Rare diseases in orthopedics: algodystrophy and aseptic osteonecrosis

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The term “rare disease” is commonly reserved for pathological conditions with an extremely low incidence and prevalence. According to the “Rare Disease Act”, enacted in the United States in 2002 to be defined as rare a disease has to affect fewer than 200,000 Americans with a prevalence equal or less than 1 in 1,500 individuals (1). These number changes all over the world, i.e. in the European Community to identify a rare disease the prevalence has to be less than 1 in 2,000 (2) and in Japan less than 1 in 2,500 (3). The numerical discrepancies reveal several uncertainties, especially regarding the etiology and pathogenesis, in the field of human pathology. Moreover, the term "rare disease" in Europe and in the United States is often synonymous of "orphan disease" or "orphan-drug-disease", underlining the lack of an adequate pharmacological and non-pharmacological treatment for these diseases. The World Health Organization (WHO) assumes that, of the 30,000 known diseases, among 6,000 to 8,000 might be defined as rare (4). Many rare diseases involving the musculoskeletal system are caused by variations in genes responsible to modulate the skeletal development and regulation. Recent advances of the molecular genetics have allowed understanding the genetic basis and the phenotypic correlations, depending on the type and location within the same gene. Up to now almost 400 different forms of skeletal dysplasias have been described (5). However the skeletal system might be affected also by rare diseases of uncertain etiology, for which it has not been recognized a genetic etiology but only a genetic predisposition. Among these conditions, algodystrophy and aseptic osteonecrosis of the femoral head have an important historical and clinical role in the field of orthopedics. The algodystrophy is currently considered as a form of Complex Regional Pain Syndrome (CRPS) type 1, characterized by a specific set of clinical signs and symptoms related to specific pathogenic mechanisms involving both bone and soft tissues of the affected extremity. It is a typically orthopedic disease following a trauma of bone or soft tissues, or a surgical intervention. The symptomatology usually appears after at least one month from the traumatic event, precipitating with a wide range of temporal variability (6). A typical case is that of a patient who suffered a fracture of the distal extremity of the radius and, after removing the plaster cast and radiographic fracture healing, complaints of a persistent pain with neuropathic characteristics (hyperalgiesia and allodynia). It is very frequent in these situations to observe a positive scintigraphy with the presence of hyperaccumulation of the radioactive tracer or the presence of edema at the Magnetic Resonance Imaging (MRI). At the same time in an advanced stage it might be experienced a diffuse demineralization of the skeletal segment (known as Sudeck’s bone atrophy). The disease usually resolves spontaneously, but in some cases it might develop into a chronic pain syndrome, constituting a real CRPS type 1. Therefore, it is essential to identify predisposing factors that might influence the genesis and the natural history of the disease. The type of trauma, the mode of treatment, the type of anesthesia, and the early pharmacological treatment might influence the evolution of the process. The Avascular Osteonecrosis of The Femoral Head (ANFH) is another rare, but challenging disease for orthopedic surgeon. This condition is characterized, in advanced stages, by hip pain and functional limitation, with lameness, dysmetria, collapse of the subchondral bone, and consequent osteoarthritis of the hip joint that often requires subsequent total hip replacement. Prevalence of ANFH is not precisely known, but it is believed that there are approximately 15,000 new cases per year in the US (incidence is approximately 1 in 20,000). Most cases are associated with harmful traumatic events involving the hip, blood disorders, metabolic disorders, abuse of alcohol and/or smoke, and use of corticosteroids. There are also very rare familiar forms of ANFH linked to genetic alterations such as the autosomal dominant one involving the gene of type II collagen (COL2A1) (7). The most reliable pathogenic hypothesis attributes the process to the combined effects of a genetic predisposition, metabolic factors, and local factors (microvascular damage, increased intraosseous pressure, and increased mechanical stress) interfering with the adequate nutrition supply, resulting in an ischemic bone necrosis (8, 9). The diagnosis of ANFH is performed based on clinical evaluation and imaging assessment, in particular the MRI (a broader description is given in one of the papers of the supplement, included advanced MRI and ultra-high field magnets). The natural history of the disease appears to be very variable and its progression is not clearly defined, making it difficult to judge the validity of the chosen treatment. The conservative and surgical management, in the pre-collapse phase, might improve the clinical manifestations, in particular reducing the disabling pain, although up to date there is no a conservative, surgical or mixed treatment that
could certainly avoid or delay the progression of ANFH towards the collapse, the secondary osteoarthritis, and joint replacement.

Epidemiological and etiopathogenic issues and latest advances for conservative and surgical management of CRPS and ANFH were discussed during the works of the Congress of the Italian Orthopedic Group for the Study of Severe Osteoporosis (GISOOS) and the Italian Society of Osteoporosis Surgery (SICOST), of which this supplement is a written testimony.

References

2. Communication from the commission to the European Parliament, the council, the European economic and social committee and the committee of the regions - on Rare Diseases: Europe’s challenges. Brussels: 2008.