CLINICAL MANIFESTATIONS OF GOUT NEPHROPATHY. PRINCIPLES OF DIAGNOSIS AND TREATMENT.

Rakhmatov A.M., Jabbarov O.O., Kodirova Sh.A., Zaripov S.I.
Tashkent Medical Academy, Tashkent, Uzbekistan
bolavaz@gmail.com +998977096004

Abstract: Gout is a systemic tofus disease that develops due to inflammation in organs and systems at the sites of deposition of sodium monaurate crystals in people with persistent hyperuricemia caused by environmental and/or genetic factors (Nasonova V.A., Barskova V.G., 2004).

Key words: gout, gouty nephropathy, gene, hyperuricemia

Metabolic disorders are associated with a violation of purine metabolism, which is characterized by an increase in uric acid in the blood and deposition of sodium salt of uric acid (urates) in the tissues of the musculoskeletal system and internal organs with the development of recurrent acute arthritis and the formation of gouty nodules (tofuses).

For a long time, gout was considered a disease of wealthy families. It is known from history that such famous people as Alexander the Great, Darwin, Goethe, Kant, Newton and many others were ill with it.

In recent years, the incidence of gout has been increasing in all countries. Epidemiological surveys conducted in the United States revealed that cases of gout increased 7 times from 0.2 to 1.5%. The same level of infection of the population with gout has been established in England and Hungary.

In an epidemiological survey of 5,000 residents of Tashkent, 5.8% were diagnosed with various joint diseases, including gout in 0.04%. Hyperuricemia is detected in 4-18% of the Russian population, 0.1% of the country's residents suffer from gout.

Gout is more common in men (80% according to the American Rheumatology Association). Men over the age of 40 are more likely to get sick compared to women (7:1). In women, the frequency of detection of purine metabolism disorders and gout increases during menopause, which is apparently associated with a decrease in estrogen levels. But, today, most researchers note the occurrence of the disease at a younger age with an increase in the number of gout patient among women.

Observations show that there was a "rejuvenation of gout" because instead of the previous 50 years, the peak incidence of it falls by 30-40 years of age. Whiter, the period of development of gouty nodes in soft tissues or bones has decreased. If earlier they developed during 10-20 years of the disease, now it happens in 5-10 years.

In recent decades, there has been a steady increase in the incidence of gout worldwide, both due to an increase in life expectancy, an increase in the proportion of protein foods in the diet, with a high standard of living, which is associated not only with significant consumption of products rich in purine bases (meat, poultry, meat products, alcoholic beverages), but also with an increasing decrease in physical activity, as a result of which the uric acid reaction decreases.

In the human body, uric acid is the end product of the cleavage of purines. The reserves of uric acid in the body are normally 1000 mg at the rate of their renewal within 650mg / day, i.e. 650mg of uric acid decreases from the reserves every day and is replenished the same amount.The source of uric acid formation in the body are purine compounds that come from food, and are also formed in the body during the exchange of nucleotides.

In the blood plasma, uric acid is in the form of free sodium urate and is 0.3mmol/l for men, 0.24 mmol/l for women. The upper limit for men is 0.42 mmol/l, for women 0.36mmol/l. The uric acid content above these figures is regarded as hyperuricemia with a high risk of developing gout. Previously, the level of uric acid >420 mmol/l was considered hyperuricemia, this is the point of super saturation of serum with urates, at which uric acid crystals begin to form

Today, according to the recommendation of the European Anti-Rheumatic League for the diagnosis of gout, it is proposed to consider the level of uric acid > 360 mmol/l (6 mg/dl) as hyperuricemia. This position is based on the results of a number of studies that have shown a 4-fold increase in the risk of developing gout in men and a 17-fold increase in women if the uric acid level is > 360 mmol/L.

The mandatory and most important risk factor for gout is hyperuricemia. The concentration of uric acid in serum depends on gender and age, and in adults — on height, weight, blood pressure, kidney function and alcohol consumption. In most children, it is 180 – 240 mmol/l (3-4 mg%). The upper limit of the normal concentration of uric acid in serum in women of childbearing age and in adult men is 360 and 416 mmol/l, respectively (6 and 7 mg%). In postmenopause, the concentration of uric acid in the serum of women increases and approaches the concentration characteristic of men. Hyperuricemia may occur due to increased production (10%) and/or decreased renal excretion of MC (90%)

In addition to hyperuricemia, factors and processes leading to the formation and deposition of urate crystals in tissues with the subsequent development of inflammation are important for the development of gout. Such factors include insufficient vascularization of tissues (tendons, cartilage, ligaments), a high concentration of urates, local temperature (hypothermia of peripheral joints promotes the formation of microtofuses), pH (at acidic pH values, urates crystallize, in an alkaline environment, the solubility of MK increases). The development of gout is based on urate dysmetabolism, which leads to an increase in the level of uric acid in the blood serum - hyperuricemia and deposition of salts of MK (urates) in organs and tissues. The main mechanism for the development of gout is prolonged hyperuricemia, in response to which a number of adapted reactions occur in the body aimed at reducing the content of uric acid in the blood, in the form of increased uric acid excretion by the kidneys and the deposition of urates in the tissues.The main role in the pathogenesis of hyperuricemia is played by genetically determined disorders in the enzyme system and, first of all, the insufficiency of the enzyme taking part in the resynthesis of nucleides from purines. The most common cause of secondary hyperuricemia is renal failure. Some blood diseases - essential polycythemia, chronic myeloid leukemia, chronic hemolytic anemia, pernicious anemia, myeloma - may be accompanied by hyperuricemia due to the breakdown of cell nuclei and increased catabolism of cellular nucleotides.Urates (sodium uric acid) it is deposited selectively in the joints, vagina, bursae,

skin, kidneys, due to morphological changes in these tissues. Of particular importance is the deposition of uric acid in the kidneys.

Pathogenesis of an acute attack of gout. An acute attack of gout usually develops after persistent and long-term hyperurekemia. Its occurrence is associated with a number of provoking factors, leading mainly to a significant violation of uric acid excretion by the kidneys.

It has been established that an acute attack of arthritis develops due to the deposition of sodium urate microcrystals into the joint cavity, which causes an inflammatory reaction of the synovial membrane. Needle-like double-stunning crystals of sodium urate, well detected in polarizing light, are constantly present in synovial fluid (freely or in the cytoplasm of leukocytes) in patients during an acute attack of gout.Gouty nephropathy is a collective concept that includes the entire renal pathology observed in gout; tofuses in the kidney parenchyma, urate stones, interstitial nephritis, glomerulonephrosis and arteriosclerosis with the development of nephrosclerosis.

Tubular tofuses are formed in 50%, and urate stones in the pelvis in 10-25% of patients. Both processes create .conditions for urinary tract infection. A distinctive feature of gout is kidney damage - interstitial nephritis (due to the widespread deposition of urates in the interstitial tissues of the kidneys). Kidney damage can occur many years before the joint syndrome! Urate nephrolithiasis: Increased risk of stone formation at acidic urine pHГипеурикозурия

- • Long (years) asymptomatic existence, often preceding gouty arthritis
- • Episodes of renal colic
- • Frequent complication of pyelonephritis
- • Frequent combination with obesity and arterial hypertension
- • Slowly progressive chronic renal failure
- Chronic urate tubulointerstitial nephritis:
- • Decrease in the relative density of urine
- • Nicturia
- • "Trace" proteinuria
- • Microhematuria
- • Arterial hypertension
- • Slowly progressive chronic renal failure (decreased GFR, hypercreatininemia...)

Laboratory tests. The most important for the diagnosis and treatment of gout is the study of uric acid metabolism: the content of uric acid in blood serum, in daily urine and the determination of uric acid clearance.

During the attack, ESR increases in patients with gout (usually 25-40mm / h), moderate leukocytosis, a positive reaction to C-reactive protein and other indicators of the acute phase of inflammation may be observed. In the intercrime period, these indicators are normal, but in the presence of urate arthropathies, they may be weakly positive.

According to experts of the European Anti-Rheumatic League, the "gold standard" for the diagnosis of gout is the detection of sodium monaurate crystals in synovial fluid or in the contents of tofus, which reflects the pathogenetic essence of the disease. On ultrasound of the kidneys, it

is possible to identify stones in the cup-pelvic system, but the deposition of uric acid in the pyramids is characteristic of the gouty kidney, which is manifested by their sclerosis.

In the presence of a classic picture of gout with a typical localization of the process in the I metatarsophalangeal joint, a rapid increase in symptoms of acute arthritis and its complete reverse development in a few days, suspicion of the possibility of developing this disease (especially in men) may arise already in the early period of the disease after 1-2 attacks. The diagnosis is confirmed by the detection of hyperuricemia, rapid relief of the attack with colchicine, especially the detection of sodium urate crystals in the synovial fluid.

In 1963, at the International Symposium on the Diagnosis of RB in Rome, the criteria for the diagnosis of gout were developed:

1. Increased uric acid content in blood serum (more than

0.42 mmol/l for men and 0.36 mmol/l for women),

2.Tofuses,

3.Sodium urate crystals in synovial fluid or in

tissues, detection by microscopic or chemical studies

4. Acute attacks of arthritis occur suddenly, with complete remission within 1-2 weeks.

A. Every patient with gout should be fully informed

about the pathophysiology of the disease, the availability of effective treatment methods, comorbid diseases, the principles of therapy for acute

arthritis attack and elimination of urate crystals by lifelong lowering of the serum uric acid level below the target level

B. Every patient suffering from gout should receive lifestyle recommendations: weight loss if necessary, refusal of the intake of alcohol (especially beer and strong alcoholic beverages) and sweetened beverages, the exclusion of overeating, excessive consumption of meat and seafood. Should be encouraged

consumption of low-fat dairy products. Regular physical exercises should be recommended

. Every patient with gout should be systematically screened for the detection of comorbid diseases and cardiovascular

risk factors, including renal failure, coronary

heart disease, heart failure, stroke, atherosclerosis

of peripheral arteries, obesity, hyperlipidemia, hypertension,

diabetes and smoking, the prevention and therapy of which should be considered as an integral part of the treatment of gout

The treatment has the following objectives:

I) stop the attack with anti-inflammatory drugs,

2} avert relapses of acute attacks (if they are too frequent with daily prophylactic intake of colchicine,

3) to prevent further complication of urate crystals and eliminate already existing topuses) that will give. by reducing the concentration of urates in the body fluids.

It is also necessary to prevent kidney damage and possible disability due to the erosion of bones and joints, cartilage.

Specific therapy is determined by the stage and severity of the disease. In addition, it is necessary to treat hypertension, hyperlipidemia and obesity associated with gout.

Drugs that reduce the level of uric acid in the blood should be prescribed only after the acute inflammation subsides, against the background of daily intake of colchicine. This is due to the fact that hypouricemic agents in the first weeks of their use can lead to acute attacks of gout, these attacks often occur during a decrease in the level of uric acid in the blood. With prolonged use of colchicine, nephropathy or myopathy may develop. Side effects: nausea, persistent diarrhea.

Contraindications: HF, CRF, YABZH, pregnancy.

With hypurekemic therapy, the level of uric acid should be periodically determined, monitoring the effectiveness of treatment. The choice of a specific drug and its dosage should ensure a significant reduction in the concentration of uric acid in the blood. It may take months or years for topuses to dissolve. From uricosuric agents, probenecid is prescribed (table 0.5 g) or sulfinpyrazone (table 100 mg). The optimal dose is selected so as to maintain the concentration of urate in the blood at a normal level. The starting dose of half a tablet 2 times a day is gradually increased to 4 tablets. in the day. Sulfinpyrazone has a stronger uricosuric effect than probenecid, but is more toxic. Salicylates counteract the uricosuric effect of both drugs, so they should be avoided; acetaminophen is used as an analgesic.

Inhibition of uric acid synthesis caused by allopurinol at a dose of 200-600 mg / day (several doses) also provides a decrease in its level in the blood. In addition to blocking the enzyme (xanthine oxidase), responsible for the synthesis of uric acid, allopurinol also suppresses the excessive synthesis of purines. This is of particular importance in urolithiasis (caused by the deposition of urates) and in significant violations of kidney function. With the help of allopurinol, it is possible to achieve the dissolution of already formed uric acid stones. Side effects may be minor disorders of the gastrointestinal tract, skin rash and leukopenia. In cases where this is achieved, extracorporeal ultrasound lithotripsy can be used. It is necessary to adhere to the following basic principles in allopurinol therapy:

1. It is not recommended to start therapy with allopurinol in the presence of an acute articular attack, it is necessary to completely stop the articular syndrome.

2. It should be remembered that during an attack of arthritis, the level of uric acid is usually lower than in the intercrime period, therefore, repeated studies of its level are required after the implementation of arthritis.

3. Start therapy with a small dose (more often 100 mg per day and up to 300 mg).A reflection of the correct selection of the dose of the drug is the rate of decrease in the level of hyperuricemia-no more than 0.6-0.8 mg% or 0.1-0.6 mg \ dl or 10% of the initial figures during 1 month of therapy.

4. It is generally accepted to adapt the dose according to creatinine clearance: at a level below 30 ml / min, it is advisable to reduce the dose of allopurinol to 50-100 mg per day.

5. To prevent an acute attack at the beginning of taking allopurinol, it is possible to use low doses of colchicine or NSAIDs.

6. When canceling allopurinol, the uric acid level increases rapidly (3-4 days

Auxiliary methods of treatment.

Additional fluid intake (3 liters per day) is useful for all patients with gout, especially with a tendency to form uric acid stones in the urinary tract. In these cases, it is also recommended to alkalize urine with sodium bicarbonate or trisodium citrate (5 g x 3 p. per day Hypouricemic agents so effectively reduce the level of uric acid in the blood that strict restriction of purines in the diet is not required. During the intercrime period, obese patients need to take measures to reduce body weight. Large tofuses can be surgically removed, while others (with the exception of those whose shell has undergone significant fibrosis) usually gradually dissolve against the background of adequate preventive therapy.

Idiopathic hyperurcemia.

The question of specific treatment for asymptomatic hyperuricemia, not accompanied by gout, has been little studied. I believe that the daily use of probenecid or sulfinpyrazone is indicated only to persons under 40 years of age who have persistent hyperuricemia (> 9mg%), provided that the daily excretion of urates in urine is normal, if it is elevated, allopurinol should be prescribed.

In recent years, the use of calcium antagonists in the treatment of gout has been described in the literature. Of these, corinthar increases the excretion of uric acid in the urine, and the more the lower the tone of the kidney vessels.

Physiotherapy and spa factors in the treatment of gout.

An integral part of the comprehensive treatment of patients with gout is physical factors.

The purpose of physiotherapy is to help the dissolution of tissue uric acid compounds and their excretion by the kidneys and sweat glands, which leads to improved blood circulation and metabolic processes in the joints and periarticular tissues, the ability to eliminate pain, as well as an increase in the volume of movements in the affected joints.

Methods of physiotherapy are diverse:

1. Ultrasound has analgesic, desensitizing and anti-inflammatory effects.

2. Induction therapy, ultrasound and infrared irradiation, diadynamic (DDT) and sinusoidal modulated currents (SMT), electrophoresis of medicines, the use of ozokerite, paraffin, therapeutic mud also have anti-inflammatory, analgesic effects improve blood circulation, oxidative. regenerative processes, stimulate compensatory, adaptive, protective mechanisms.

Spa treatment is a powerful factor in primary and secondary prevention, treatment and rehabilitation of rheumatological patients, including patients with gout.

In the intercrime period, with intermittent and chronic gout, patients are prescribed sanatorium-resort treatment.

Radon and hydrogen sulfide baths, which have a general effect on the course of the disease and blood circulation, contribute to the improvement of metabolic processes, enhance the excretion of uric acid compounds by the kidneys and skin. Radon baths normalize purine metabolism, which is expressed in a decrease in the absorption and excretory function of liver parenchymal cells, favorably affect lipid metabolism, reducing the content of total lipids and cholesterol in the blood.

Hydrogen sulfide baths enhance microcirculation, as well as trophic processes in joint tissues, increase the secretory function of the synovial membrane, improve cartilage nutrition, have a stimulating effect on enzymatic systems, metabolic and immunological processes.

References:

1. Jabbarov, O. O., Maksudova, M. H., Mirzayeva, G. P., & Rakhmatov, A. M. (2023). The Relationship of Blood Group with Human Diseases. *Web of Semantic: Universal Journal on Innovative Education*, *2*(3), 331-334.
2. Rakhmatov, A. M., & Jabbarov, A. A. KodirovaSh. A., Jumanazarov SB (2022). CLINICAL MANIFESTATIONS OF GOUTHY NEPHROPATHY. THEORETICAL ASPECTS IN THE FORMATION OF PEDAGOGICAL SCIENCES, 1 (6), 140–141.
3. Реймбаева, А. А., Аляви, А. Л., Ходжанова, Ш. И., Жаббаров, А. А., Сайдалиев, Р. С., Кодирова, Ш. А., & Максудова, М. Х. (2023). Особенности Течения Хронической Сердечной Недостаточности, Резистентной К Антиагрегантной Терапии.
4. Умарова, З. Ф., Жаббаров, О. О., Жуманазаров, С. Б., Кенжаев, М. Л., & Ибинхужаев, Э. Т. (2023). Эффективность Антиоксидантной Терапии У Больных С Хронической Болезнью Почек Ii-Iii Стадии Диабетической Этиологии. *Central Asian Journal of Medical and Natural Science*, *4*(2), 68-73.
5. Tursunova, L. D., & Jabbarov, O. O. (2021). APPLICATION OF SAKABUTRIL/VALSARTAN IN PATIENTS WITH CHRONIC KIDNEY DISEASE WITH TYPE 2 DIABETES MELLITUS. *Art of Medicine. International Medical Scientific Journal*, *1*(1).
6. Максудова, М. Х., Кодирова, Ш. А., Мирзаева, Г. Ф., & Рахматов, А. М. (2023). Эффективность Системного Применения Стрептокиназы У Больных ОКС С Подъемом Сегмента ST. *Central Asian Journal of Medical and Natural Science*, *4*(3), 93-98.

7. Жаббаров, О. О., Умарова, З. Ф., Турсунова, Л. Д., Нодирова, Ю. И., Сайдалиев, Р. С., Жуманазаров, С. Б., & Хужаниязова, Н. К. (2023). Ассоциация Полиморфных Маркеров Leu28pro Гена Apoe И Pro12ala Гена Pparg2 При Диабетической Нефропатии У Больных Сд 2 Типа. *Central Asian Journal of Medical and Natural Science*, *4*(1), 146-152.
8. Jumanazarov, S., Jabbarov, O., Maksudova, M., & Mirzayeva, G. (2023). SPECIFICS OF THERAPEUTIC NUTRITION IN GLOMERULONEPHRITIS.
9. Sh, R. A. J. O. K., Mirzaeva, A. T. L. J. S., & Tojiboev, G. B. N. (2022). THE GENETICS OF HYPERURICEMIA AND GOUTY NEPHROPATHY.
10. Jumanazarov, S., Qodirova, S., Tursunova, L., Nadirova, Y., & Raxmatov, A. (2023). TIBBIYOT SOHASIDA IT TEXNOLOGIYASINING TUTGAN O'RNI.
11. Jumanazarov, S., Qodirova, S., Tursunova, L., Nadirova, Y., & Raxmatov, A. (2023). TIBBIYOT SOHASIDA IT TEXNOLOGIYASINING TUTGAN O'RNI.
12. Fayzullaevna, M. G., Otakhanovich, J. O., Tokhirovna, B. N., Mamatovich, R. A., & Bakhadirovich, J. S. (2022). Gout Therapy With Reduced Kidney Function. *Central Asian Journal of Medical and Natural Science*, *3*(6), 198-203.
13. Zaripov, S. I., & Abdurakhmanova, N. M. (2023). Quality of life of End-Stage Renal Disease (ESRD) patients receiving hemodialysis: influencing factors and approaches to correction. *Texas Journal of Multidisciplinary Studies*, *21*, 14-17.
14. Nazarova, N. O. K., Jabbarov, A. A., Madazimova, D. H., Mirzayeva, G. P., & Buvamuhamedova, N. T. (2021). DECREASED GENE TGF-B1 ARE ASSOCIATED WITH RENAL DAMAGE IN FEMALE PATIENTS WITH LYUPUS NEPHRITIS. *Oriental renaissance: Innovative, educational, natural and social sciences*, *1*(11), 1200-1203.
15. Abdurakhmanova, N. M., Zaripov, S. S., & Turaev, I. A. (2023). THE EFFECT OF CLIMATE-GEOGRAPHICAL FACTORS ON RHEUMATOID ARTHRITIS ACTIVITY. *World Bulletin of Public Health*, *18*, 67-69.
16. Istamovich, Z. S., Sadullayevich, A. K., & Mirza-Bakhtiyarkhanovna, A. N. (2023). THE SIGNIFICANCE OF AUTOANTIBODIES IN THE PATHOGENESIS OF SYSTEMIC SCLEROSIS (LITERATURE REVIEW). *JOURNAL OF BIOMEDICINE AND PRACTICE*, *8*(2).
17. Rakhmatov, A. M., Kodirova, S. A., & Xodjanova, S. I. (2023, June). Acute Kidney Injury: Comment on "Trends in the Incidence of Acute Kidney Injury in Patients Hospitalized With Acute Myocardial Infarction. In *International Conference on Multidisciplinary Research* (Vol. 1, No. 2, pp. 52-54).