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CASE REPORT

Pain amplification syndrome in the elderly. Case report and literature review*

Síndrome de amplificação dolorosa no idoso. Relato de caso e revisão da literatura

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SUMMARY

BACKGROUND AND OBJECTIVES: There are very few publications on pain amplifIcation syndrome in the elderly (PAS), in spite of its importance for them, because it may have multiple consequences during aging. This study aimed at reporting a case of PAS in the elderly represented by fIbromyalgia (FM), describing its diagnostic approach and therapeutic management, and at presenting a literature review on the subject.

CASE REPORT: Female patient, 73 years old, with moderate diffuse muscle pain, ‡eeting morning stiffness, anhedonia, sadness, anxiety, major fatigue and sleep disorders for four years. She was initially diagnosed as rheumatic polymyalgia and was under regular prednisone in spite of the progressive worsening of her functional capacity and quality of life (QL). One year ago her diagnosis was reviewed by our service and we conflrmed it was PAS, spectrum of FM. Prednisone was then withdrawn and non-pharmacological therapy was indicated with pain self-management program; multimodal pharmacological therapy was also instituted with non-opioid (lysine clonixinate) and opioid (tramadol) analgesics and a pain modulator (duloxetine). Six months later there has been major pain, sleep, depression, anxiety, functional capacity and QL improvement.

CONCLUSION: Accurate diagnosis and adequate therapeutic intervention are paramount for PAS cases, especially in the elderly population with FM, which has unique characteristics in such population. There are major probabilities of symptomatic, functional and QL improvement in the elderly with PAS if we pay attention to differential diagnoses and introduce adequate therapies.

Keywords: Differential diagnoses, Elderly, Fibromyalgia, Pain amplifIcation syndrome.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Pouquíssimas são as publicações sobre a síndrome de amplifIcação dolorosa no idoso (SAD), a despeito da sua importância para aqueles indivíduos, pois pode ter múltiplas consequências no envelhecimento. O objetivo deste estudo foi relatar um caso de SAD no idoso; representada pela fIbromialgia (FM), descrevendo sua abordagem diagnóstica e seu manuseio terapêutico, bem como apresentar uma revisão bibliográfIca do assunto.

RELATO DO CASO: Paciente do gênero feminino, 73 anos, há 4 anos iniciando um quadro de moderada dor muscular difusa, rigidez matinal fugaz, anedonia, tristeza, ansiedade, importante fadiga e distúrbio do sono. Inicialmente, diagnosticada polimialgia reumática, assim, vinha fazendo uso regular de prednisona, apesar de progressiva piora da sua capacidade funcional e qualidade de vida (QV). Há um ano, no nosso serviço, foi revisto o diagnóstico, e verifIcado tratar-se de SAD, espectro da FM. Suspendeu-se, então, a prednisona e orientado terapia não farmacológica com programa de autogeren-

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ciamento em dor, e farmacológica multimodal com analgésicos não opioide o clonixinato de lisina e opioide o tramadol, e um modulador da dor, a duloxetina. Após 6 meses de tratamento verifícou-se grande melhora na dor, sono, depressão, ansiedade, capacidade funcional e QV.
CONCLUSÃO: É de suma importância o diagnóstico correto e uma intervenção terapêutica adequada nos casos de SAD, especialmente tratando-se da população idosa e da FM, a qual apresenta características peculiares naquela população. Há grandes probabilidades de melhora sintomática, funcional, e na QV dos idosos com SAD ao se atentar para aos diagnósticos diferenciais, bem como ao se introduzir terapêuticas adequadas.
Descritores: Diagnósticos diferenciais, Fibromialgia, Idoso, Síndrome de ampliflcação dolorosa.

INTRODUCTION

Population aging is a worldwide phenomenon with unprecedented levels. Only in Brazil, the elderly population shall double in the next two decades and may reach 30 million of individuals[1]. This fact is followed by increased frequency of cases related to pain complaints.
Pain, for its prevalence and impact, is considered today a major public health problem. Older people are especially more susceptible to chronic pain, which ends up contributing to functional impairments and also worse quality of life scores (QL)[2].
Pain ampliflcation syndrome (PAS) has signiflcantly increased in recent years, also including the aging population. However, there are still few studies speciflcally addressing it in the elderly.
Fibromyalgia (FM) is a major PAS presentation, which is seldom addressed and discussed in aging people, especially in Brazil.
This study aimed at reporting a PAS case as well as at reviewing FM spectrum in the literature, describing diagnostic approaches and adopted therapies, in addition to presenting a scientiflc-literary review on the subject.

CASE REPORT

Female patient, 73 years old, artisan, with hypertension, spinal osteoporosis and osteoarthritis, who referred paresthesia and sensation of edema on hands, moderate diffuse muscle pain, ‡eeting morning stiffness, anhedonia, sadness, anxiety, major fatigue and sleep disorders for four years. She was being followed by other health service since the beginning of symptoms with diagnosis of polymyalgia rheumatica.
So, since that time she was under regular steroids with 10 mg prednisone/day. She referred initial pain improvement but her functional capacity was progressively worsening.
She is being followed by our service for one year and was initially submitted to evaluation especially addressing the different aspects of her pain: moderate intensity by the verbal scale, and equal to 5 by the numerical verbal scale, continuous, diffuse and heavy chronic pain but with exacerbation periods, interference with her executive functionality with partial dependence for complex daily life activities, interference with her affection with depression and anxiety followed by fatigue and sleep disorders.
Physical evaluation has shown just hyperalgesia in upper and lower limbs. We suspected of PAS, FM spectrum, and requested several laboratory tests, including in‡ammatory tests, vitamin D, CPK, thyroid, parathyroid, kidney and liver function, among others, and all were within reference values, except for VHS of 40 mm in the flrst hour. Compared to tests of three years ago, VHS was 43 mm in the flrst hour. We have also requested shoulders ultrasound, which has not shown signiflcant changes. Bone densitometry was not performed because she missed her appointments several times.
With the higher possibility of really being FM, we have gradually withdrawn prednisone and established a new treatment: pain self-management program with guidance and exercises, educational measures, physical measures at home, such as the use of stupes, coping, cognitive-behavioral measures and multimodal pharmacological therapy with non-steroid analgesic (125 mg lysine clonixinate every 8 hours) and opioid analgesic (50 mg tramadol every 8 hours) intercalated by 14 days of duloxetine (60 mg/day).
Six month later she returned referring that she was accurately complying with our guidance and that there had been major improvement in her general status with signiflcant pain, sleep, depression and anxiety improvement with major improvement of her functional capacity and QL.

DISCUSSION

In this case, it was observed that only after three years of medical follow-up and prolonged treatment with steroids the correct diagnosis was established. Since the beginning, a major disproportion between symptoms and flndings was observed. Pain was not severe but interfered a lot with her affection, functionality and sleep, and was associated to major fatigue.

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In the "pain puzzle", PAS is considered a new piece that, in turn, belongs to a group of conditions especially characterized by pain without associated organic cause, or even by symptoms disproportional to flndings. So, there is chronic pain the intensity of which is not objectively explained[3]. Such condition has also been called functional pain syndrome.

Traditionally, most patients affected visit many physicians, including different specialties according to predominant symptoms and in general, abnormalities which could fully explain the symptoms are not identified.

PAS has a wide presentation spectrum being most frequent the musculoskeletal forms. But in addition to PAS musculoskeletal forms, other chronic conditions have been observed in recent years, such as chronic fatigue syndrome, headaches, irritable colon and bladder syndromes, restless legs syndrome, and periodic limbs movement syndrome, among others. They have similar conditions with common features based on their biopathophysiological knowledge[4,5].

PAS musculoskeletal spectra, for being very frequent, will be deeper discussed. They are classifled into localized and generalized forms.

Localized musculoskeletal PAS are especially recognized by the following syndromic diagnoses: complex regional pain syndrome type 1, which is less common in the elderly; miofascial pain syndrome, more frequent above 60 years of age; and temporomandibular dysfunction syndrome[5]. These forms affect just some body regions, being characterized by hyperalgesia and allodynia, but also by trophic changes in affected tissues. It is less frequent in hands and feet, very often preventing the use of shoes or socks, which ends up limiting daily activities[6].

These localized forms tend to generalization when they are not adequately treated, so accurate diagnoses and approaches are relevant. Miofascial pain syndrome is highly prevalent in the elderly and is associated to excessive muscle use thus being also called muscle stress syndrome. It is characterized by muscle pain, strained muscle bands and trigger-points (TP) located in muscles, skin, tendons, periosteum and ligaments very sensitive to stimulations, generating local and/or referred pain[7]. TP may be evident with biological aging, causing motor incoordination by excitability disorders and motoneurons nervous conduction, preventing the synchronization of nervous contractions of synergist muscles.

Generalized musculoskeletal PAS are characterized by the presence of muscle and joint pain symptoms, the latter less frequent, which are diffuse in different body regions. These symptoms are followed by neurovegetative disorders. Some changes in normally presented characters are typical of generalized PAS and very often external in‡uences may be recognized as causing them[8]. Most people affected report more severe pain during weather changes or when the weather is cold and wet. They feel better in warm and dry weather and physical stress worsens a lot the disorders[8]. Major nosological entity of this group is FM.

Among risk factors for the onset and maintenance of generalized PAS there are age, female gender, family history of chronic pain, obesity and more deflcient mental and/or physical status[9]. Factors negatively in‡uencing generalized form results are: high levels of psychological disorders, somatization, fatigue, poor sleep, higher number of painful areas, pain intensity, mental status and impaired functional capacity, comorbidities and higher number of medical visits to primary care institutions[9]. Mild alcohol consumption and individualized social support seem to have protective effects[9].

As to genesis, PAS has been described as multifactorial. It is believed that involved factors are especially genetic, environmental such as traumas, infections, emotional stress, adverse childhood experiences and patterns learned to face pain. It seems clear that this is not a primary psychiatric condition and that there is no need for psychological factors for its genesis, because most patients do not have active psychiatric diseases or even a speciflc type of personality, such as obsessive-compulsive disorders. However, depression is very frequent. It is impossible to determine whether psychological factors are primary, simultaneous or secondary[8].

As to involved pathophysiological mechanisms, there are major associations with somatosensory system dysfunction, with abnormal pain processing by central nervous system, with neuroendocrine system dysfunction evidencing changes in the hypothalamic-pituitary-adrenal axis and with failure of the stress response system, with adaptation deflcit to physical or psychical overload[8].

Experimental studies have shown the presence of high nitric oxide levels in the muscles, in addition to low phosphorylation and muscle oxidative capacity potential, such as decreased muscle phosphocreatine, ATP and increased substance P. Such changes could help pain sensitization and amplifIcation shown by primary afferent nociceptors changes, with increased neuronal and receptive neuronal flelds excitability, that is, there would be an increase in the referred pain area, or afferent hypersensitivity.

There is central sensitization with increased substance P and dynorphin in the CSF, increased temporal summation and somatosensory potential by skin stimulations, decreased nociceptive inhibitory control system activity, with serotoninergic dysfunction evidenced by decreased serotonin and its precursors levels[10]. Among neuroendocrine changes and abnormal responses to stress there are abnormal ACTH and urinary cortisol levels with decreased cortisol response and sympathetic nervous system hyperactivity[11].

In general, PAS diagnosis is based on clinical flndings because laboratory and imaging results are normal. Its identifIcation depends on a good communication between patients and physicians, which will allow the observation of sensory, emotional and cognitive involvement of patients. Sometimes the elderly have communication limitations, such as visual and auditory deflcits[12]. SpecifIcally for elderly people, one should always check chronic pain impact on functional capacity, that is, impact on physical, mental, social and executive-functional dimensions, in addition to QL. PAS represents a major impact on their lives[13]. From the physical and mental point of view, chronic pain often contributes to gait disorders with ambulation impairment, thus leading to loss of fltness and also to falls.

In terms of executive functionality, chronic pain often brings a higher degree of functional dependence for instrumental and basic daily life activities. In the social dimension, there is increased use of medical services and higher family expenses, which frequently helps impairing QL, isolating individuals from important social stimulations and amplifying functional and emotional losses caused by untreated pain. In general, patients experience major physical distress, fatigue, depression and sleep disorders, in addition to other potentially debilitating overlapping conditions[14].

It is important to understand PAS effects on functional independence and QL of the elderly for effective treatment strategies. Moderate chronic pain has negative in‡uences, so health professionals should be always alert and use evaluation methods which may identify the magnitude of the pain, since very often the elderly are unable to adequately express their pains, thus offering all necessary health support[15].

Central desensitization is critical for an adequate therapy. Antidepressants, anticonvulsants, NMDA receptor antagonists, psychotherapy and sleep improvement may be very successful. So, pharmacological and non-pharmacological approaches are always required and currently they may be powerful interventions to manage PAS.

Among PAS in the elderly population, FM deserves attention since there are few scientific studies addressing this subject specifically in Geriatrics. It is believed that FM in the elderly population is often inaccurately diagnosed and as a consequence is inadequately treated and this is why further investigations and disclosures on the subject are justified. A very important fact is that the elderly experience different levels of "fibromyalgia symptoms" as compared to younger people[16].

There are many studies on FM prevalence but most of them address the population where this disease is more frequent – between 30 and 60 years of age[17]. Considering the Brazilian population one more fact should be taken into consideration: those prevalence studies were carried out in countries with different characteristics from our study.

Most frequent FM cases in the population are found in the program The Community Oriented Program for Control of Rheumatic Disease (COPCORD) created by the World Health Organization (WHO) and the International League of Associations of Rheumatology (ILAR). However, the studies involved in this program address major age intervals and several rheumatic diseases, thus impairing FM prevalence results, especially in the elderly. In addition, among them, just one Brazilian study has specifIcally addressed the elderly population. This latter has found FM prevalence of 1.9% in older individuals between 55 and 74 years of age[18].

An American study with more specifIcity for FM has found prevalence of 5.4% for people above 60 years of age[19]. A French study has found prevalence of 2.8% and 4.1% for ages between 65 and 74 years and 75 to 84 years, respectively[20].

Little has been discussed in published studies about FM characteristics in the elderly, so it is unknown whether ethnic, cultural and / or environmental variables would differ in addressed elderly populations. In general, there is always predominance of the female gender, which in turn would consider gender as pain predisposing factor, based on biological, hormonal and social factors.

There are currently two diagnostic criteria for FM. According to the American College of Rheumatology (ACR), whose criteria are internationally recognized, it has to be diffuse pain for three months or more and have 11 out of 18 tender points (anatomical areas with excessive pain sensitivity at palpation, being typically areas of muscles and tendons insertion)[21]. More recently, Wolfe et al criteria[22] require the presence of 4 or 5 tender points and several overlapping symptoms such as cog-

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nitive changes, fatigue, sleep disorders and depression. What has encouraged discussions about these recently developed criteria was the determination of the tender points, which are very subjective and vary according to the examiner and the occasion.

Some patients may identify factors triggering or worsening their pain, among them virus infection, physical and psychical traumas, weather changes, inactivity and anxiety. In general, in addition to persistent pain, most have fatigue[14] in addition to other complaints, among them: sleep disorders, tension headache or migraine, irritable colon, Raynaud phenomenon, subjective edema of soft tissues, concentration difflculty, dry mouth and eyes, palpitation, paresthesia in upper and / or lower limbs, sensitivity to some foods and medications, depression and / or history of depression[23]. Some diseases are very similar to FM.

A study comparing 31 individuals with FM onset after 60 years of age and other 63 individuals where its onset was before 60 years of age, has found that in 40% of them rheumatoid arthritis or polymyalgia rheumatica had been incorrectly diagnosed[17]. These individuals were submitted to oral steroids, which is a problem especially for the elderly population. An important observation in this same study was the recognition that FM was present in just 17% of the elderly with that condition.

With aging, FM symptoms become unique. Younger people refer pain as the worst symptom while the elderly refer more fatigue, swelling and depression[16], being less frequent headaches, self-report of anxiety and depression, symptoms worsening by weather conditions, mental effort or sleep disorders[16]. The elderly may even be less symptomatic than middle-age adults, as shown by a recent study[24], however the importance of their clinical status is still noted.

Peripheral nociceptive reductions are still very useful to treat FM in the elderly, particularly for muscles, improvements or preventions of central sensitization and the management of associated negative effects, especially depression. In studies involving pharmacological therapy efflcacy in the elderly, in addition to efflcacy, tolerability and comorbidities were also very important. Treatments for elderly individuals should be adapted to meet their unique needs, taking into account their individual health.

The pharmacological treatment includes some classes of drugs. Non-steroid anti-in‡ammatory drugs (NSAIDs) seem to have a synergic effect when combined to drugs acting on the central nervous system, however one has to be more cautious with the elderly.

Antidepressants, among them tricyclic[25], amitriptyline and nortipritlyne, are the drugs of choice and may improve, pain, sleep, depression, stress and anxiety. However they should also be carefully used by the elderly due to their adverse effects. Double-action inhibitors are more on focus, with evidences for duloxetine. In a multicenter study also involving the elderly with FM, but with mean age of 49 years, duloxetine during 12 weeks has considerably improved females' pain intensity, stiffness and QL[26].

Antiepileptic drugs, such as gabapentin[27], pregabalin[28], topiramate, carbamazepine and lamogrigine may also be used. A recent study using duloxetine and pregabalin for 12 months, also involving the elderly but with mean age of 50 years, has shown different dose patterns for each drug[29]. In this study, mean daily duloxetine dose was relatively more stable along time, while there has been signiflcant pregabalin dose increase during the period, with mean daily dose of 55.6 mg/person for duloxetine and 195.7 mg/person for pregabalin, thus implying higher costs for pregabalin.

Neuromuscular blockers, such as cyclobenzaprine[30], carisoprodol and tizanidine are also part of the therapeutic armamentarium, as well as dopaminergic agonists.

As to non-pharmacological therapy, of major importance, the key-aspect would be patients' education by explaining the disease. Exercises, in their different modalities, are also mandatory. Strength training, especially for elderly patients, is becoming an area of major interest due to several functional health benefits[31]. Physical exercises should be carefully oriented otherwise the may pose risks to the elderly because factors such as age, fltness level, exercise intensity and overlapping conditions determine favorable or unfavorable results[12]. Cognitive-behavioral therapy, yoga and all types of massages may bring symptoms relief[32]. Acupuncture has obtained results for FM, however for a short period. In summary, to date, FM treatment is symptomatic and should be multidisciplinary with the association of pharmacological and non-pharmacological therapies, highlighting multimodal therapies.

Polymyalgia rheumatica in the elderly may really have several differentials (Table 1)[33], so one should be cautious because a wrong treatment with steroids, which are the drugs of choice for polymyalgia rheumatica, may bring severe problems, especially for the elderly. Mild HSV increases are common in the geriatric population and very often have no clinical signiflcance. Currently, shoulders ultrasound is being useful to help differential

polymyalgia rheumatica diagnosis and usually shows bilateral subacromial/subdeltoid bursitis[34,35]. This latter has high sensitivity and specifIcity for polymyalgia rheumatica and has been suggested as a new diagnostic criterion since it is altered both in cases of high or normal HSV[35].

After a correct diagnosis and guided and carefully followed clinical treatment, there has been signifIcant PAS improvement.

Supported by literature review, multimodal pain therapy is very effective and is based on the premise that, whenever possible, drugs and techniques with synergic pharmacokinetic and / or pharmacodynamic effects should be associated to relieve pain. This would allow a more rational use with lower drug doses and less side effects. The pain self-management program[36] adopted in this clinical case was very important for the analgesic treatment and aimed at decreasing pain, improving mood and psychosocial functioning of the patient. There has been also contribution of the pharmacological therapy with prescription of opioid analgesics such as tramadol, of non-opioid analgesics such as lysine clonixinate, this latter with proved analgesic effIcacy and tolerability for the elderly[37], and prescription of duloxetine, a pain-modulating drug.

PAS management in the elderly is still a major challenge. In our case, patient was submitted to a long treatment with steroids, which represented at least a major problem for her with signifIcant increase of the risk of fractures.

It is very important to identify PAS in the elderly knowing that in younger people pain is the worst symptom while in the elderly most common symptoms are fatigue, swelling and depression[11]. They have also less complaints of chronic headache, self-report of anxiety and stress, symptoms worsening by weather factors, mental effort or sleep disorders. Due to the major distress and functional impairment that PAS may bring, health professionals should pay attention to the list of possible diagnoses for the elderly with diffuse pain. Currently, even other aspects have been studied with regard to diffuse pain, such as the speed of psychomotor processing which is very important during aging. A study has found association between generalized chronic pain and slower cognitive processing speed in community elderly people[38].

So, PAS should not be overlooked in the elderly. All attention should be driven to diagnosis and treatment, looking for releasing symptoms which may impair a successful aging. There are major probabilities of symp-

Table 1 – Differential fIbromyalgia diagnoses

Diagnoses	When to consider	Suggestions
Hypothyroidism	Consider almost always, but seldom its treatment improves FM symptoms	TSH, free T4
Hyperparathiroidism	Bone and kidney manifestations	Serum calcium, PTH
Polymyalgia rheumatica	Pain in scapular and pelvic girdle, morning stiffness and arthritis.	HSV, PCR, and shoulders US or MRI, also as an option
Polymyositis	Muscle weakness	CPK, aldolase
Multiple myeloma	Diffuse bone pain, emaciation, renal failure, anemia, serum calcium increase	Protein electrophoresis, Bence Jones U.
Osteomalácia	Bone loss, bone pain, Anserine gait, pseudofractures	Vitamin D, calcium, phosphorus, alkaline phosphatase
Sjögren S.	Sicca symptoms, fatigue, arthritis	Anti-Ro, anti-La
Drug myopathy	Statines, fIbrates, H2 blockers, steroids, cocaine, canabis	Withdraw the drug
Early Parkinson's disease	Bradykinesia, shivering, stiffness, fatigue	Parkinson's disease management

US = ultrasound; MRI = magnetic resonance imaging; FM = fIbromyalgia.

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tomatic, functional and QL improvement of the elderly with PAS if we pay attention to their differential diagnoses and introduce adequate therapies.

CONCLUSION

PAS in the elderly is still poorly diagnosed in spite of the major clinical importance of its repercussion, especially in the case of FM spectrum, which has unique features in patients. Signiflcant clinical improvement of our clinical case implied considering several differential diagnoses and guidance for multimodal therapy.

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