ACUTE GOUT ATTACK WITH NORMAL SERUM URIC ACID LEVELS

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ACUTE GOUT ATTACK WITH NORMAL SERUM URIC ACID LEVELS (Abstract): Aim: The paper aims to determine the prevalence of clinical cases with acute gout attacks and normal serum uric acid levels. Material and methods: This retrospective study was conducted between October, 2013 and June, 2014 in 30 patients diagnosed with acute gout attack admitted to the 1st Clinic of Rheumatology of Iaşi. The diagnosis was based on clinical manifestations and positive response to therapeutic test with colchicine. Results: Normal serum uric acid levels were found in 63.3% of the patients with acute gout attack. The inflammatory syndrome was detected in 76.6% of patients with high erythrocyte sedimentation rate (ESR) levels and in 30% of patients who had elevated C-reactive protein levels. The urinary excretion of uric acid was measured in 11 patients and it was found increased in 55% of them. Conclusions: The diagnosis of acute gout attack should not be excluded in the presence of normal serum uric acid levels if the clinical manifestations or the positive response at colchicine are suggestive of gout. The low uric acid level is correlated with increased inflammatory factors and urinary excretion of uric acid.

Keywords: ATTACK, GOUT, URIC ACID, PCR, COLCHICINE

Described since antiquity and named by Hippocrates the "disease of kings and queen of diseases", emphasizing the importance of overeating and heredity in the pathogenesis of this disease, gout is today known as an inflammatory arthritis caused by an abnormality of purine metabolism. The prevalence of this disease is 0.16 to 1.36%, with higher rates among men (male: female ratio = 2-7: 1) and a mean age of onset of 50 years. The natural history of this inflammatory arthritis has four stages: asymptomatic hyperuricemia, acute gouty arthritis, intercritical phase and chronic tophaceous gout. In asymptomatic hyperuricemia high blood uric acid levels are not accompanied by clinical manifestations, which occur during acute attacks of gout. Intercritical phase is by definition asymptomatic with a variable time between gout attacks and chronic tophaceous gout is the advanced stage of this disease characterized by accumulation of urate crystals in tissues and formation of tophi (1, 2, 3).

Clinical expression of gout is the appearance of inflammatory symptoms predominantly in the metatarsophalangeal joint of the big toe, which can then affect other joints such as the ankle, knee, wrist and small joints of the hands. From a biological perspective, hyperuricemia (uric acid > 7 mg /dl) forms a part of diagnostic criteria in gout, although only one fifth of the patients with increased uric acid levels become symptomatic (1,4). The presence of inflammatory syndrome (high ESR, C-reactive...
protein, and fibrinogen) and radiological changes (swelling of soft tissues in the early stages reaching erosions, "blown bone" appearance, tophi in advanced stages) suggest a diagnosis of gout. The laboratory tests for determining the urinary uric acid excretion are also discussed as they establish the type of excretion (hyperexcretion or normal excretion) important to know when choosing the hypouricemiant treatment (5). The correct diagnosis can be made only by demonstration of uric acid crystals in the synovial fluid of the joint. These crystals have an acicular appearance under optical microscope and negatively birefringent on polarizing examination (6, 7).

This study aimed to determine the prevalence of acute gout attack cases with normal serum uric acid levels, considering that data in the literature suggest that at least 10% of patients with acute gouty arthritis are normouricemic.

**MATERIAL AND METHODS**

We present a retrospective study conducted between October 2013 - June 2014 including 30 patients admitted to and diagnosed with acute gout attack in the 1st Rheumatology Clinic of Iasi/Rehabilitation Hospital. The diagnosis was made based on both clinical manifestations and favorable response to colchicine administration (therapeutic trial).

**RESULTS**

Of the 30 patients 25 (83.3%) were males and 5 (16.6%) females (fig. 1); mean age was 64.3 years (range 44-82 years). It is important to note that the age at the onset of gout attacks in men was younger in our study (44 years) than in the cases reported in the literature (50 years). Analyzing the home treatment in our patients, we found that only 4 (13.3%) were on different doses of allopurinol prior to admission.

![Fig. 1. Patient distribution by gender](image)

The serum uric acid levels among the study patients was within normal range in 19 cases (63.3%) and elevated in 11 cases (36.6%) (fig.2). The inflammatory syndrome was present in most cases: elevated ESR and C-reactive protein were found in 76.6% and 30% of the cases, respectively (fig. 3). From this point of view, the limitation was the fact that C-reactive protein was not measured in all cases.

![Fig. 2. Concentration of uric acid](image)

In 11 of the 30 study patients the 24-hour urinary uric acid excretion was determined. It is known that this investigation gives us information on the hyper- or normo secretor status of the patient, which helps in selecting the therapeutic approach. The results showed that 55% of the 11
cases had increased levels of renal uric acid excretion.

**Fig. 3.** Inflammatory syndrome

### DISCUSSION

According to literature data, normal serum uric acid levels can be found in at least 10% of patients with acute gout attack; however, some studies show a proportion close to 50% of patients. A normal amount of uric acid during an acute gout attack can be explained by the increased urinary uric acid excretion resulting from ACTH release followed by adrenal stimulation caused by the stress of the painful process (1, 4, 5). Inflammation plays an important role in acute gout attack as it is believed that increased levels of inflammation markers (ESR, CRP), and IL6 and IL1β are directly correlated with lower serum uric acid levels (5).

An important aspect is the correct diagnosis, especially in elderly patients where symptoms can be intricate with a number of other co morbidities. A differential diagnosis of osteoarticular pains is required, as they can be of many causes, such as arthritis, multiple myeloma, autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus), bursitis, tendonitis and not the least gout. Elderly patients require a more detailed history not to miss a possible equivalence of angina pain (8). Also, the treatment of gout in elderly can be challenging in part because of increased colchicine and nonsteroidal antiinflammatory drug toxicity and low compliance to treatment and diet (9).

### CONCLUSIONS

In our study we highlighted the fact that normal serum uric acid is not a criterion for exclusion of the diagnosis of acute gout attack, especially in the presence of a suggestive clinical picture or therapeutic response to colchicine. Low uric acid levels may be related in direct proportion to the elevated acute phase reactants as well as increased renal uric acid excretion.

### REFERENCES

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ROSAI - DORFMAN DISEASE – A RARE CAUSE OF CERVICAL LYMPHADENOPATHY

Rosai-Dorfman Disease is a rare histiocytic disorder affecting various groups of lymphnodes in the human body. Rosai and Dorfman in 1969 described this disorder under the term Sinus Histiocytosis with Massive Lymphadenopathy. Majority of patients are children or young adults. Males are more commonly affected. Cervical Lymphnodes are commonly affected; however other lymphnodal groups like axillary, inguinal and mediastinal may also be involved. Extra-nodal involvement is seen in 25-40% cases. Various extranodal sites have been reported including the upper respiratory tract, gastrointestinal tract, paranasal sinuses, orbit and even meninges. In most of the cases patients are usually asymptomatic except for cervical lymphadenopathy however they may present with symptoms due to extranodal involvement and infiltration of vital organs. The disease usually has a self limiting, benign course and may not need any treatment. Episodes of remissions and exacerbations are characteristic however few patients may die from their disease. Etiology is not exactly known however like any other histiocytic disorder responds well to systemic steroids. Histologically it is characterised by pericapsular fibrosis with dilated sinuses, heavily infiltrated by large histiocytes, lymphocytes and plasma cells. Emperipolesis is characteristic of lymphnodal involvement. Poor prognosis in the disease is due to wide spread dissemination and involvement of vital organs like kidney and liver or presence of immunological abnormalities. Otherwise the disease has a very stable and benign course. Diagnosis of Rosai-Dorfman disease is based on clinical suspicion and histopathological confirmation. Histologically there is infiltration of the tissue by lymphocytes, histiocytes and plasma cells. Demontration of emperipolesis i.e. engulfment of lymphocytes and erythrocytes by histiocytes, is usually diagnostic of Rosai-Dorfman Disease. Immunohistochemistry is usually necessary for confirmation of diagnosis. Characteristically S100 is always positive. Also some other markers like CD68, CD163, α1 antichymotrypsin and α1 antitrypsin may also be positive (2). Systemic symptoms in this disease may be related to enhanced production of such cytokines (5). In general the disease has a benign course and is self limiting. However massive lymphadenopathy and multisystemic involvement, especially vital organs like CNS, Liver, Kidney and lungs is usually associated with poorer prognosis. The treatment in Rosai-Dorfman Disease is non-specific and depends on the site of involvement. Isolated Lymphadenopathy may not be treated at all except for cosmetic reasons. However if any vital organs are involved or if the lesion is causing some obstructive symptoms or pressure symptoms, aggressive treatment may be indicated. In conclusion, Rosai-Dorfman Disease should be kept as a differential diagnosis in young patients presenting with massive cervical lymphadenopathy. High degree of clinical suspicion with typical histopathological features and immunohistochemistry are diagnostic. These patients respond well to systemic steroids and aggressive surgical treatment is needed only in life threatening complications. However it is necessary that both clinicians and pathologist keep this entity in their list of differential diagnosis for massive lymphadenopathy (Shelkar R., Ekhar VR, Rane S, et al. Rosai - Dorfman Disease – A Rare Cause of Cervical Lymphadenopathy. MedPulse – International Medical Journal, 2014; (2): 50-52).

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