occupational stress (Lovell, 1997; van der Merwe et al., 2012).

Unfortunately, there is no way to know if these traumatic lesions occurred prior to or following the onset of DISH.

Lifestyle and Its Implications

The diagnosis of lesions observed in individual UE-140062 includes three independent pathologies: DISH, DSS, and trauma. The emergence of DSS and possibly occupational stress-related trauma (in the tibia and ribs) suggests that individual UE-140062 may have suffered high occupational stress in life, mainly related to the back. This evidence indicates an active lifestyle for this individual. Although DISH is almost asymptomatic, and only some cases present with low-mild pain and stiffness, individual UE-140062 may have suffered from chronic leg pain. Tibia fractures can cause peripheral neuropathy related to damage in the tibial nerve, even once the healing process has ended (Waldron, 2003). Consequently, the movement and sensitivity of the leg may be damaged. On the other hand, healed rib fractures do not generally cause excessive discomfort (Lovell, 1997).

DISH has largely been associated with a high status and monastic lifestyle in paleopathological contexts. This hypothesis, referred to as the 'monastic way of life', is based on a comparative study (Rogers & Waldron, 2001; Waldron, 1985) that discusses the high prevalence of DISH in church and chapel burials (11.5-23.1%), ascribed to high status individuals, in contrast to lay or civil burials (0-6.5%). Additionally, some published case reports seem to confirm this association (Fornaciari & Giuffra, 2013; Jankauskas, 2003; Verlaan et al., 2007), and it has been referenced in several books and reviews (e.g., Bombak, 2012; van der Merwe et al., 2012; Waldron, 2008). These paleopathological analyses support the finding from clinical studies suggesting an association between DISH and metabolic syndrome, based on a statistical correlation (Kiss et al., 2002; Sarzi-Puttini & Atzeni, 2004). The metabolic syndrome is a heterogeneous disorder related to hyperinsulinemia, type two diabetes mellitus, obesity, dyslipidaemia, and cardiac disease. For this reason, the emergence of DISH in monastic and high status burials is explained as a consequence of the monastic way of life, characterized by a sedentary lifestyle and a high intake of caloric foods (Waldron, 1985; Rogers & Waldron, 2001).

In contrast, individual UE-140062 was excavated from a lay burial and, like the rest of the skeletal sample, exhibits evidence of occupational stress indicating a non-sedentary lifestyle. Other published paleopathological cases of DISH also do not seem to fit into the monastic way of life hypothesis, including those found in hunter-gatherer societies (Arriaza, 1993; Crubézy & Trinkaus, 1992; Ostendorf Smith et al., 2013), or in the later Spanish Roman period and Visigoth societies (Menéndez Bueyes, 2013). These examples exhibit strong evidence for occupational stress and could support an association between DISH and a less sedentary lifestyle. Moreover, Waldron (2008) points out that DISH cases are not necessarily always related to high-status burials; the current case provides an additional example to illustrate this. Further examples come from clinical studies, such as that by Resnick et al. (1975) in which 57% (n=12/21) of the sample comes from individuals with occupations requiring a moderate to high degree of physical activity (e.g., construction workers, ranchers, etc.). Conversely, a study by Holton and colleagues (2011) did not find clinical evidence for a statistical correlation between physical activity and DISH. Therefore, the relationship between physical activity and DISH remains unclear.

Holton and colleagues (2011) also found no correlation between body mass index and the occurrence of DISH, demonstrating that DISH is not always associated with obesity and the metabolic syndrome. Moreover, diet is not the only determining factor for overweight and obesity. Obesity is multifactorial, and genetics or environment can play an important role (Doo & Kim, 2015). Thus, relationships between the monastic way of life, diet, sedentary lifestyle, obesity, the metabolic syndrome, and DISH do not seem clear, in spite of previously observed differences between high status clerical and lower status lay burials.

We propose that the association between DISH and high socioeconomic status or a monastic way of life could be explained by sample bias. The onset of DISH has largely been associated with advanced age (e.g., Forestier & Rotes-Querol, 1950; Holton et al., 2011; Resnick et al., 1975; Vidal, 2000), and monastic communities usually have more advanced age-at-death than non-monastic communities (DeWitte, Boulware, & Redfern, 2013). Therefore, the higher presence of DISH reported in the literature for monastic burials (Waldron, 1985; Rogers & Waldron, 2001) may be related to the over-representation of advanced age groups. More studies surrounding the relationship between socioeconomic status, sex, age-at-death, and incidence of pathology are necessary. Accurate epidemiological studies are fundamental in order to confirm or reject the causal relationship between socioeconomic status, lifestyle, and DISH.

Some clinical authors propose alternative pathogenetic mechanisms of DISH other than metabolic disorders, including genetic, environmental, or toxic factors (Sarzi-Puttini & Atzeni, 2004). Ohishi and colleagues (2003) suggest that mechanical stress on ligaments is important to the progress of ossification, and may explain the onset of enthesopathies. In fact, enthesopathies, a typical feature of DISH, are classically interpreted as occupational stress markers (Villotte et al., 2010). For individual UE-140062 this hypothesis seems more parsimonious than the 'monastic way of life' due to evidence for spinal lesions and occupational stress markers. In the future, clinical studies could contribute to improved understandings of the factor, or factors, that triggers DISH onset, allowing the recognition of historical cases.

Conclusion

The Avinganya individual UE-140062 has been identified as a probable case of DISH. In this individual, DISH coexists with marginal and focalised cases of DSS as well as tibial and rib fractures. We interpret these traumatic lesions as the possible consequence of a repetitive activity or occupational stress, indicative of a non-sedentary lifestyle. In contrast, much of the paleopathological literature associates DISH with monastic and high status communities who experience low occupational stress. We suggest that this association is less clear than has often been assumed. Medieval non-monastic communities have a lower survival rate than monastic communities, where individuals may be more likely to develop DISH as a result of living to a more advanced age. Finally, we suggest that mechanical stress is the most likely aetiology for DISH in this case. However, further research into this potential association is necessary. In a paleopathological context, a deeper insight into the relationship between socioeconomic status, sex, age-at-death, and the incidence of pathology could be beneficial in elucidating the causal factors that can trigger disease onset.

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