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Epidemiology of Paget's disease of bone in an area of Barcelona

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Summary

Paget's disease of bone (PD) is a focussed disorder, asymptomatic in the majority of cases and of an unknown etiology. The epidemiology of this disease is little characterised; its global prevalence or incidence in Spain is not known. The objective of this study is to determine the prevalence and incidence of PD in an area of the city of Barcelona (Barceloneta) which has a health care system in which primary, hospital and specialised care are integrated, and in which digitised archives of complementary investigations, diagnoses and treatments are available.

Patients and Methods: The population of the area of Barceloneta is 18,509 inhabitants (1996 Census) with 6,989 people older than 55 years. The process for the identification of patients affected by PD in the area of Barceloneta was carried out through a review of the digitized archives of diagnoses, treatments, analyses, pathological anatomy, and bone radiography and gammagraphy from the primary care centre (CAP), the Rheumatology service and other services of the Hospital del Mar. In cases detected the diagnosis was confirmed through a review of the clinical history by the researchers.

Results: 16 patients were found to have the disease (10 women and 6 men). The average age was 79.2 years (range 65-92). Monostotic/Polyostotic: 8/8. Symptomatic/Asymptomatic: 9/7. The apparent prevalence in the population over 55 years of age was 0.23%. In the period 1996-2000, five new cases were diagnosed, the incidence being 1.78/10,000 person/years. Assuming that only 20% of cases are symptomatic it is possible to infer that the total number of patients is 45, real P being calculated at 0.64%.

Conclusions: In the area of Barceloneta (Barcelona, Spain), the real prevalence calculated is 0.64% and the estimated incidence is 1.78/10,000 person/years, all figures referring to the population over 55 years of age.

Key words: *Osteitis deformans, Prevalence, Incidence.*

Introduction

Paget's disease of bone (PD), also called "osteitis deformans", is a focussed disorder of bone remodelling, of unknown etiology, which occurs usually in an asymptomatic form. It is characterised by an increase in bone resorption followed by an increase in formation which gives rise to bone which is disorganised, with anomalous characteristics and altered biomechanical properties. All this drives the appearance of enlarged bone, deformed and fragile, which is the cause of its clinical manifestations and orthopaedic and neurological complications. Its imaging techniques, which to the greatest extent, allow the diagnosis of the disease. Biochemical markers for remodelled bone and gammagraphic studies are the complementary investigations which serve to assess the activity and extent of the disease. At present biphosphonates are the medical treatment of choice. The indication for treatment with anti-resorptive drugs should be individualised, taking into account metabolic activity, age, the location of the disease and presence of complications¹.

PD is the most frequent bone metabolic disease in the countries of our region, after osteoporosis. Its prevalence and incidence show great variability in relation to geographic location, age, gender and race. In general, it affects adults, being infrequent in those below 40 years of age. The distribution by gender is similar predominantly in men. Its racial distribution is heterogeneous, it being non-prevalent in the native black population of Africa, Japan and South-east Asia. PD predominates in the Caucasian Anglo-Saxon race².

The epidemiology of PD in Spain has not been well characterised until recently by Guañabens N et al³, who estimate it at at least 1% in those older than 55 years. This data concurs with previous data which estimates it at around 0.9-1.3%⁴, with a focus of higher prevalence in Sierra Cabrera (Madrid)⁵ and in Vitigudino (Salamanca)⁶. The objective of this study is to approximate the prevalence and incidence of PD in an area of the city of Barcelona (Barceloneta).

Patients and Methods

The study was carried out in 1998 in an area of the city of Barcelona (Barceloneta, Spain), in which the health care of the population is provided, almost completely through the primary care centre (CAP Barceloneta) and the University Hospital (Hospital Universitario del Mar), which is the hospital for referrals from the area. The population of the area is, according to the census of 1996, 18,509. 97% are of Caucasian origin, the remaining 3% being made up largely of people from the Magreb. The age distribution is the following: 9.9% (0-14 years), 63.8% (15-64 years) and 26.2% (> 65 years), of which 6,984 patients are over 55 years of age (2,816 men and 4,168 women).

80% have an open and active clinical history at the University Hospital (Hospital Universitario del Mar) and/or at the CAP (Centro de Asistencia Primaria) Barceloneta.

The University Hospital and the CAP Barceloneta have available digitized archives of diagnosis, treatment and complementary investigations. The search for probable cases of PD was carried out by means of a review of the digitised archives of: clinical diagnoses (CAP Barceloneta, and the Rheumatology Service and general archive of the University Hospital), anti-Paget treatments, anatomical-pathological diagnoses (the archive of the Anatomy Pathology Service of the University Hospital), diagnoses of the Nuclear Medicine Service of the University Hospital, and clinical analyses. A case was considered to be probable when the total values of alkaline phosphatase in the blood were higher than 300 UI in patients older than 55 years, and with normal liver tests (AST, ALT, GGT and bilirubin). When a probable case was identified the diagnosis of PD was confirmed through a review of their clinical history by the researchers trained in the diagnosis of PD (JB and ME). Following the confirmation of diagnosis a form was completed to gather data including: age and gender, monostotic/polyostotic form, year of diagnosis and possible complications.

Results

A total of 16 patients were identified (6 men and 10 women). The average age: 79.2 (range 65-92). The distribution according to age and gender is shown in Figure 1. What stands out is that not one case was found in anyone younger than 65 years old, and that prevalence increases with age. Also, the distribution by gender only showed a clear predominance of the female sex in the group older than 85 years. The apparent prevalence in the population studied > 55 years old was 0.23%. The symptomatic cases registered were 9 (9/16), which represents 56%. Kanis JA⁷ says that only 20% of patients with PD show any clinical manifestation. Following from this premise it could be inferred that the total number of symptomatic patients in our population is 45, with a prevalence calculated at 0.64%. The polyostotic (8) and monostotic (8) forms are present with the same frequency.

In the period 1996-2000 5 new case of PD were diagnosed in patients older than 55 years, giving an apparent incidence of 1.78/10,000 person-years.

A difficulty with the study is that in assessing prevalence in a predominantly asymptomatic disease there is a dissociation between detected cases and real cases. Detected cases allow us to define the apparent prevalence and the real cases (symptomatic detected + non-detected cases) as the real prevalence.

Discussion

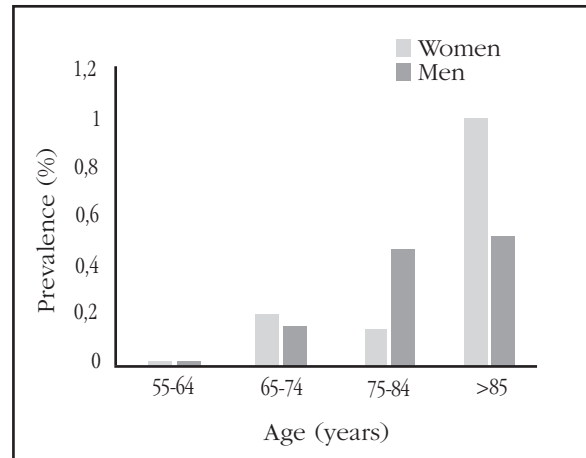
The importance of epidemiological studies of PD reside in the fact that they permit the establishment of a hypothesis on the etiology and pathology of the disease, thus providing social/public health data which could help managers in the assignment of resources in an efficient way.

In 1932 in Germany, Schmorl⁸ was the first to calculate the prevalence of the disease by carrying out 4,614 autopsies on people who had died aged 40 or more years, establishing a prevalence of 3%. In England, Collins DH⁹, in 650 autopsies, found a prevalence of 3.7%. Pygott F¹⁰ in 1957 determined, through a radiological review of the pelvis and lumbar spinal column, a prevalence of 3-4% in Great Britain.

Detheridge FM et al⁴, evaluated the prevalence in western Europe through a postal questionnaire carried out with radiographers in 13 cities in 9 European countries. Confirming the high prevalence of this disease in Great Britain, at around 5-6%, much the same as the findings of the Barker DJ et al^{11,12}. These authors evaluated the radiological prevalence of PD in 14 cities of Great Britain, the study widening 3 years later with the inclusion of 31. The result of both studies show an average prevalence of 5%, being higher in the cities of the north east (focussed on Lancashire) where it varies between 6 and 8%. In a recent study van Staa TP et al¹³ found, through the review of the centralised diagnostic archives (General Practice Research Database) of England and Wales, a prevalence for clinical PD of 0.3% in the population over 55 years old. The incidence found at 75 years, was 5/10,000 patient/years in males and 3/10,000 patient/years in females, with a decline in incidence in the last 11 years. Studies carried out in France, with a similar methodology, show a prevalence of 1.5-2.5%¹⁴. In a recent study, Lecuyer et al¹⁵, through a review of radiographies of dorsal and lumbar spinal column carried out in the course of an epidemiological study of osteoporosis (EPIDOS), found a prevalence in women over 75 year of between 1.1 and 1.8%. In the Netherlands Eekhoff M et al¹⁶, using the results of the Rotterdam Study of the incidence and risk factors of various chronic diseases, identified cases of PD in this population by studying those subjects who had high levels of total alkaline phosphatase in the blood (higher than 2 DE on average) and the presence of radiographic signs of PD. The prevalence was estimated at 3.6%. In the rest of the European countries the prevalence is lower: Sweden (Malmo) 0.4; Italy (Palermo) 0.5%; Greece (Athens) 0.5%. In Spain an intermediate prevalence is observed, 1.3% in Valencia and 0.9% in La Coruña, similar to that of Portugal (Oporto 0.9%), Italy (Milan 1%) or Germany (Essen 1.3%)⁴. The rarity of this disease in the Nordic countries has also been confirmed in other studies carried out in Norway and Finland¹⁷. In Ireland the prevalence was 1.7% in Dublin, less than might be expected in a country which neighbours Great Britain. However, the prevalence of 0.7% found in Galway, in the north west of Ireland is comparable with the rest of Europe¹⁸.

The prevalence in the United States is estimated at around 1-2% in the general population, with no differences in gender, or ethnic group, except in Native Americans, in whom it is very low. The prevalence of 3% in New York compared to 1% in Atlanta, shows a pronounced variation in the dis-

Figure 1: Prevalence of Paget's disease of bone, according to age and gender



tribution of this disease between the cities of the north and the south of the country^{19,20}.

The few epidemiological studies carried out on the non-Caucasian population of Africa reveal prevalences of between 1.3 and 2.4% in those over 55 years old²¹.

Countries with predominantly Anglo-Saxon immigration, such as Australia or New Zealand, show a high level of prevalence. It has been suggested that this could be attributed to emigration from Great Britain. The prevalence in British immigrants to Australia is 4%, intermediate between the 5% for Britons who have stayed in Great Britain, and the 3.2% for native Australians with British origins²².

In summary the prevalence varies between the 5% seen in the population of people over 50 years old in Great Britain and the 0.4-1.3% seen in the other countries of Europe, with New Zealand, the United States and Australia being similar to that of Europe. In countries such as the Scandinavian nations, Japan, China and the Middle East PD is rare.

The heterogeneous geographical distribution of this disease, as has been commented on, is well known, as is the existence of areas of very high prevalence, "hot spots" which have motivated the study of possible etiopathogenic factors. In the "hot spot" of Lancashire, Great Britain, with a prevalence of 6.3 – 8.3% in those over 55 years of age, the existence of any exclusive climatic or geological characteristics which could give some inkling of an explanation of the etiology of PD¹¹, has not been found. In the "hot spot" of the Sierra de Cabrera, in Madrid (Spain), with a prevalence of 6.37% in those over 40 years of age, a probable genetic conditioning has been postulated, through the detection of a group of 6 families with 15 members affected by the disease⁵. In Vitigudino, Salamanca (Spain), the prevalence is

Table 1: Description of the principal characteristics of the most relevant studies on the prevalence of Paget's disease of bone

Authors and bibliographical reference	Year	Location	Methodology	Prevalence (%)
Gardner MJ et al ²¹	1978	Australia	Abdominal X-ray review, barium study and endovenous urography	3.2-4
Barker DJ et al ¹⁰	1980	Great Britain	Abdominal X-ray review	5
Barker DJ et al ⁹	1980	Great Britain (Lancashire)	Abdominal X-ray review	6.3-8.3
Guyer PB et al ⁸	1980	USA	Abdominal X-ray review	1-3
Detheridge FM et al ³	1982	Europe	Postal survey and abdominal X-ray review	0.4-4.6
Detheridge FM et al ¹⁷	1983	Ireland	Postal survey	0.7-1.7
Morales-Piga A et al ⁴	1990	Spain (Madrid)	Determination of total alkaline phosphatases and radiological confirmation	6.3
Renier JC et al ¹³	1995	France (Anjou)	Endovenous urography review	1.8
Miron-Canelo JA ⁵	1997	Spain (Salamanca)	Questionnaire, radiological study and determination of total alkaline phosphatases and radiological confirmation	5.7
Altman RD et al ¹⁹	2000	USA	Pelvic X-ray review.	1-2
van Staa TP et al ¹²	2004	England and Wales	Review of diagnoses from population database (General Practice Research Database)	0.3 *
Eekhoff M et al ¹⁵	2004	Netherlands (Rotterdam)	Determination of total alkaline phosphatases and radiological confirmation	3.6
Guañabens N et al ³	2008	Spain	Abdominal X-ray review	1,0

* Clinical prevalence

5.7% in those over 40 years of age, much greater than that reported in other parts of the country, and higher than that estimated for the south of Europe⁶. Recently, new areas of high prevalence have been described in Spain²³. Table 1 describes the characteristics of the principal studies of prevalence.

The polyostotic form of the disease is more common than the monostotic form, as has been shown in a range of studies. Monfort et al²⁴, through an evaluation of 250 patients, found that 73% had the poliostotic form.

Recent studies seem to indicate "secular" changes concerning the age of presentation, the severity of the disease (evaluated by the extent of the affection of the bone and/or levels of alkaline phosphates in the blood), predominance of one gender or other, and geographic location. The data for prevalence, standardised by age and gender, of Cooper et al²⁵ in great Britain, indicate a

reduction in prevalence from 5% in 1974, to 2%, twenty years later, this decrease being more marked in certain zones, such as Lancashire, considered "hot spots" of high prevalence. In the United States a similar phenomenon has been described²⁶. The majority of the studies confirm that the age of presentation continues to get higher. Cundy et al²⁷, show that at the beginning of the 70s the average age of presentation was 62 years, lower than that of 71 years of the last decade. The number of certificates of disability due to PD or its complications has diminished in the last 30 years, in the same way as the disease, which suggests a tendency to less severe forms²⁸⁻³¹.

The results obtained in this study in Barceloneta, a district of the city of Barcelona, show that the real prevalence calculated for this area is in the region of 0.6-0.7%. In Europe, with the exception of Great Britain, it varies between 0.4 and 1.3%⁴. The prevalence found is lower than

that found in two Spanish cities – Valencia, 1.3% and La Coruña, 0.9 – by Detheridge FM et al⁴. In respect of this last work, what stands out is that the results are the product of a postal questionnaire carried out in radiological services in diverse cities of Europe with the limitations that this methodology can bring.

We do not know of the existence of other studies carried out using the same methodology, at present, in Spain. The results obtained, very probably, approximate to the reality of the prevalence in our locality, an area in which health care is provided almost exclusively by the Primary Care Centre and by the referent hospital, and having had systemic access to the digitized registers of diagnosis and complementary investigations which makes it probable that non-diagnosed cases are scarce. Differently from other studies, in which one might question the certainty of the diagnosis of PD, the cases were confirmed through an exhaustive review of the clinical history. The population studied does not differ much in its distribution by age, gender and ethnicity, from that of the Spanish population, which allows the extrapolation of the results to the rest of the country, except that the average age is somewhat higher than the average for the Spanish population as a whole, and that this study was carried out in an urban area. To which can be added the fact that it was carried out in a mixture of the hospital and extra-hospital population.

In conclusion, the prevalence of PD in the area of Barceloneta (Barcelona, Spain), is similar to the average prevalence in Europe, and very close to that in other parts of Spain, despite the non-existence of truly representative studies of the global impact of this disease in our country. We would support any study which might answer the epidemiological questions raised by this interesting and complex illness.

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