

Crystal-Induced Arthropathy in Elderly Patients Hospitalized for Acute Conditions

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ABSTRACT: **Background:** Arthritis and arthralgia are painful symptoms experienced by many elderly patients during hospitalization. Crystal-induced arthritis (CIA) is one of the most common causes of arthritis worldwide and represents the most common cause of acute arthritis in the elderly.

Objective: To determine the incidence of both acute new onset or acute exacerbation of CIA among elderly patients hospitalized due to an acute medical illness.

Method: This study comprised 85 patients. Patients aged 70 years and older who complained of any articular pain were included. Exclusion criteria were signs of septic arthritis, chronic use of steroids or non-steroidal anti-inflammatory drugs, or admission to the hospital due to an acute attack of CIA.

Results: Synovial aspiration was performed in 76 patients (89%). Joint aspiration yielded a diagnosis in 67 of them (79%). The predominant type of crystal was calcium pyrophosphate dehydrate (68%) followed by monosodium urate (20%). The main causes of hospitalization were acute infectious disease (57%) followed by neurologic and cardiac diseases, 14% and 9% respectively, and orthopedic problems (6%). Among patients with acute infectious disease, the main causes were pulmonary (57%) and gastrointestinal (22%) infections. In 9 patients (12%) who underwent synovial aspiration, visible crystals were identified without a definite diagnosis.

Conclusion: Our study showed that hospitalization could be a risk factor for the development of CIA, and the time to diagnose CIA is during hospitalization for other acute illnesses.

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KEY WORDS: crystal-induced arthritis (CIA), monosodium urate (MSU), calcium pyrophosphate dehydrate (CPPD), gout, pseudogout

mation and joint damage via biomechanical and biochemical pathways. Monosodium urate (MSU) crystal deposition disease (gout) represents the highest known burden of CIA and is likely the most common type of inflammatory arthritis in adults in the United States [1,2]. Calcium pyrophosphate dehydrate (CPPD) arthropathies (pseudogout) are less common [3]. The diagnosis of CIA is based on clinical presentation and laboratory findings. The gold standard is the demonstration of crystals in the joint synovial fluid using polarizing light microscopy [4-7].

The purpose of this study was to determine the incidence of both acute new onset or acute exacerbation of CIA among elderly patients hospitalized in an internal ward due to acute medical illness.

PATIENTS AND METHODS

We performed a retrospective analysis of electronic patient records of all patients ≥ 70 years of age who were hospitalized due to an acute medical problem and who complained of articular pain during hospitalization. The study was conducted in two internal departments of Meir Medical Center, Kfar Saba, Israel from January 2005 to December 2013. The study protocol was approved by the Meir Medical Center Ethics Committee (Declaration of Helsinki). All participants provided informed written consent.

During the study period all patients aged 70 years and older who complained of any articular pain were included. Excluded were patients diagnosed with septic arthritis, chronic use of steroids or non-steroidal anti-inflammatory drugs, or admission due to an acute attack of CIA. The study population comprised 85 patients.

The electronic medical records included medical history (e.g., cardio/cerebrovascular diseases, diabetes mellitus, renal diseases, arthritis), physical examination, and demographic and laboratory data.

RESULTS

The mean age of the 85 patients was 82.2 years (range 70–106) and most were female (67%). A previous history of CIA was found in 21% of the patients. On admission 21% of patients received diuretic treatment.

Crystal-induced arthritis (CIA) represents a heterogeneous group of disorders where minerals are deposited in musculoskeletal tissue resulting in pathological alteration. CIA is among the most common causes of arthritis worldwide and represents the most common cause of acute arthritis in the elderly. Intra-articular crystals may cause acute and chronic inflam-

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Table 1. Characteristics of patients who underwent synovial fluid aspiration

	CPPD (n=52)	MSU (n=15)
Age (yr)	83.5	82.0
Females	39 (75%)	8 (53%)
Previous history of CIA	7 (13%)	6 (40%)*
Current diuretic drug use	6 (12%)	2 (13%)
Cause for hospitalization		
Infectious disease	31 (60%)	7 (47%)
Pulmonary	14 (27%)	6 (40%)
Acute gastroenteritis [‡]	8 (15%)	
UTI [§]	4 (8%)	
Cholecystitis	4 (8%)	
Neurologic disease	9 (17%)	2 (13%)
Cardiologic disease	4 (8%)	3 (13%)
Orthopedic disease [‡]	2 (4%)	6 (40%)

* $P = 0.022$, $^{\ddagger}P < 0.0001$, § Yate's correction 11.238 ($P < 0.0008$)
CIA = crystal-induced arthritis, UTI = urinary tract infection

Table 2. Characteristics of patients hospitalized due to infectious disease

	n=50
Age, mean \pm SD	83.5 \pm 11.7
Females	28 (58%)
Primary infection foci	
Pulmonary	27 (54%)
Acute gastroenteritis	11 (22%)
UTI	4 (8%)
Cholecystitis	4 (8%)
Other	4 (8%)
Previous history of CIA	11 (22%)

CIA = crystal-induced arthritis, UTI = urinary tract infection

Synovial aspiration was performed in 89% of the patients. Joint aspiration yielded a diagnosis in 79%. The predominant crystal type was CPPD (68%) followed by MSU (20%). In 12% of those in whom synovial aspiration was performed, visible crystals were identified without a definite diagnosis [Table 1]. A previous history of CIA was more prevalent in patients with MSU than in those with CPPD (40% vs. 13%, respectively, $P < 0.001$).

The main causes of hospitalization were acute infectious disease (57%), followed by neurologic and cardiac diseases, 14% and 9% respectively, and orthopedic problems (6%). Among patients with acute infectious disease [Table 2], the main causes were pulmonary (57%) and gastrointestinal (22%) infections.

DISCUSSION

Gout and pseudogout are two forms of inflammatory arthritis with periodic attacks caused by deposition of crystals (MSU and CPPD, respectively) [8,9]. In both types of arthritis there

is sterile infiltration of phagocytic cells into the synovial fluid causing damage to the joint.

Intra-articular deposition of CPPD crystals is an age-related phenomenon [10]. Acute pseudogout is an age-related disease and is more common in advanced age [11-13]. In our study, we found a high prevalence of CPPD arthritis (78%) compared to MSU arthritis (22%).

We demonstrated that hospitalization for acute medical problems in elderly patients can be a precipitating factor for exacerbation of previous known CIA, or it may precipitate new-onset disease. Known triggers for exacerbation of CIA include hospitalization [14], trauma, surgery, acute medical illness, stroke, and myocardial infarction [15-17]. Several mechanisms that can precipitate CIA attacks were suggested: fluid shift, local pH reduction due to influx of neutrophils and lactic acid production, changes in renal urate handling, initiation or discontinuation of medication [18-22], increased secretion of endotoxins, and increase of local temperature [23].

In our study the main cause for hospitalization of patients diagnosed with CIA attacks during the hospital stay was an infectious disease (57%). Infectious diseases explained 57% of the admissions of patients who developed CIA in our study. Dubreuil et al. [18] reported that acute infection was the cause of hospitalization in 25% of CIA attacks, but the mean age in their study was lower (54.5 years).

In the study by Fam and co-authors [24] the first attack of pseudogout occurred in 40% of hospitalized patients, and in 25% of them the precipitating factor was infectious disease. In our study we focused on the first attack of CIA. CPPD arthritis was documented in 88% of patients and the first attack of MSU arthritis in 60%.

Concomitant use of diuretics in elderly patients with renal insufficiency is well known and a high prevalence has been noted in elderly populations with CIA [10]. Renal insufficiency, which may cause decreased renal excretion of urate, is a known risk factor for gout. Choi et al. [20] showed that chronic renal failure is strongly associated with the incidence of gout.

Estrogen appears to have a uricosuric effect and older women are therefore prone to experience CIA attacks more often than young women. The preponderance of women in our study may be due to the higher proportion of female patients in the hospitalized population rather than to the high incidence of CIA in females.

In conclusion, the results of our study suggest that hospitalization, especially due to infection, can be a trigger for CIA (mainly CPPD) attacks in elderly patients, including patients without a known history of CIA. Physicians taking care of patients in medical wards should keep in mind that these patients may be at increased risk for CIA attack during hospitalization, especially those hospitalized for infectious problems.

Non-specific clinical signs in patients with CIA are not uncommon. Fever, confusion, disorientation, nuchal rigidity or

leukocytosis may be present [15,16,25]. A delay in the accurate diagnosis of CIA can lead to high morbidity and prolonged pain [15]. Careful examination of the joints followed by a precise diagnosis will help minimize the rate of CIA complications in elderly patients.

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**“I tire so of hearing people say
Let things take their course.
Tomorrow is another day.
I do not need my freedom when I’m dead.
I cannot live on tomorrow’s bread”**

Langston Hughes (1902-1967), American poet, social activist, novelist, playwright, and columnist. Hughes is best known as a leader of the Harlem Renaissance in New York City