

The "Braids Lady" of Arezzo: A case of rheumatoid arthritis in a 16th century mummy

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ABSTRACT

Objective. To diagnose a probable case of rheumatoid arthritis in a mummified female body from the 16th century and to backdate the first clinical diagnosis, entering the diatribe regarding the ancientness of the disease.

Methods. Image techniques such as normal X-ray, X-ray by mammography, total body CT and high resolution CT were used. Microscopic examination by stereomicroscopy was performed. Samples of tissue were submitted to histology. These data and the review of past literary references, of artistic representations and of paleopathological cases provided an interesting contribution to reconstruct the history of the disease.

Results. The body of the "Braids Lady" showed all the "stigmata" of the disease. The left hand revealed large erosions of the metacarpophalangeal joints of both the third and the fourth fingers, volar metacarpophalangeal subluxation of both the third and the fourth fingers and lateral deviation of all the fingers. The carpus showed some minute and marginal erosions of the bones. The bases of the first phalanges were slightly flared. The toes showed partially overlapped fibular deflection. CT evidenced subluxations of the joints. The body showed no involvement of sacroiliac articulation.

Conclusions. The "Braids Lady" was affected by rheumatoid arthritis. A large number of features typical of the disease were recorded. Differential diagnosis supported the findings. The death of the lady was established at the end of 16th century, namely 200 years before the first clinical diagnosis worked out by Landré Beauvais in the early 1800s.

Introduction

The church of San Francesco in Arezzo

(Tuscany) - well known for the Renaissance frescoes of "The Legend of the True Cross", painted by Piero della Francesca from 1453 to 1464 - is composed of two churches, one above the other. The lower church was built at the end of the thirteenth century, while the upper church was completed in 1377. The restorations of the floor, carried out in 1996, revealed some wooden coffins containing nine well preserved natural mummies (1). A mummy is a body in which the processes of putrefaction do not occur due to a rapid dehydration, resulting in the preservation of the soft tissues, dried and reduced in mass and in weight. In the present case the mummy is natural and its preservation is due only to microclimatic conditions.

The unexpected burials found in the church were positioned to the left and in front of the high altar, in a hollow space between the cross vaults of the lower church and the floor of the more recent building (Fig. 1). The dry and stable environmental conditions of the space explain the good preservation of the bodies. Identification of the individuals is currently impossible; we can only assume that they were eminent members of the Renaissance wealthy class of Arezzo and certainly benefactors of the Franciscan Order.

A first survey brought to light nine bodies, including that of the so-called Lace Lady, which represents a dramatic case of puerperal death already studied in the past (2). The present study concerns the case of another woman, who we have nicknamed the Braids Lady because of her dark hair gathered into two long braids resting on the breast, held together by a green silk ribbon. The style of her dress indicates that the burial took place at the end of the 16th century.

External examination evidenced a number of bone lesions suggesting a severe form of arthritis. In order to investigate the nature of these lesions the body was at first studied by several imaging techniques (normal X-ray, X-ray by mammography, total body CT, high resolution CT, 3-D virtual reconstruction). Microscopic examination by stereo microscopy was also performed and samples of tissue were submitted to histology. The review of past literary references, of visual arts sources and of paleopathological cases provided an interesting contribution to the history of the disease.

Combination of the results allowed us to diagnose a case of rheumatoid arthritis (RA). The present study enters also the diatribe regarding the ancientness of this disease. Our diagnosis, based on the findings of numerous features typical of RA, made it possible to confirm the presence of the disease in Europe during the second half of the 16th century and to backdate the first clinical diagnosis worked out by Landré Beauvais at the beginning of the 19th century (3).

Historical background

Past literary sources

Inaccuracy and approximation of the descriptions reported in past literary references make it difficult to find positive evidences for RA in both ancient and modern times.

The first account of a disease which could have the features of RA was made by Julius Caesar's doctor, Scribonius Largus (40 BC). Arateus (81-138 AD) described a joint disease in which alternate periods of remission and new acute phases were observed. In his treatise "Chronic Diseases", Soranus from Ephesus (98-138 AD) reports some joint disease features, such as onset in adult age, deformation of the joint, rotation and overlapping of the fingers. The disease could reasonably be interpreted as RA but the description of a later appearance of a typical tophus suggests a case of gout (4). In his recent studies on important historical figures suffering from rheumatic diseases, Appelborn (5) suggests that the deforming polyarthritis affect-



Fig. 1. The Braids Lady's wooden coffin at the moment of the discovery.

ing the Emperor Constantin IX Monomachus (980-1055 AD) may have been a case of RA, and that the painter Peter Paul Rubens was probably affected by RA (6).

During the 17th century Thomas Sydenham (1624-1629) elaborated a theoretically acceptable description of RA (7). However, we must wait until the 19th century for the first unmistakable clinical description by Landré Beauvais, called "primitive asthenic gouty"

(3). Finally, in 1859 sir Alfred Garrod named the disease with its current name: rheumatoid arthritis (8).

Visual arts sources

Figurative arts have given an interesting contribution to the history of RA, with two probable representations of the disease in paintings. In "The temptations of Saint Anthony", produced at the end of the 17th century by an anonymous Flemish painter, the right hand

Table I. Comparison between the morphological findings in the RA literature and in the “Braids Lady”.

Reported cases	Types of damage recorded
May, 1897 (11) mummy (V Dynasty)	Proximal interphalangeal joint lesions Distal interphalangeal joint lesions Ulnar (or lateral) deviations of the fingers
Ruffer, 1913 (12) mummy (III Dynasty)	Ankylosis
Rogers, 1981 (13) English man (X-XI century AD)	Symmetric lesions Marginal erosion at x-ray examination
Ortner-Uthermole, 1981 (14), Kodiak Isle (1200 AD)	Symmetric lesions Marginal joint erosions
Ortner-Putschar, 1985 (15), English medieval man	Symmetric lesions Detection of osteoporosis at x-ray examination Ankylosis
Bennike, 1985 (16) Danish man (late Iron Age)	Marginal joint erosions Distal interphalangeal joint lesions
Leaden, 1986 (17) Swedish man A (2500-900 BC) (late Iron Age)	Symmetric lesions Joint lesions of the carpus Lesions of the elbows Lesions of the knees Shoulder joint lesions Detection of osteoporosis at x-ray examination Ankylosis
Leden, 1986 (17) Swedish man B (2500-1900 BC)	Lesions of the elbows Lesions of the feet Ankylosis
Woods, 1988 (18) Late Woodland's population, Ohio (800-1100 AD)	Symmetric lesions Proximal interphalangeal joint lesions Distal interphalangeal joint lesions Joint lesions of the carpus Joint metatarso-phalangeals lesions Detection of osteoporosis at x-ray examination Marginal erosion at x-ray examination
Rothschild, 1988 (19) Tennessee's population, Alabama (3000-1000 BC)	Symmetric lesions Joint lesions of the hand Proximal interphalangeal joint lesions Distal interphalangeal joint lesions Joint lesions of the carpus Lesions of the feet Joint metatarso-phalangeals lesions Joint atlanto-occiput lesions Detection of osteoporosis at x-ray examination Marginal erosion at x-ray examination
Kilgore, 1989 (20) Kulubnarti's woman, Sudan (700-1450 AD)	Distal interphalangeal joint lesions Joint lesions of the carpus Marginal erosion at x-ray examination
Ciranni-Fornaciari, 2000, the “Braids Lady”, Arezzo, Italy (1550-1650)	Symmetric lesions Marginal joint erosions Joint lesions of the hand Proximal interphalangeal joint lesions Ulnar (or lateral) deviations of the fingers Joint lesions of the carpus Lesions of the feet Shoulder joint lesions Detection of osteoporosis at x-ray examination Marginal erosion at x-ray examination

of the beggar shows dislocation of metacarpus, contraction of the flexed fingers and lateral deviation of the fingers.

“The Painter’s Family” by Jacob Jordaan (1593-1678) shows a serving maid, holding a basket of fruit, whose hands present dislocation of the metacarpus and swelling of the metacarpophalangeal and interphalangeal joints (9).

Extremely evocative, but not entirely convincing, is “The Portrait of a Young Man” (1483), painted by Sandro Botticelli, where the young age of the man can suggest a juvenile form of the disease (6).

Paleopathological sources

The first paleopathological description of possible RA was performed by Page May, in 1897, on an Egyptian mummy from Vth dynasty (2750-2625 BC). The body showed a series of anomalies such as ulnar deviation of the fingers, hyperextension of the metacarpophalangeal articulations, flexion of the interphalangeal joints and joint tumefaction, typical but insufficient for a RA diagnosis (10).

Table I reports all the cases which regard ancient human remains suggestive of RA (2,10-19); up until 1988 none of these had been accepted as sure case of RA. In 1974, Short placed the origin of RA in the modern age, probably for industrialization, environmental pollution of new compounds and diffusion of new antigens (4).

In 1988 Woods and Rothschild had the opportunity to study a skeletal population dated to Late Woodland (800-1100 AD), northern Ohio, with 7 males and 2 females displaying a symmetrical erosive disease (17). In the same year the authors discovered along the Tennessee River (Alabama, USA) 84 individuals, 3000-5000 years old. Six of the skeletons, 4 females and 2, exhibited a very interesting clinical picture. The morphology of the lesions, X-ray results, prevalence in the females and differential diagnosis made it possible to diagnose a disease similar to RA (18).

Short’s observations and the scarce descriptions made in the Old World be-

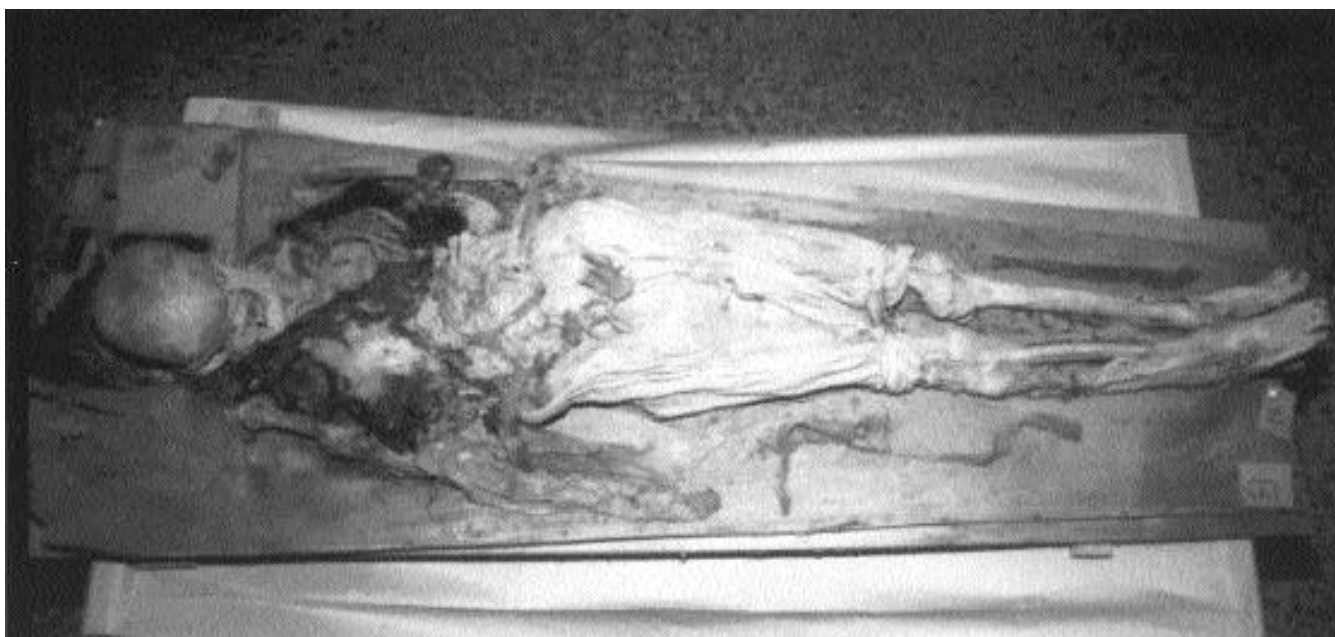


Fig. 2. The mummy of the Braids Lady: the hair, taken off the skull, is arranged in two braids on the breast.

fore 1800, suggested to Rothschild to set the origin of the disease in the New World and its exportation to Europe after 1492, through pathogens and allergens (20).

Materials and methods

The Braids Lady is a natural mummy, partially skeletonized (Fig. 2), belonging to an adult female 50-55 years aged (21) and about 1.44 m tall.

To avoid autopsy, after external examination, we studied the mummy using a large field digital fluoroscopy system for the acquisition of digital radiographic images.

Total Body CT. CT study was performed using a spiral equipment (HiSpeed Advantage, GEMS, Milwaukee, Wis, USA). The mummy was scanned with a beam collimation of 3 mm, pitch 1 (3 mm/sec of table incremental speed), 1 sec tube rotation, tube current 250 mA with 80 kVp, FOV 35 cm. All axial images were reconstructed with 180° linear interpolation at 1 mm spacing by using a standard reconstruction algorithm. Spatial resolution of slices was 512 x 512 x 12 bit (384 K bytes of memory occupied). The total number of images reconstructed for each study ranged between 75 and 90 (28 - 33.8 Mbytes) (22).

Left Hand CT. Using the same method

the left hand was detailed examined by a high resolution volumetric study with a beam collimation of 1 mm, pitch 1, interpolation at 1 mm and field vision of 12 cm.

Left Hand Radiography. The left hand was submitted to a radiography both by mammography, using a Compact Mammo HF type (Italray, Italy) with manual technique, microfire and a range of 65 cm on 18x24 film that made it possible to point out thinnest contrasts with a very good settlement, and by digital method using an apparatus "Clinodigit X- FRAME" (Italray, Italy) applying the following technical parameters: 5 mAs; 52-55 KVP (kilovolt Pico); maximum field; ionization chamber of 6 inches; no diaphragm; automatic exposition and laser print.

Left Hand Photography and Stereomicroscopy. The left hand was studied and photographed at stereomicroscope both entire and after dorsal-longitudinal section of the fingers and of the metacarpus. The most of the joints were well documented.

Left Hand Histology. The samples chosen to perform histology were taken from parts of the hand, resulted highly diagnostic at radiographic examination. Fragments (1 x 1 cm) of the metacarpophalangeal and carpo-metacarpal joints were processed as routine surgi-

cal tissue: rehydrated and fixed by Sandison's method (23), dehydrated by alcohol, decalcified in EDTA (etilendi-amintetracetic acid), embedded in paraffin, then cut in slices and stained on slides with haematoxylin-eosin to screen significant samples. The slides were analysed by light microscopy.

Results

External examination

The body revealed a partial mummification (Fig. 2) and a number of severe



Fig. 3. The head of the right humerus shows deformation and erosions.

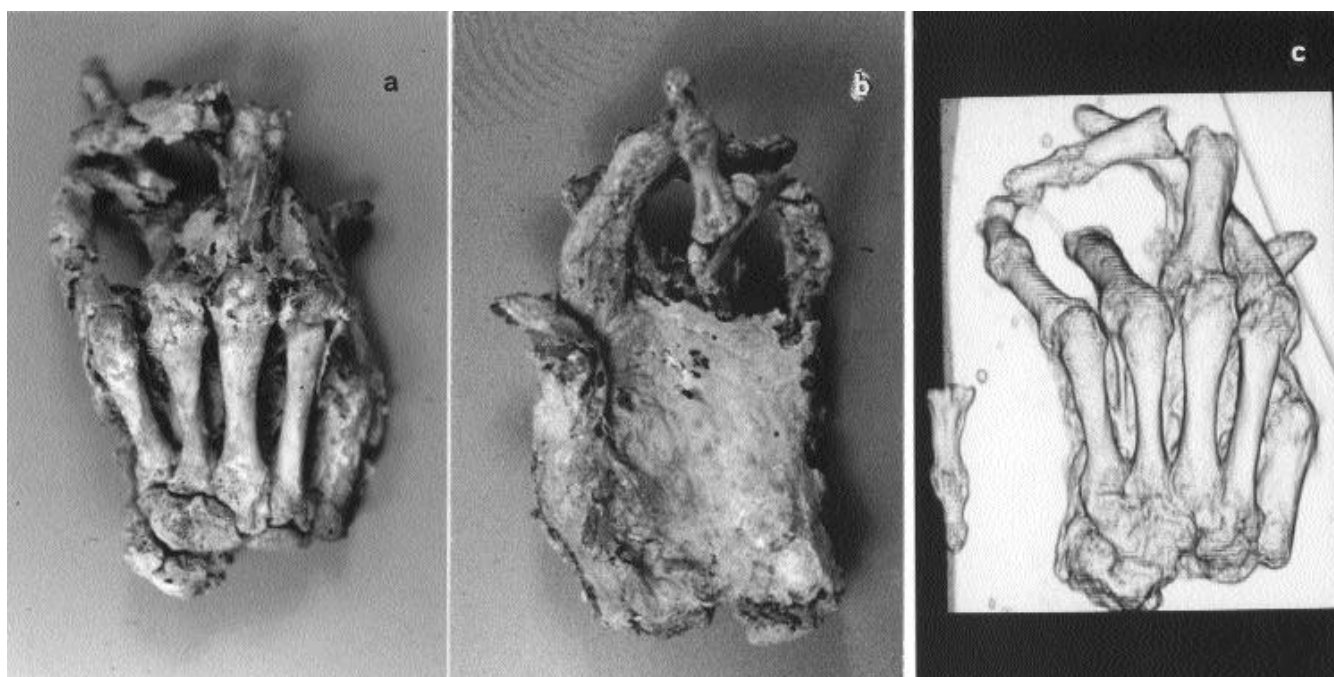


Fig. 4. Dorsal (a) and plantar (b) surfaces of the left hand: the typical “z” deformation of the 1st finger is well evident. Three-dimensional reconstruction of the same hand (c).

alterations of the bones, especially at the joint level. The skull, showing a post mortem fracture of the left superciliary arch and detached from the body at C2 level, was positioned on the occiput. The inferior and superior teeth were mostly lost intra-vitam. The head of the right humerus resulted dramatically deformed and eroded (Fig. 3). A less severe form of the same features was evident on the left humerus as well. The forearms were positioned on the abdomen. The right hand was almost totally skeletonized and the metacarpal bones had lost the skeletal connection with phalanges.

The left hand represents (Fig. 4a, b) a very peculiar finding and will be described in detail in the next paragraph. In her left hand the Braids Lady gripped a rosary, made of opaque green stones and enriched by a crucifix inlaid with pearl-shells. The lady was wearing a short linen tunic fastened at the knees by a strip (Fig. 2). Bureaucratic reasons made it impossible to undress the body and to perform external examination of the trunk and the pelvis.

Legs were parallel and extended. The feet, which were very well preserved, showed marked deformities of the toes consisting in fibular deviation, partial

overlapping and joint tumefaction (Fig. 6a).

Left hand examination

The left hand (11 x 7 cm) was partially mummified: the palmar surface (Fig. 4b) was totally covered with dry, dark and crumbly skin, while the dorsal surface (Fig. 4a) showed skeletonization of the carpus and the metacarpus (II, III, IV and V bones). The fingers were partially covered with skin; many tendons and nail-prints resulted still visible. Some bones of the carpus were lost; those still present showed a reduction of the joint spaces. All the metacarpophalangeal and interphalangeal joints appeared subluxed, with reduction of the articular spaces.

The 1st finger showed the typical “z” deformation caused by the hyperextension of the interphalangeal joint (Fig. 4b). The 2nd finger presented a subluxation of the metacarpophalangeal joint and lateral deviation of the first phalanx; the first and the second phalanges formed an angle corner of about 45°. The 3rd finger showed a lateral deviation of the metacarpophalangeal joint and post-mortem loss of the 2nd and the 3rd phalanges. The lateral deviation was well evident also at the level

of the 4th and 5th fingers, with flexion of the distal interphalangeal joint in the last finger.

CT and radiographic studies

Total body CT examination, with multiplanar reconstruction along different planes, made it possible to visualize the left and right humeri. The head of the right humerus confirmed the severe deformation and erosions (Fig. 3). The head of the left humerus appeared less compromised than the right; however the cortical bone showed marked thinning.

The left hand was submitted to both X-ray examination and CT which yielded the same results. X-ray study was carried out using antero-posterior (AP) and latero-lateral (LL) projections. The AP projection (Fig. 5a) revealed lateral deviation of all the fingers and large erosions of the articular surfaces of the metacarpophalangeal joints of both the 3rd and 4th fingers. The bases of the first phalanges showed a slight flaring. Some minute marginal erosions of the carpal bones are also present, with only minimal fusion between the cuneiform and the semi-lunar.

The LL projection showed volar metacarpophalangeal subluxation of both

the 3rd and the 4th fingers (Fig. 5b). The feet, likewise, presented fibular deflection of the toes with partial overlapping (Fig. 6 a,b).

Stereomicroscopic study

Stereomicroscopy of dorsal-longitudinal sections of the fingers confirmed the presence of subluxations, reduction and deformation of the joint spaces, articular erosions, cortical bone thinning and osteoporosis (Fig. 7a-d).

Histology

Histological examination revealed reduction of the joint spaces, cortical bone thinning and osteoporosis as well. The bad preservation of soft tissues made it impossible to observe inflammatory cells.

Discussion

Rheumatoid arthritis is a dramatic form of synovitis that leads to the destruction of affected joints. About 1% of the world population is affected and women suffer from RA three times more than men. Usually the disease starts between 30 and 40 years of life (24). Clinical diagnosis is often very difficult to perform, especially in its early stage: the joint deformities typical of RA are not yet present and there



Fig. 5. Radiography of the left hand. Antero-posterior projection (a), latero-lateral projection (b). The metacarpophalangeal joints show erosions, joint subluxation, lateral deviation of the fingers and joint enlargement. The carpus shows marginal erosions.

are not pathognomonic lesions.

A correct diagnosis is deeply bound to the number of lesions and typical symptomatic, but not exclusive, features of RA. For this reason "American

Rheumatism Association" in 1988 listed a number of criteria useful in epidemiological studies and based on easily recognizable lesions (25). The criteria were, of course, referred to a living

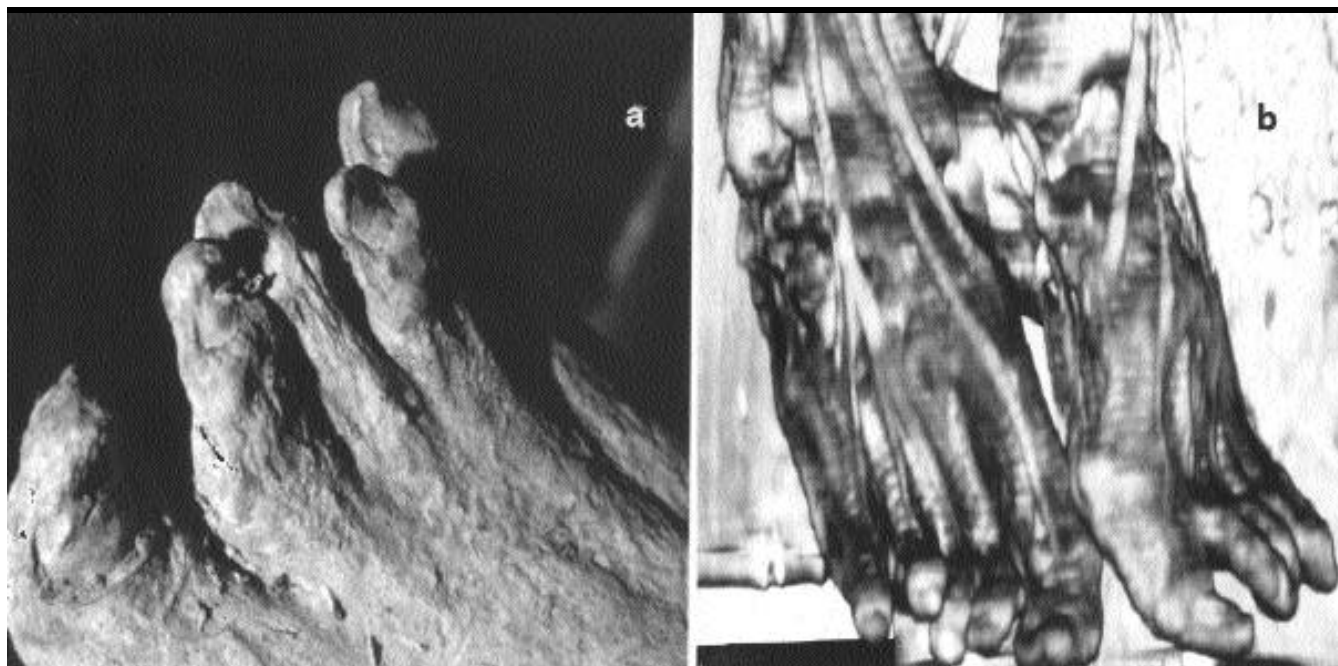


Fig. 6. The feet are characterised by fibular deviation of the toes, partial overlapping and joint tumefactions (a). Three-dimensional reconstruction of the feet (b).

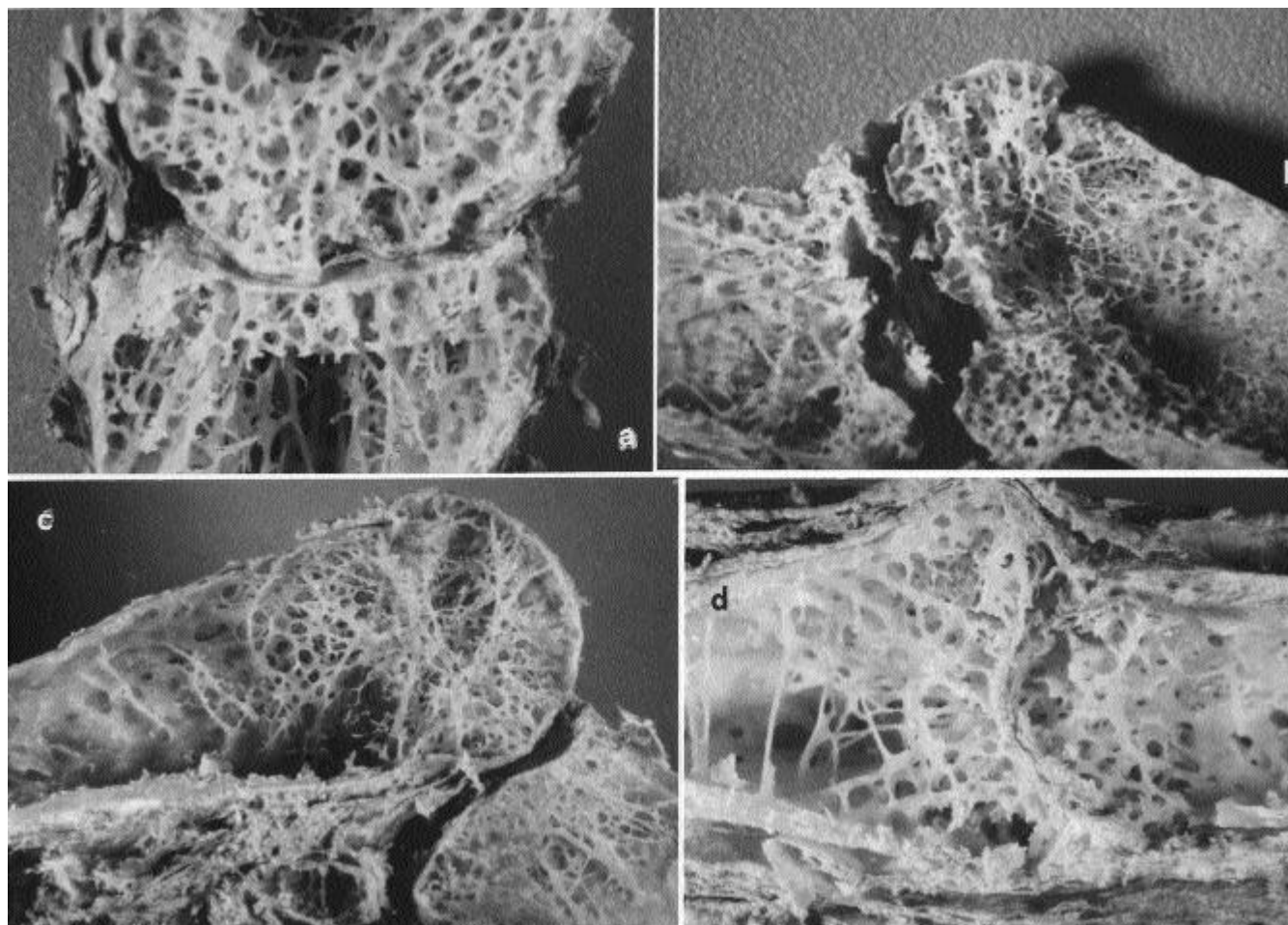


Fig. 7. Dorsal longitudinal sections of some fingers: the 2nd shows (a, d) reduction of the joint space and thinning of the cortical bone (4x); (b) subluxation, deformities and irregularity of the metacarpophalangeal joint of the 3rd finger (3x); the 5th finger shows (c) metacarpophalangeal subluxation (3x).

population and could not be completely applied to the present ancient case. However, our study allowed us to record a relevant number (10 on 16) of typical features making the diagnosis of RA certain. Comparison between the number and the type of lesions recorded on the body of the "Braids Lady" and those recorded in past discoveries (Table I), showed a number of alterations typical of RA, very similar those present in the individuals examined by Rothschild, whose diagnosis was considered certain. The minimal fusion of the carpal bones observed in the Italian case can be easily explained as the expression of a post-traumatic event. Our conclusions are strongly supported by the differential diagnosis. For instance, RA does not involve the sacroiliac articulation, a typical feature of ankylosing spondylitis; psoriatic arthritis is much more asymmetric, and involves sacroiliac and distal interphalan-

geal articulations; finally, in osteoarthritis of the hand there are not joint erosions.

The oldest unmistakable European clinical description – made by Landré Beauvais in 1880 – is an unprecedented occurrence in the history of medicine. The apparent deficiency of previous descriptions of RA forced Short (1974) to speculate the origin of the disease in the modern age, as a result of the process of industrialization that introduced new environmental antigens and allergens (4). Some doubts about this hypothesis were voiced by Domen (1981), who considered underestimated the number of ancient recorded cases. A more detailed observation of skeletal materials would have made it possible to recognize other cases of RA: as a matter of fact the hands and the feet, parts of the skeleton which are highly diagnostic for RA, are the segments more suitable to be lost and/or destroyed (26).

Rothschild suggested a new theory after his new American findings: rheumatoid arthritis arose in the New World and, only after the arrival of Columbus, was exported to Europe carried by some pathogens (20).

In this scenario the case of the Braids Lady acquires remarkable importance. The burial took place between the vaults of the lower church and the floor of the more recent building. Therefore the year 1377 is the earliest possible dating for the tomb but, considering the style of the dress, the indicative date of the burial can be included between 1550 and 1650, most probably at the end of 16th century (Devoti, 1997, personal communication).

The definition of this range of time allowed us to backdate by 250-150 years the first certain diagnosis, before the description made by Landré-Beauvais in 1800.

This finding rejects Short's hypothesis

who set the origin of RA after the XVII century and, probably, Rothschild's hypothesis as well. Indeed, if we consider the discovery of America by Columbus in 1492 and the foundation of New Amsterdam (New York) in 1623, 30 years before the more recent limit in which we set the death of the Braids Lady, it is quite difficult that in 100 years the moving of pathogens or allergens from America may have given origin to rheumatoid arthritis in Europe. The emigration movement was in fact extremely limited before the 17th century and commerce across the Atlantic of tobacco, potatoes and other potential vehicles of disease, took place in a period following that of the life of the Braids Lady, who moreover lived in Arezzo, a town in internal Tuscany, in this period rather far from commercial routes.

Our results support the presence of rheumatoid arthritis in Europe during ancient times, even if the impact on the population must have been low. In the course of time its frequency has obviously grown, reaching recently the modern impact (0.5-1%), probably as a result of a major sensitization due to the diffusion of new antigens.

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