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Diagnostics of Granulomatosis with Polyangiitis

Belovol A.N.[1], Knyazkova I.I.[1], Kuzminova N.Y.[2], Osovskaya N.Y.[2]
1- Kharkov National Medical University
2- Vinnitsa National Pirogov Memorial Medical University

Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis, granulomatous vasculitis associated with anti-neutrophil cytoplasmic antibody) is a rare disease of unknown aetiology with multisystemic failure characterized by necrotizing granulomatous inflammation and the signs of vasculitis of autoimmune genesis involving predominantly small vessels [8]. In 1954 Goodman and Churg described the triad of pathologic signs of GPA including (1) systemic necrotizing vasculitis, (2) necrotizing granulomatous respiratory tract inflammation and (3) necrotizing glomerulonephritis.

Epidemiology. There are no exact data on the prevalence of the disease. In the USA the prevalence of GPA in population is 25-60 cases per 1 million, and the incidence of the disease is 3-12 cases per 1 million persons [23]. GPA occurs at any age but mostly at 40-65 [18]. The disease is considered to occur with similar frequency in men and women. In Europe GPA occurs more often in men than in women with the ratio 1.5:1 [21].

Aetiology and pathogenesis. An exact aetiology of GPA is unknown. An infectious agents (Staphylococcus aureus, parvovirus B19) or ecologic factors in the persons with genetic predisposition are supposed to be the initiating factor triggering the onset of the disease [14]. Patients- carriers of Staphylococcus aureus in the nose have more severe GPA course and more frequent exacerbations [16]. GPA patients are shown to have more frequent allergic reactions as well [14].

GPA is characterized by vasculitis of small- and medium-size vessels, "geographic" necrosis (see below) and granulomatous inflammation, particularly that of the airways. Cellular immune processes are suggested to form the basis of initial pathologic lesion, the granuloma. Tissue damage is associated with activation of cellular immune reactions and inflammatory processes. Determination

of anti-neutrophil cytoplasmic antibody IgA (ANCA) in most patients with GPA confirms the significance of humoral autoimmune response. GPA is usually associated with detection of diffuse cytoplasmic-staining ANCA (cANCA). One of the antigens is serine proteinase 3 (PR3-cANCA). The pathogenic role of PR3-cANCA in GPA is confirmed by detection of active phase of the disease in 80-90% of patients with GPA [5]. Experiments in vitro showed activation of neutrophils to be one of the effects of PR3-cANCA leading to the formation of active oxygen and elastase and PR3 secretion which in its turn contributes to tissue damage [16]. Research data in vitro confirmed the role of complement in ANCA-associated systemic vasculitis and suggested the involvement of ANCA in neutrophil activation and endothelium damage. On the whole the processes mentioned lead to the development of necrotizing vasculitis [9].

Clinical presentation. The onset of the disease may be either subacute (the development of clinical symptoms lasts for several weeks) or primary-chronic. Upper respiratory tract involvement is found in 90% of patients with GPA. Often it is the first and the only manifestation of the disease for a long time along with general inflammatory symptoms (fever, loss of weight, increased ESR). These patients often present to the otolaryngologist with nose congestion, manifestations of "sinusitis", ear pain and decrease of hearing (Table 1). These symptoms are attributed to the development of granulomatous proliferation and nasopharyngeal ulcerations. Nasal septum, hard palate as well as sinuses are usually involved. If nasal cartilages are damaged the nasal septum is subjected to destruction and saddle nose deformity formation. In prolonged course of the disease (months) erosions of sinus bones characteristic to GPA may develop.

Table 1. Clinical manifestations of GPA.

Process localization	Clinical symptoms
Nose involvement	Persistent rhinorrhea, purulent and bloody discharge from the nose, nose bleedings, difficulty in nose breathing, dry brown crusts in nasal cavity, hyposmia and sometimes anosmia, perforation of nasal septum, formation of "saddle" nose

	deformity
Nose sinuses	Sinusitis with radiographic evidences of bone destruction, maxillary sinus walls in particular
Auditory organ involvement	Hearing impairment caused by granulomatous inflammation of the middle ear, possible destruction of temporal bones, including mastoid process, followed by the development of hearing loss; hearing impairment caused by obliterating and ossifying labyrinthitis
Oral cavity	Hyperplastic gingivitis, ulcers of the tongue and oral cavity, rare involvement of palates
Visual organ	Conjunctivitis, scleritis (often necrotizing), episcleritis, anterior uveitis, nasolacrimal tract obstruction, orbital granulomatosis (pseudotumor) presented as exophthalmus, limited mobility of eye fundus, keratitis, chemosis (edema of eye wall conjunctiva) and optic disk edema resulting in its atrophy and blindness
Pharynx, larynx and trachea involvement	Sore throat, hoarseness, stridor, sublaryngeal stenosis
Lungs	Cough, occasionally exhausting, pain in the chest, dyspnea, hemoptysis. In some patients the changes are seen only on chest radiograms. Secondary diffuse alveolitis with massive pulmonary hemorrhage is possible. Bronchiole involvement leads to impaired bronchial patency and secondary bronchial asthma. Bronchial obstruction of large trunks may cause segmental or lobular atelectasis
Heart	Pericarditis, myocarditis, endocarditis. Rare mitral and tricuspid valves involvement followed by their defect. Painful or silent myocardial infarction develops in coronaritis. Potential formation of granuloma in cardiac conduction system associated with rhythm disturbances (complete atrioventricular block, paroxysmal tachycardia, atrial fibrillation, supraventricular tachyarrhythmia)
Gastro-intestinal tract	Rare vasculitis of mesenteric vessels, spleen infarctions are possible (usually determined in sectional investigation). Formation of granuloma in gastric mucosa may mimic the tumor. Pancreatic involvement is manifested by acute or chronic pancreatitis. Ischemic enteritis with possible development of gastro-intestinal bleeding, intestinal wall perforation.

Kidneys	Glomerulonephritis (vasculitis of renal small size vessels). Renal biopsy occasionally shows vasculitis of renal medium size vessels
Skin involvement	Includes palpable purpura, subcutaneous nodes (Churg-Strauss granulomas),ulcers, papules, vesicles
Joints	Migrating arthralgias or polyarthritis (of large and small joints) with no persistent deformity
Peripheral nervous system	Peripheral mononeuritis (of mixed sensor and motor character)
Central nervous system	Its involvement is not common. Clinical picture of chronic meningitis is observed. Intracerebral and subarachnoid bleeding is possible.

In GPA conductive and sensorineural (perceptive) forms of deafness develop. Conductive and sensorineural hearing loss implies the involvement of the middle ear often followed by severe otitis media. Granulomatous inflammation of the middle ear may also compress the seventh cranial nerve, going along the acoustical nerve (the eighth cranial nerve) which enters the structure of the middle ear causing facial paresis. Sensorineural (cochlear) hearing loss develops as a result of internal ear involvement and may be associated with vestibular dysfunction (manifested by nausea, lightheadedness, ringing in the ears). “Combined” deafness is often observed in GPA resulting from conductive and sensorineural hearing loss.

Visual organ involvement. In GPA various inflammatory lesions of the eyes occur. Orbital granulomatosis (pseudotumor) can lead to exophthalmos and loss of sight because of optic nerve ischemia. In scleritis photophobia, pain and redness of sclera are observed. The disease may progress to necrotizing scleritis, chronic ulcers of sclera and corneal coat resulting in vision loss. Peripheral ulcerative keratitis may lead to “cornea melting”. In GPA episcleritis and conjunctivitis frequently occur, they being not only the symptoms of the disease but also the first manifestations of its recurrence. Anterior uveitis and nasolacrimal tract obstruction may develop as well. Posterior uveitis is not common in GPA.

Oral cavity involvement. Inflammation of the gums and tongue ulcers are the classic signs of GPA. Strawberry-like appearance of inter-dental papilla is a characteristic feature of gum inflammation in this case. These symptoms are characterized by marked tenderness and rapid improvement after the initiation of glucocorticoid therapy.

Pharynx, larynx and trachea involvement. Some patients, basically young women, develop the so-called subglottic laryngitis with granulomatous inflammation in the larynx and trachea. It has a long asymptomatic course and is manifested only by mild impaired phonation with further development of subglottic segment stenosis resulting in acute asphyxia.

Pulmonary involvement. It is an essential sign of GPA. Clinical symptoms of pulmonary involvement include cough, occasionally exhausting, hemoptysis, dyspnea, sometimes pain in the chest. In some patients the disease has asymptomatic course and is detected only by chest roentgenography.

Kidney involvement. It is an essential diagnostic sign of GPA (see below). Kidney damage is observed in about 20% of patients at the time of diagnostics of GPA and considerably increases (up to 80%) together with disease progression.

Arterial hypertension is not characteristic to GPA and it is a rare occurrence.

Abnormalities of other organs and systems. Nonspecific arthralgias and evident arthritis are often observed at early stages of GPA. Migrating arthralgias or polyarthritis of joints - from large joints of lower extremities to small joints of upper extremities - with no persistent deformity occur in GPA. Occasionally there are ischemia and gangrene of fingers resulting from finger artery inflammation.

Skin involvement occurs rather rarely. Skin manifestations of GPA include the signs intrinsic to skin vasculitis: palpable purpura, papules, ulcers, vesicles and bullae. Inspection of skin cover should include thorough examination of nodes. For instance, Churg-Strauss granulomas (cutaneous extravascular necrotizing granulomas) are usually localized on the extensor surfaces of the elbows and other areas. Hemorrhagic rash developing in GPA increases the diagnostic confusion with endocarditis.

Changes of peripheral nervous system in GPA are presented as peripheral neurites resembling those in nodular polyarthritis. But neurites in GPA have milder course than in nodular polyarthritis and are limited by the involvement of one nervous trunk. Involvement of central nervous system is not common. Cerebral thrombosis, intracerebral and subarachnoid bleedings are described in GPA patients.

Diagnostics.

Laboratory diagnostics. Routine laboratory data as well as other specific findings in GPA are presented in Table 2. All these indices are essential at the first stage of diagnostic search in suspected GPA. At the same time exclusion of renal pathology is of great significance not only at the initial investigation but also during the follow-up period in the patients with GPA.

Table 2. Laboratory values in GPA [1]

Test	Typical results
Complete clinical blood count	- anemia normochromal, normocytic; in alveolar bleeding severe acute anemia is possible - leukocytosis from mild to moderate, usually not more than 18×10^9/l - thrombocytosis from moderate to severe (platelet count - 400×10^9/l, occasionally up to 1000×10^9/l)
Electrolytes	Hyperkalemia in case of marked renal dysfunction
Liver function tests	Liver involvement is representative of GPA, but serum aspartate aminotransferase and alanine aminotransferase is increased in liver damage
Complete clinical urinalysis	-hematuria (от from mild to severe) -red blood cell casts - proteinuria
ESR/C-reactive protein	Considerable increase in acute phase; good correlation with disease activity
Antinuclear antibodies	Negative
Rheumatoid factor	Positive in 40-50% of patients
C3, C4	Complement levels from normal to increased in GPA
ANCA	Positive in 60-90% of patients in GPA. Proteinase 3

	antibodies are found in 90% of patients with respiratory tract and kidney involvement and only in 70% of patients with no kidney lesion
Glomerular basal membrane antibodies	Found in a small number of patients with GPA

Erythrocyte sedimentation rate and serum C-reactive protein concentration are useful (though incomplete) biomarkers in long-term observation to evaluate disease activity.

Imaging methods.

It should be noted that asymptomatic pulmonary involvement is detected by **chest roentgenography** in one third of patients with GPA. Granulomatous inflammation of alveolar capillaries and arterioles of the lungs results in severe pulmonary capillaritis. Pulmonary infiltrates develop which can undergo destruction with cavity formation resulting in hemoptysis and pulmonary hemorrhage. Besides, infiltrates which can increase and decrease are often misdiagnosed as pneumonia. Lung dissemination may be observed as well. Unilateral small nodule shadows on X-ray can often be misinterpreted as lung cancer. Usually multiple bilateral nodules, often with the cavity, are seen. Furthermore, venous thrombosis (deep vein thrombosis in particular) and thromboembolism of pulmonary artery are established to be rather common GPA complications.

Magnetic resonance imaging of the chest is referred to the basic methods of investigation in patients with suspected or confirmed GPA. Magnetic resonance imaging detects various abnormalities (with rare exception of root lymph nodes and mediastinum) including pleural effusion and nonspecific infiltrates. In the lungs multiple bilateral nodules and destruction cavities are determined. Pathologic changes are often presented as peripheral wedge- or coin-shaped lesions and are misdiagnosed as thromboembolism of pulmonary artery or malignant tumors.

Biopsy. Because of various masks of GPA and imperfect methods of ANCA detection the biopsy of the organ involved is required to confirm the

diagnosis. Among common organs which most often undergo biopsy in GPA are (in order frequency) the lungs, the kidneys and upper airways (the nose or its sinuses). In GPA the necrotizing zones are so extensive that they are often called "geographic necrosis". But even if all three signs of GPA are present (granulomatous inflammation, vasculitis and necrosis), the diagnosis requires thorough integration with clinical symptoms, laboratory and radiologic data. Acid-resistant agents and pathogenic fungi should be excluded as well.

The biopsy results are not always positive in definite diagnosis of GPA. It depends on the stage of the disease, previous therapy and frequently joined infection. For instance, complete diagnostic triad detected by upper respiratory tract biopsy (nose, accessory sinuses of the nose and infraglottic area) is determined only in 15% of cases. However, upper respiratory tract biopsy is usually more safe than that of the lungs and the kidneys. In typical symptoms of GPA negative histologic findings do not deny the clinical diagnosis. But even some of the triad symptoms detected by biopsy of the nose and sinuses confirm the diagnosis of GPA only if other signs of the disease are present.

It should be noted that pathologic process is presented most completely in the patients with GPA in lung biopsy results because of large samples of tissue. Kidney biopsy findings in GPA are unrepresentative (the results may be similar to the other forms of autoimmune glomerulonephritis) [19].

Serologic methods of ANCA detection

At present fluorescence immunoassay and immune-enzyme analysis are widely used in ANCA detection. Both methods complement each other and are recommended in diagnostics of suspected GPA. Negative tests for ANCA do not exclude the diagnosis of GPA. But it should be considered that about 10% of patients with active untreated generalized GPA may have negative ANCA tests and in 30% of cases ANCA may be undetermined. Low specificity and low positive prognostic value of fluorescence immunoassay is observed in GPA. In patients with vasculitis detection of fluorescent type cANCA (in about 90%) corresponds to the detection (by immune-enzyme assay) of proteinase 3 antibodies (PR3-

cANCA). Detection of both fluorescent type cANCA by fluorescence immunoassay and PR3-cANCA by immune-enzyme assay has high prognostic value in GPA.

Most of serums inducing perinuclear type of immunofluorescence react with myeloperoxidase (MPO) – the principal microbicidal enzyme of azurophilic granules generating oxygenic radicals. As opposed to PR3 antibodies, pANCA/anti-MPO have no high specificity in diagnostics of any particular vasculitis and are detected in all types of ANCA-associated vasculitis and all related diseases. MPO antibodies occur in the majority of patients with idiopathic necrotizing demilune vasculitis, microscopic polyangiitis as well as in GPA without anti-PR3/cANCA antibodies.

The use of cANCA as a screening test permits to increase the GPA detection frequency, especially on its early stage, in the patients with limited and atypical forms of the disease or in those with crossed angiitis syndroms as well as to verify the diagnosis in some of the patients with kidney failure undergoing hemodialysis. In ANCA-vasculitis serial investigation of ANCA is recommended. Persistent remissive cANCA in patients with GPA requires more prolonged use of immunosuppressive preparations (about 5 years).

At the same time, it would be a mistake to equate ANCA positive test and GPA diagnosis before the consequent serologic and histologic investigations are performed [22]. ANCA can be detected not only in vasculitis. They have been found in the serum of patients with ulcerative colitis and Crohn’s disease as well as in healthy relatives of those patients [17], and in the serum of patients with bacterial endocarditis [2], recurrent polychondritis, rheumatic arthritis and systemic lupus erythematosus [6]. Certain drugs as propylthiouracil and hydralazine are considered to be involved in induction of ANCA formation and pathogenesis of vasculites. There are evidences of possible effect of penicillamine, allopurinol and sulfasalazine, antibiotics, anticonvulsants, narcotics and others [11]. Several cases of ANCA detection in cholesterol embolism [4], post-

streptococcal glomerulonephritis and pulmonary thromboembolism [24] are reported.

Three **periods in GPA course** are commonly suggested:

- Onset of disease: local changes in upper respiratory tract, middle ear or eyes;
- generalization period: involvement of inner organs, primarily the lungs and kidneys (rapidly progressive glomerulonephritis);
- terminal period: development of renal and/or pulmonary and heart failure.

In the USA classification criteria of GPA diagnostics suggested by American College of Rheumatology (ACR) are used (Table 3). The diagnosis of GPA is based on the signs of vasculitis in the presence of at least two of four criteria noted below.

Table 3. Criteria of GPA diagnostics by American College of Rheumatology (ACR) [15]

1. Inflammation of nose and oral cavity
Development of painful or painless mouth ulcers, purulent or bloody discharge from the nose.
2. **Pathologic changes on lung roentgenogram**
Small nodules, fixed infiltrates or destruction cavities on roentgenogram
3. Changes in urinary sediment
Microhematuria (>5 erythrocytes per high power field) or erythrocyte casts
4. Granulomatous inflammation in biopsy
Hystologic changes presented as granulomatous inflammation within vascular wall of the artery or in perivascular or extravasal area (of arteries or arteriols).
Number of required criteria: 2
Sensitivity: 88,2%
Specificity: 92%

The **principal diagnostic criteria** of GPA are [7]:

1) ulcerative necrotizing rhinitis, sinusitis (purulent bloody discharge from the nose, dry crusts, nose bleeding);
2) destruction of the cartilage and bone tissue of nasal septum, maxillary sinus cavity, orbit, “saddle” nose deformity;
3) pulmonary infiltrates with destruction (coughing, dyspnea, chest pain hemoptysis, pulmonary hemorrhage);
4) rapidly progressive glomerulonephritis (proteinuria, microhematuria, impaired renal function);
5) serum antineutrophil cytoplasmic antibody, primarily cANCA and PR3/cANCA.

According to the guidelines of The Eropean League Against Rheumatism (EULAR), the investigation of antineutrophil cytoplasmic antibody (both by indirect immunofluorescence reaction and enzyme immunoessay) should be performed depending on the clinical setting (level of evidence – 1A, strength of recommendation - A). Positive biopsy findings are a significant factor in confirmation of vasculitis. In case of suspected vasculitis this investigation should be done for both verification of the diagnosis and further evaluation of patients with this disease (level of evidence – 3, strength of recommendation - C). At every out-patient examination of the patient with vasculitis clinical studies should be performed in a certain order including urinalysis and other basic laboratory tests (level of evidence – 3, strength of recommendation - C). This approach allows not only to monitor the course of the disease but also to correct the treatment modality including early detection of side effects of immunosuppressive therapy.

The prognosis is rather unfavourable in GPA: in case of late diagnostics the patients die during the first year from pulmonary-cardiac and renal failure, development of infection. In generalized form of the disease death results within 5 months [10]. Prognosis of GPA is considered to change greatly after introduction into clinical practice the combination of glucocorticoids and cyclophosphane [20]. Four-year survival rate is 93% in patients treated with cyclophosphane and glucocorticoids [13]. Life span of GPA patients is shown to be

20 and more years [12]. However, current mode of therapy does not lead to full recovery. Complications resulting from prolonged use of cyclophosphane, primarily severe infections, hemorrhagic cystitis and toxic hepatitis are potential causes of death in patients with GPA [11].

Thus, early GPA diagnostics and prompt start of treatment targeted at prevention of irreversible organ changes are of decisive importance. For instance, simultaneous detection of signs of pulmonary and renal pathology in one and the same patient requires exclusion of GPA or microscopic polyangiitis, and the recurrence of sinusitis and middle otitis in adult patients of middle age, especially in those resistant to antibacterial therapy, should arouse a suspicion of GPA. Knowledge of diagnostic search directions is of great importance to all medical professionals as early GPA diagnostics and further proper management of patients with this disease greatly affects the prognosis.

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Belovol A.N.[1], Knyazkova I.I.[1], Kuzminova N.Y.[2], Osovskaya N.Y.[2]

3- Kharkov National Medical University

4- Vinnitsa National Pirogov Memorial Medical University

Department of Clinical pharmacology; e-mail:iknyazkova@ukr.net

A b s t r a c t

Actuality: Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis, granulomatous vasculitis associated with anti-neutrophil cytoplasmic antibody) is a rare disease of unknown aetiology with multisystemic failure characterized by necrotizing granulomatous inflammation and the signs of vasculitis of autoimmune genesis involving predominantly small vessels There are no exact data on the prevalence of the disease. GPA occurs at any age but mostly at 40-65. In Europe GPA occurs more often in men than in women with the ratio 1.5:1.

Objective: the analysis of clinical course of the disease, its diagnostics and prognosis of GPA is presented in this review

Materials and methods we present the major clinical features of its course, approaches to diagnostics, and prognosis of GPA based on the review of literature data.

Results and discussion. The onset of the disease may be either subacute (the development of clinical symptoms lasts for several weeks) or primary-chronic. Upper respiratory tract involvement is found in 90% of patients with GPA. Often it is the first and the only manifestation of the disease for a long time along with general inflammatory symptoms (fever, loss of weight, increased ESR). These patients often present to the otolaryngologist with nose congestion, manifestations of "sinusitis", ear pain and decrease of hearing. The diversity of GPA clinical variants are presented in the article. Stages of diagnostic search in suspected GPA including laboratory tests, visualization methods, biopsy and serologic methods of anti-neutrophil cytoplasmic antibody detection are presented. The article emphasizes important diagnostic criteria of GPA and discusses possible prognoses of the disease.

Conclusions: Knowledge of diagnostic search directions is of great significance for doctors of various specialities as early GPA diagnostics and proper management of patients with this disease influences greatly its prognosis.

Key words: Granulomatosis with polyangiitis, Wegener's granulomatosis, clinical manifestations, diagnostics, diagnostic criteria, anti-neutrophil cytoplasmic antibody, prognosis.

Діагностика гранулематозу з поліангіїтом

Біловол О.М. [1], Князькова І.І. [1], Кузьмінова Н.В. [2], Осовська Н.Ю. [2]

1- Харківський національний медичний університет

2 - Вінницький національний медичний університет ім. М.І. Пирогова

Кафедра клінічної фармакології; e-mail:iknyazkova@ukr.net

Реферат

Актуальність: Гранулематоз з поліангіїтом (ГПА) (гранулематоз Вегенера, гранулематозний васкуліт, що асоціюється з антинейтрофільними цитоплазматичними антитілами) - рідкісне захворювання невстановленої етіології з поліорганними ураженнями, яке характеризується розвитком некротизуючого гранулематозного запалення і ознаками васкуліту аутоіммунного генезу, що вражає переважно судини малого калібру. Точних даних про поширеність захворювання немає. ГПА зустрічається у будь-якому віці, але частіше в 40-65 років. В європейській популяції ГПА дещо частіше виявляється у чоловіків в співвідношенні чоловіки-жінки 1,5:1

Мета дослідження: У представленому огляді розглянуті особливості клінічного перебігу та діагностики та прогноз хворих з ГПА

Матеріали та методи На підставі аналізу даних літератури представлені основні особливості клінічного перебігу, підходи до діагностики та прогноз пацієнтів з ГПА.

Результати досліджень та їх обговорення: початок хвороби може бути підгострим (з розвитком клінічної симптоматики впродовж декількох тижнів) або первинно-хронічним. Ураження верхніх дихальних шляхів виявляється у 90% хворих з ГПА і часто є першим і впродовж тривалого часу єдиним проявом захворювання, разом із загальнозапальними симптомами (лихоманка, схуднення, прискорена ШОЕ). Ці хворі частіше звертаються до отоларинголога із скаргами на відчуття закладеності носа, прояву "синуситу" та погіршення слуху. Розглянуто різноманіття клінічних варіантів захворювання, кроки діагностичного пошуку при підозрі на ГПА, зокрема, результати лабораторних тестів, значення методів візуалізації, біопсії і серологічних методик виявлення антинейтрофільних цитоплазматичних антитіл. Виділені важливі діагностичні критерії ГПА, розглянуті питання прогнозу.

Висновки: Знання напрямів діагностичного пошуку украй важливі для лікарів різного профілю, оскільки рання діагностика ГПА і подальше правильне ведення пацієнтів з цим захворюванням істотно впливають на прогноз.

Ключові слова: гранулематоз з поліангіїтом, гранулематоз Вегенера, клінічні прояви, діагностика, критерії діагностики, антинейтрофільні цитоплазматичні антитіла, прогноз

Диагностика гранулематоза с полиангиитом

Беловол А.Н. [1], Князькова И.И. [1], Кузьминова Н.В. [2], Оссовская Н.Ю. [2]

1- Харьковский национальный медицинский университет

2 - Винницкий национальный медицинский университет им. Н.И.Пирогова

Кафедра клинической фармакологии; e-mail:iknyazkova@ukr.net

Реферат

Актуальность. Гранулематоз с полиангиитом (ГПА) (гранулематоз Вегенера, гранулематозный васкулит, ассоциированный с антинейтрофильными цитоплазматическими антителами) – редкое заболевание неустановленной этиологии с полиорганными поражениями, характеризующееся развитием некротизирующего гранулематозного воспаления и признаками васкулита аутоиммунного генеза, поражающего преимущественно сосуды малого калибра. Точных данных о распространенности заболевания нет. ГПА встречается в любом возрасте, но чаще в 40-65 лет. В европейской популяции ГПА несколько чаще выявляется у мужчин в соотношении мужчины-женщины 1,5:1

Цель исследования. В представленном обзоре рассмотрены особенности клиники и диагностик и ГПА.

Материалы и методы. На основе анализа данных литературы представлены основные особенности клинического течения, подходы к диагностике и прогноз пациентов с ГПА.

Результаты и обсуждение. Начало болезни может быть подострым (с развитием клинической симптоматики в течение нескольких недель) или первично-хроническим. Поражение верхних дыхательных путей выявляется у 90% больных ГПА и часто является первым и в течение длительного времени единственным проявлением заболевания, наряду с общевоспалительными симптомами (лихорадка, похудание, ускоренное СОЭ). Эти больные чаще обращаются к отоларингологу с жалобами на ощущение заложенности носа, проявления «синусита», боли в ухе и ухудшение слуха. Рассмотрено многообразие клинических вариантов заболевания, шаги диагностического поиска при подозрении на ГПА, в частности, результаты лабораторных тестов, значение методов визуализации, биопсии и серологических методик выявления антинейтрофильных цитоплазматических антител. Выделены важные диагностические критерии ГПА, рассмотрены вопросы прогноза.

Выводы. Знание направлений диагностического поиска крайне важны для врачей различного профиля, поскольку ранняя диагностика ГПА и дальнейшее правильное ведение пациентов с этим заболеванием оказывают существенное влияние на прогноз.

Ключевые слова: гранулематоз с полиангиитом, гранулематоз Вегенера, клинические проявления, диагностика, критерии диагностики, антинейтрофильные цитоплазматические антитела, прогноз