Was true gout? New interpretations of the skeletal disease(s) of the Medici family

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It was well known that several members of the Florentine Medici family were affected by skeletal disorders, as documented by medical reports and by the stitched nicknames, as the famous “Piero The Gouty”. However, it is difficult to decipher from the several paintings and sculptures dedicated to the Medici grand dukes the nature of the osteo-articular disease(s). The reasons of this are either the fact that often the artist’s portraits were produced after the death of the V.I.P. or the tentative of the artist to hide physical deformities that could unplease the person who commissioned the masterpiece.

It is also true that evident deformities of the most exposed parts of the body, and therefore visible to the lay people were remembered in time. This happened in the case of Cosimo The Old, patre patriae, commissioned to the great painter Pontormo in 1520 from the secretary of Lorenzo duke of Urbino 50 years after the death of Cosimo. Pontormo could not neglect the hands’ deformities of Cosimo, presented in the portrait as the Florentine people remembered them, contorted, with evident deformities of the first finger of the right hand and hypertrophy of the metacarpophalangeal joints (Figure 1).

Differently from what happened with the paintings, reliable and unquestionable are the paleopathological observations performed on three different times in the bones taken from the Medici cadavers from the tombs of San Lorenzo church in Florence: in 1924 by Pieraccini, in 1955 by Costa and Weber and in 2009 by Fornaciari (1-3). From pathological, histological and radiological exams it did not appear a clear diagnosis of gout, but for a big toe’s phalangeal joint of Ferdinando I of the Medici family, who died at 60 years of age. Conversely, the deformities of the majority of the joints, mostly in males, were characterized by ossification of the anterior longitudinal ligament of the dorsal vertebral column with a typical wax casting or candy shape (the Zuckerusswirbestäule described by Rokitansky in 1856). Together with these vertebral lesions, other enthesopathies of the appendicular skeleton, in particular, ossifications of the Achilles and kneecap tendons, were described in the skeleton of Cosimo I (3). Other frequently described alterations were carpal and tarsal hyperostoses and sclerotic appearance of the cortical bone in the appendicular skeleton.

Altogether these phenotypes were interpreted as the consequence of the syndrome that Forestier and Rotes-Querol interpreted as spondilo-ankylosing hyperostosis (4), later named diffuse idiopathic skeletal hyperostosis (DISH) and considered a systemic disease of the entire skeleton (5).

The DISH syndrome is frequently familiar and affects mostly males in the family, with a tardive expression in patients over 50 years of age, as the disease is asymptomatic for several years. Predisposing conditions are diabetes and hyperuricaemia. The symptoms are evident when the ossification of the enthese causes acute joint flogosis.

Reading the history of the Medici family joint pain is described mainly in elderly people. From notes of the personal physician of Cosimo I the description of the primary crisis was referred as an painful swelling of the knee, without signs of flogosis and with a rapid return to normality. Differently, Piero The Gouty had a dramatic disease course, that made him practically uncapable to walk, with a low quality of life, and the possibility to move nothing else but the tongue.

References

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Italian Society of Osteoporosis, Mineral Metabolism and Skeletal Diseases: www.siommms.it
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American Society for Bone and Mineral Research: http://www.asbmr.org/
European Calcified Tissue Society: www.ectsoc.org/
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Scope
The Journal encourages the submission of case reports and clinical vignettes that provide new and exciting insights into the pathophysiology and characteristics of disorders related to skeletal function and mineral metabolism and/or highlight practical diagnostic and/or therapeutic considerations. The format of these papers should follow the one described in the “Preparation of Manuscript” section, with the added consideration of providing case historical data as appropriate.

General Information
Manuscripts should be sent in two copies to the Editor-in-Chief: Maria Luisa Brandi, M.D., Ph.D., Department of Internal Medicine, University of Florence, Viale Pieraccini, 6 - 50139 Florence, Italy. Fax +39 055 2337867. E-mail: mb@chunifi.it.
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To simplify the typesetting process and speed up the processing of the manuscript, text, tables and figures, prepared using Word for Windows or Macintosh, should also be submitted in electronic format or by e-mail. High resolution illustrations (graphs included) should be submitted in TIF, JPG or EPS format, or in original prints of such good quality that they can be photographed.

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Articles are definitive and comprehensive descriptions of major research findings of broad significance for readers of Clinical Cases in Mineral and Bone Metabolism. The results described should be both novel and of wide interest. Articles may be of any length and may contain as many display items as appropriate for the subject matter.

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Manuscripts consider the step-by-step process of clinical decision making. Information about a patient is presented to an expert clinician(s) in stages to simulate the way such information emerges during clinical practice. The clinician responds as new information is presented, sharing his or her reasoning with the reader. The text should not exceed 2500 words, and there should be no more than 20 references. The use of clinical illustrative materials, such as x-ray films, is encouraged.

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Articles are evidence-based results of clinical trials relevant to practicing physicians, both primary care providers and specialists. These studies are scrutinized for the strength of the hypothesis, the rigor of the experimental design, the evaluation and interpretation of the data, and the clinical implications of the study. In addition, clinical trials are subjected to a separate statistical reviewer. Articles detail the pharmacology and the use of specific drugs used to treat particular diseases. Because the essence of Clinical Trials articles is the evolution of therapeutic intervention, the Journal expects that the Authors of such articles will not have financial associations with a company (or competitor) that makes a product discussed in the article.

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Usually provide commentary and analysis concerning an article in the issue of the Journal in which they appear. They may include an illustration or table. They are nearly always solicited, although occasionally, unsolicited proposals may be considered. Commentaries are limited to 1200 words, with up to 5 references.

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Are generally solicited. We are willing to consider proposals for book reviews, but please contact the editorial office before submitting a review.
Assunto è stato studiato in sperimentazioni cliniche che hanno coinvolto circa 8.000 persone. La sicurezza a lungo termine è stata valutata con studi di fase III, in donne in postmenopausa con osteoporosi, trattate fino a 60 mesi con 2 g/die di ranelato di stronzio approssimativamente del 60-70%. Pertanto, la somministrazione di OSSEOR e di tali prodotti deve essere distanziata di almeno 2 ore per evitare interazioni farmacologiche. Il cibo, il latte ed i suoi derivati, e le specialità medicinali contenenti calcio possono ridurre la biodisponibilità del ranelato di stronzio approssimativamente del 70-80%. Pertanto, la somministrazione di OSSEOR e di tali prodotti deve essere distanziata di almeno 2 ore (vedere paragrafo 5.2). 

2 bloccanti ed inibitori della pompa protonica, ACE-inibitori, antagonisti dell'angiotensina II, agonisti selettivi dei recettori beta-2-adrenergici, anticoagulanti orali, inibitori dell'aggregazione piastrinica, statine, fibrati e derivati delle benzodiazepine.

**Tromboembolismo venoso (TEV)**
- In assenza di dati relativi alla sicurezza ossea in pazienti con insufficienza renale grave in trattamento con il ranelato di stronzio, OSSEOR non è consigliato nelle pazienti con clearance della creatinina inferiore a 30 ml/min (vedere paragrafo 5.2). Nel rispetto di una buona pratica clinica, si raccomanda un controllo periodico della funzionalità renale nelle pazienti con insufficienza renale cronica. 

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**Insufficienza renale**
- **Granulato per sospensione orale.** Granulato giallo.
- **La sicurezza e l'efficacia di OSSEOR nei bambini di età inferiore ai 18 anni non sono state stabilite. Non ci sono dati disponibili.**

**Classe terapeutica:**
- **Non stereoidei (compreso l'acido acetilsalicilico), anilidi (come il paracetamolo), H
curazione.**

**Effetti indesiderati**

- **Frequenza non nota:**
  - Stato confusionale
  - Insonnia

**Classificazione per sistemi e organi**

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