



A recording form for differential diagnosis of arthropathies

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ABSTRACT

The present study is focused on a group of arthropathies that may have very similar bone manifestations (rheumatoid arthritis, ankylosing spondylitis, reactive arthritis, psoriatic arthritis, osteoarthritis and diffuse idiopathic skeletal hyperostosis), which makes it more difficult to diagnose them in human remains from archaeological contexts. A stepwise recording form was designed in order to improve the identification and differential diagnosis of these pathological conditions in bone remains, particularly in joint manifestations of the spine, pelvis, hands, feet and other limb joints. This recording form was applied in the analysis of two medieval individuals from the Basque Country (Spain) who presented very severe arthropathic manifestations. The use of this recording form allowed the researchers the diagnosis of ankylosing spondylitis in one of them and diffuse idiopathic skeletal hyperostosis in the other.

1. Introduction

Arthropathies are the most frequent post-cranial diseases in bone material, in both current and ancient human populations (Rogers and Waldron, 1995). Joint pathology can be caused by different factors, with those of inflammatory and degenerative nature being the most common ones. Inflammatory arthropathies are a group of autoimmune diseases triggered by the inability of the immune system to recognize and tolerate one's own antigens. In general, autoimmune diseases do not cause visible lesions in bone tissue, except for a group of arthropathies, among which the following stand out: Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Reactive Arthritis (ReA) and Psoriatic Arthritis (PsA) (Rajic Sikanjic and Vlaskovic, 2010). On the other hand, degenerative arthropathies are illnesses, generally chronic, that worsen in the course of time, with Osteoarthritis (OA) and Diffuse Idiopathic Skeletal Hyperostosis (DISH) being the most common.

For the diagnosis of arthropathies, it is necessary to know which are the most relevant skeletal manifestations to increase the certainty of the diagnosis. In archaeological remains, which present poor preservation, descriptive data of the preserved bone portions are usually taken, without reaching a differential diagnosis in most cases. Therefore, the aim of the present study is to propose a way to record data using a recording form focused on “key” skeletal joints (vertebral, sacroiliac, hands and feet, among others) to establish a diagnosis, and in the case of partial preservation of the skeleton, to reach a presumptive diagnosis. In order to validate the viability and effectiveness of the proposed recording form, it was applied to analyse one individual recovered from

the medieval necropolis of San Miguel de Ereñozar (Bizkaia, Basque Country) (13th-15th century) and another one from Cathedral of Santa María de Vitoria-Gasteiz (Álava, Basque Country) (11th-19th), both presenting very severe arthropathic manifestations.

2. Methodology

A literature review of specialized archaeological, anthropological and biomedical journals and textbooks was performed, with the aim of gathering the most important bone manifestations of diseases studied (Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Reactive Arthritis (ReA), Psoriatic Arthritis (PsA), Osteoarthritis (OA) and Diffuse Idiopathic Skeletal Hyperostosis (DISH)).

We describe the diagnostic bone manifestations of the arthropathies included in the recording form.

2.1. Rheumatoid Arthritis (RA)

Rheumatoid Arthritis (RA) characteristically involves the small joints of the hands and feet, especially the metacarpophalangeal joint (MCP), metatarsophalangeal joint (MTP) and proximal interphalangeal joint (PIP), with the distal interphalangeal joint (DIP) being rarely involved (Rogers and Waldron, 1995). It is worth mentioning that diagnosing this disease in archaeological material is impossible if no bone manifestations of the hands and feet can be demonstrated (Rogers et al., 1987). Other joints that become affected in RA are the knee, cervical spine, shoulder, elbow and hip (Resnick, 2002). Erosive lesions are very

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common in RA, as well as osteopaenia (Schett and Gravallese, 2012). The presence of erosive lesions may occur in some Spondyloarthropathies (SpAs); however, unlike in SpAs, the sacroiliac joint is not affected in RA (Rogers et al., 1987).

2.2. Spondyloarthropathies (SpAs): Ankylosing Spondylitis (AS), Reactive Arthritis (ReA) and Psoriatic Arthritis (PsA)

Spondyloarthropathies (SpAs) constitute a group of chronic inflammatory diseases that share a wide spectrum of clinical manifestations, the most important of which are the erosion or fusion of the sacroiliac joint, the involvement of no more than four joints and the formation of new bone tissue around the affected joints (Inoue et al., 1999). Indeed, this group of diseases is characterised by alterations of the fibrocartilaginous entheses, with this being a key feature of SpAs (Ball, 1971; Benjamin and McGonagle, 2001). The most prevalent spondyloarthropathies are the following:

Ankylosing Spondylitis (AS) is a chronic, rheumatic autoimmune disease that affects the spine and sacroiliac joints mostly, although other peripheral joints such as the shoulders, hips and knees may also be affected (Resnick, 2002). The structural changes are caused by inflammatory processes that destroy the bone tissue, which regenerates very quickly, developing over ligaments, tendons and fasciae (Ebringer and Wilson, 2000). The structural changes that identify AS appear in the spine and in the sacroiliac joints. In fact, the inflammation of the sacroiliac joint is the first radiographic manifestation of AS (Raychaudhuri and Deodhar, 2014). Unlike other SpAs, sacroiliitis is symmetrical, affecting both sides of the body equally. However, the changes in the extra-spinal joints are asymmetrical (Rogers et al., 1987).

Ossification begins in the sacroiliac joints and in the lumbar segment of the spine, and from there it moves toward the dorsal and cervical segments (Ebringer and Wilson, 2000) (Fig. 1A). Ossification of the ligaments of the spine joins the intervertebral discs together, resulting in some characteristic bone protuberance in the edges of the vertebral joints known as syndesmophytes. In later stages of the disease, syndesmophytes increase in size, causing the fusion of the vertebrae. In the most severe cases, the spine fuses completely and it acquires the appearance of a bamboo spine (Fig. 1B) (Slaus et al., 2012). It is worth mentioning that, in the case of AS, the growth of new bone tissue affects

the entire anterolateral surface of the vertebrae and not only one of the sides, as is the case of DISH (Rogers et al., 1987). Unlike Reactive Arthritis (ReA), in AS the affectation of the vertebrae is continuous and lacks the so-called “skip lesions” (Waldron, 2008).

Reactive Arthritis (ReA) is a disease characterised by peripheral arthritis, enthesopathy and sacroiliitis (Rogers and Waldron, 1995). In ReA sacroiliitis is asymmetrical, in contrast to AS. Moreover, the joints affected are not evenly distributed, thus it is frequent to find normal vertebrae next to fused vertebrae (“skip lesions”). The peripheral joints with more chances of being involved are those of the feet, calcaneus, knees and ankles. These changes are also asymmetrical (Rogers et al., 1987).

In **Psoriatic Arthritis (PsA)** the changes in the sacroiliac joint are usually unilateral or asymmetrical (Rogers and Waldron, 1995). Unlike in ReA, the joints of the hands are affected with the same frequency as those of the feet. The erosive changes are severe and they produce a characteristic appearance of the disease in the phalanges of the hands and feet, known as “pencil-in-cup” (Rogers et al., 1987).

2.3. Osteoarthritis (OA)

Osteoarthritis (OA), widely known as arthrosis, is a chronic, degenerative disease caused by the destruction of joint cartilage. It is the most common of all joint diseases (Ortner, 2003), with age being an important factor (Sowers, 2001). OA is characterised by (1) the formation of marginal osteophytes and/or new bone on the joint surface, (2) the reaction of the subchondral bone, (3) the presence of irregular joint surfaces and, in severe cases, (4) alterations in the contour of the joint. In the absence of (1) and (2), the changes observed in the joint can not be classified as OA. This disease can affect any synovial joint of the body, although in most cases it damages the facet joints of the vertebra, the first metatarsophalangeal joint (MTP), the hip and the knee (Rogers and Waldron, 1995). This arthropathy is characterised by the fact that the osteophytes of the spine develop horizontally from the edge of the joint, in contrast to AS, in which they develop vertically (Rogers et al., 1987). Eburnation is a pathognomonic sign of OA and it occurs when the articular cartilage has completely disappeared (Ortner, 2003).

2.4. Diffuse idiopathic skeletal hyperostosis (DISH)

Diffuse Idiopathic Skeletal Hyperostosis (DISH), also known as Forestier’s disease, is a very common degenerative disorder of unknown aetiology that appears in people of middle and advanced age (Forestier and Rotes-Querol, 1950; Resnick, 1978). The most characteristic trait of DISH is the ossification into the anterior longitudinal ligament. This results in the presence of massive vertical bone formation in the right anterolateral surface of the thoracic vertebrae, generally from T4 to T12 (Rogers and Waldron, 2001). Although this bone outgrowth is more likely to occur on the right side, some changes on the left side can be observed, particularly in the first three thoracic vertebrae and in the lumbar area due to the absence of the descending aorta (Belanger and Rowe, 2001). Its diagnosis requires at least four adjacent thoracic vertebrae to be affected (Mader et al., 2009). This disease is also characterised by the ossification and/or calcification of soft tissue such as tendons, ligaments and other non-skeletal elements (Rogers et al., 1987). In DISH, any entheses may become affected, but the common sites are the triceps insertion in the elbow, the front part of the patella and the insertion of the Achilles tendon into the calcaneus (Rogers and Waldron, 1995; Ortner, 2003). Other distinctive characteristics are the absence of both apophyseal joint degeneration and inflammation of the sacroiliac joints (Verlaan et al., 2007).

DISH is sometimes confused with AS because both have some common manifestations, such as the spinal fusion. However, unlike AS, in DISH there is a preservation of facet joints and disc spaces (Rogers and Waldron, 1995). On the other hand, in DISH the development of



Fig. 1. Characteristic joint manifestations of Ankylosing Spondylitis (AS): A) Fusion of the femur and pelvis, the sacroiliac joint, and the lumbar segment of the spine and B) fusion of the spine with the appearance of a “bamboo spine” (Images courtesy of I.M. Laza).

Table 1
Characteristic manifestations of the arthropathies studied in different bone elements (spine, pelvis, hands and feet, and other joints). (RA: Rheumatoid Arthritis; AS: Ankylosing Spondylitis; ReA: Reactive Arthritis; PsA: Psoriatic Arthritis; OA: Osteoarthritis; DISH: Diffuse Idiopathic Skeletal Hyperostosis).

Bone Manifestation	RA	AS	ReA	PsA	OA	DISH
Spine						
Fused vertebrae		x	x	x		x
Cervical segment affected	x		x	x	x	
Thoracic segment affected		x			x	x
Lumbar segment affected		x			x	x
Osteophyte formation		x	x	x	x	x
Osteophytes vertically oriented		x				x
Osteophytes horizontally oriented					x	
Symmetrical osteophytes		x				
Asymmetrical osteophytes			x	x		
Bone growth affects the entire anterolateral surface of the vertebra		x				
Bone growth only affects one of the sides of the spine ^a						x
Apophyseal joints affected	x	x	x		x	
Preservation of intervertebral space						x
Non-preservation of intervertebral space		x	x	x		
Pelvis						
Sacroiliitis ^b		x	x	x		
Symmetrical sacroiliitis		x		x		
Asymmetrical sacroiliitis			x	x		
Hands and feet						
MCP and PIP joint in hands affected	x					
MTP joint affected	x					
DIP joint affected in hands and feet		x	x	x		
Other joints						
Shoulder joint affected	x	x				
Elbow joint affected	x					
Hip joint affected	x	x			x	
Knee joint affected	x	x	x		x	
Other characteristics						
Symmetrical lesions ^c	x	x				
Asymmetrical lesions ^c		x	x	x	x	x
It usually affects five or more joints	x					
It rarely affects more than four joints		x	x	x		x
Presence of enthesal changes		x	x	x		x

MCP: metacarpophalangeal joint; MTP: metatarsophalangeal joint; PIP: proximal interphalangeal joint; DIP: distal interphalangeal joint.

^a The growth of new bone tissue in the thoracic area occurs, in most cases, at the right anterolateral side of the spine.

^b In DISH, bony bridges may form in this joint, but there is no ankylosis.

^c In AS, sacroiliitis is symmetrical; however, the changes in the extra-spinal joints are asymmetrical.

new bone in the spine has the appearance of a candle wax flowing down, which is characteristic of this disease (Rogers and Waldron, 2001). Although the sacral ligaments can ossify across the joint line, causing the fusion (bilateral or unilateral) of the sacroiliac joint, this type of fusion can be distinguished from that found in SpAs since in DISH the fusion is the result of the presence of bony bridges, not ankylosis.

3. Results and discussion

3.1. Design of the recording form for the identification and diagnosis of arthropathies in bone remains

The information recovered from the literature about the bone manifestations of the different arthropathies studied is summarised in Table 1 and it is the basis for the design of the recording form (Data 1). Both the table and the recording form are organized by bone elements, to follow an order when studying bone remains, making it quicker and simpler to draw a final conclusion on the most probable cause for the changes observed.

This recording form is focused on those bone elements (spine, pelvis, hands and feet, other joints) whose joint manifestations allow one to establish the differential diagnosis: spine segment affected, apophyseal joints affected, presence of vertebral osteophytes along with their direction and symmetry, preservation or not of the intervertebral space, enthesal changes, sacroiliac joint affected and lesion symmetry, lesions of the hands and feet (differentiating which are the affected joints) and other joints which may become affected (shoulder, elbow, hip, knee) (Table 1). In Table 1, only those spine segments which are commonly affected are shown, but it should be remembered that other regions may become affected in severe cases.

The severity of the joint lesions is measured through a scale from 1 to 3. The criteria to assess the severity are the following: Grade 1: the joint is slightly affected, with well-defined edges but without a smooth contour; Grade 2: the joint is moderately to severely affected, without neither well-defined edges nor smooth contour, but there is no joint fusion; and Grade 3: the joint is severely affected and fused. In the case of osteophytes, the criteria are: Grade 1: slight alteration in the edge of the joint (not measurable); Grade 2: the osteophyte is 5 mm in length or shorter; and Grade 3: the osteophyte is longer than 5 mm.

The recording form (Data 1) is structured into three parts. The first part includes the reference of the archaeological intervention on the burial place, the sex and age estimated, as well as the most relevant aspects of the bone elements that may help in the diagnosis. This space can be used to record the descriptions of the lesions or the preservation of each skeletal region. Estimation of age at death of non-adults (infants and juveniles) is not included because the arthropathies under study only affect adults, thus the recording form does not include lesions of juvenile-onset diseases (e.g. juvenile arthritis). The second part includes a diagram in which the bone elements available to perform the differential diagnosis are indicated. Furthermore, this diagram allows the researcher to include the number of cervical, thoracic and lumbar vertebrae available for the analysis, as well as the number of bones of the hands and feet (carpus, metacarpus, tarsus, metatarsus and phalanges). This diagram allows one to rate the degree of conservation of the skeleton, since this information will determine the reliability of the diagnosis reached. Lastly, the recording form gathers the data of the pathological traits identified in the individual. The sections included in this sheet are based on the bone manifestations that are necessary for the establishment of a differential diagnosis, which are listed in Table 1.

3.2. Case study: application of the recording form for the identification and diagnosis of arthropathies in ancient bone remains

Case 1. The recording form is applied to analyse one individual who presented very severe arthropathic manifestations (Supplementary material – Case 1) recovered from the medieval necropolis of San Miguel de Ereñozar (Bizkaia, Basque Country) (13th–15th century). Despite the poor state of conservation of this individual, enough bone elements were recovered to establish the paleopathological diagnosis, as well as the age and sex of the subject (adult male over 40 years of age) (Fig. 2).

In order to establish the diagnosis, the manifestations gathered in the recording form (Supplementary material) are compared with the diagnostic traits of each arthropathy (Table 1). This individual presents some fused vertebrae, which is a characteristic that leads to the diagnosis of some arthropathies (AS, ReA, PsA and DISH). This manifestation in the spine and the absence of lesions in the hands and feet allow the researchers to discard RA. In order to carry out the differentiation from among the previous arthropathies, it is essential to know the regions of the spine that are affected, which, in this case, are the thoracic and lumbar regions (Fig. 2C). However, since no vertebra was recovered from the cervical region, it is not possible to discard any of the arthropathies mentioned. Next, the presence or



Fig. 2. Bone remains from the medieval necropolis of San Miguel de Ereñozar (Bizkaia, Basque Country, 13th–15th century) that showed severe joint manifestations. A) Fusion of the right femur and pelvis, B) fusion of the right sacroiliac joint and C) vertebral column with “bamboo spine” appearance.

absence of affected apophyseal joints is recorded; this individual presents a complete fusion of these joints in the thoracic and lumbar regions. Of the aforementioned pathologies, this bone manifestation only occurs in AS and ReA; thereby, it is possible to discard the presence of DISH in this individual. Due to the absence of vertebral bodies and the fact that only the area of the neural arch of the spine was recovered, it is not possible to record some manifestations of the spine, such as the presence of osteophytes and their characteristics (symmetry and direction); it is also impossible to determine the preservation of the intervertebral space.

Regarding the pelvis, the right side of the sacroiliac joint is fused (Fig. 2B), and the left side of the joint was not recovered. This manifestation, as shown in Table 1, only occurs in SpAs, which definitely allows the researchers to discard DISH in this individual. However, since the symmetry of this lesion can not be determined, it is not possible to differentiate any pathology from the group of SpAs. However, the complete fusion of the thoracic and lumbar regions of the spine, without the presence of the so-called “skip lesions” characteristic of ReA and PsA, leads to the diagnosis of AS.

Case 2. The viability and effectiveness of the recording form proposed in this study are assessed by applying it to another individual recovered from the Cathedral of Santa María de Vitoria-Gasteiz (Álava, Basque Country) (11th–19th century). It is an adult male between 40 and 50 years of age (Fig. 3).

The procedure to establish the diagnosis is the one followed in Case 1. The manifestations included in the recording form for this individual (Supplementary material – Case 2), are compared with the diagnostic traits of each pathology shown in Table 1. This case presents vertebral fusion in the thoracic region of the spine and affection of the lumbar region. Both are diagnostic characteristics of AS and DISH, which allows one to discard the presence of arthropathies like RA, ReA, PsA and OA. The absence of affection in the apophyseal joints and in the sacroiliac joint, along with the preservation of the intervertebral space, ultimately allows the researchers to diagnose DISH in this individual (Rogers and Waldron, 1995). This diagnosis is reinforced by the presence of enthesitis in the patella and the calcaneus preserved and in the

iliac crest of both coxal bones (Ortner, 2003) (Fig. 3A, B and C) also highlighting the presence of massive vertical bone formation in the right anterolateral surface of the thoracic vertebrae. This new bone formation has the appearance of a candle wax flowing down, which is characteristic of this disease (Rogers and Waldron, 2001) (Fig. 3D).

These case-studies show the usefulness of the recording form designed for gathering information in a systematised manner, allowing one to compare such information with the diagnostic traits of some arthropathies (Table 1), with the aim of improving the process of diagnosing these diseases.

In conclusion, a literature review was performed on the bone manifestations of a set of arthropathies with a difficult diagnosis in archaeological human remains. The analysis allowed the researchers to design a systematised recording form, which may be a useful tool to ensure the search for some key features of a group of arthropathies, speeding up the data collection process. The recording form was applied to analyse two medieval individuals from the Basque Country (Spain) who presented very severe arthropathic manifestations. The use of this recording form allowed the researchers the diagnosis of ankylosing spondylitis in one of them and diffuse idiopathic skeletal hyperostosis in the other. The design and implementation of this recording form will improve the identification of other arthropathies in individuals recovered from burial sites.

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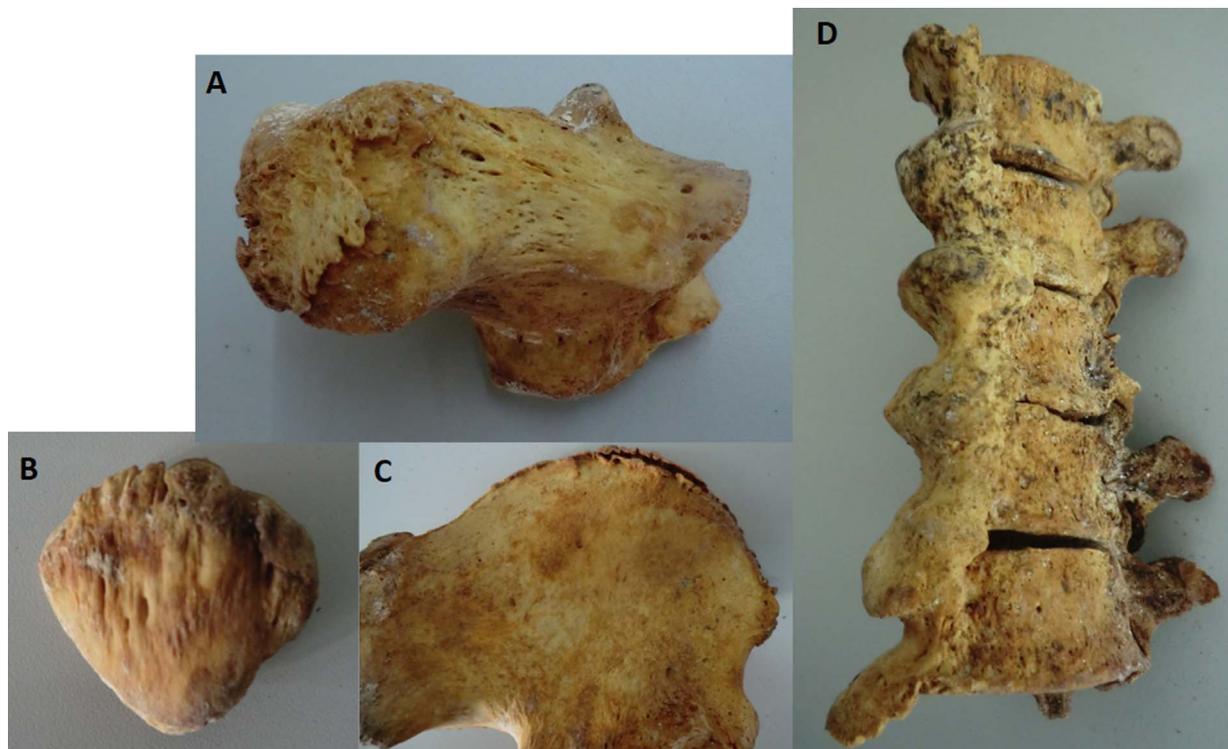


Fig. 3. Bone remains from the Cathedral of Santa María de Vitoria-Gasteiz (Álava, Basque Country, 11th–19th). A) Enthesitis in the right calcaneus, B) in the right patella and C) in the iliac crest of the right coxal bone, and D) fusion of 5 thoracic vertebrae.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.ijpp.2018.01.004>.

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