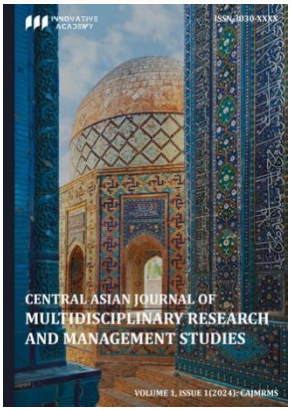


# A MODERN VIEW ON THE PROBLEM OF DIAGNOSTICS OF PATIENTS WITH ANGIOFIBROMA OF THE NASOPHARYNX BY IDENTIFYING POLYMORPHISM OF THE GSTM 1 GENE

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**ABSTRACT**

*Nasopharyngeal angiofibroma is a rare but potentially dangerous disease that requires accurate diagnosis and effective treatment methods. Current approaches to diagnosis are based primarily on visual and morphological methods, but the use of molecular markers, such as GSTM1 gene polymorphism, opens up new perspectives in this area. Genes involved in xenobiotic metabolism and antioxidant defense influence the development of tumor diseases, including angiofibroma. GSTM1 gene polymorphism, in particular its deletion, may be associated with an increased risk of tumor development, which emphasizes its importance as a diagnostic marker. The article provides an overview of existing diagnostic methods for nasopharyngeal angiofibroma and discusses the possibilities of using GSTM1 polymorphism to improve prognosis, individualize treatment, and increase the effectiveness of therapy. It is recommended to further study the role of this genetic marker in the pathogenesis of the disease and introduce it into clinical practice for more accurate diagnostics and development of personalized approaches to treatment.*

Angiofibroma of the nasopharynx is a rare benign tumor that occurs predominantly in adolescent males. Despite its morphological nature, this neoplasm is characterized by

aggressive local growth, which determines its significant clinical significance. The main difficulties in diagnosing angiofibroma of the nasopharynx are associated with its location and tendency to extensive vascular spread, which often leads to late detection and difficulties in treatment. Existing diagnostic approaches, including visualization methods and histological examination, provide high accuracy in tumor identification, but do not always allow predicting the characteristics of the disease and possible relapses [1,2]. The relevance of the study of diagnostic methods taking into account genetic markers is due to the need to improve prognostic tools and individualize approaches to therapy. Polymorphism of the GSTM1 gene, associated with metabolic and antioxidant defense features, has attracted attention as a potential predictor for assessing the predisposition and course of nasopharyngeal tumors. Thus, studying the role of GSTM1 polymorphism in the context of diagnosing nasopharyngeal angiofibroma is an important step in improving the diagnosis and treatment of patients with this disease [3,4].

Despite the progress achieved in medical imaging and pathomorphological studies, modern methods for diagnosing nasopharyngeal angiofibroma are still associated with a number of limitations. Traditional methods, including computed tomography (CT) and magnetic resonance imaging (MRI), provide a detailed image and allow one to assess the extent of tumor spread. However, these approaches are not always able to differentiate angiofibroma from other tumor and inflammatory processes with high accuracy [5,6]. Histological examination remains the gold standard for final diagnosis, but its invasiveness and dependence on the quality of biopsy material introduce additional risks and may limit timely diagnosis. The problems are exacerbated by the lack of methods capable of predicting individual growth characteristics and recurrence of angiofibroma. This is especially important due to the high vascularization of the tumor, which increases the likelihood of significant surgical blood loss and complicates biopsy [7].

In this context, there is a need for additional molecular genetic methods that can improve diagnostic accuracy and provide data for predicting the course of the disease. GSTM1 gene polymorphism is considered as a promising marker that can bring a new level of detail to the diagnosis and assessment of individual risks of development and recurrence of angiofibroma.

Objective. The aim of this article is to conduct a comprehensive review and analysis of the role of GSTM1 gene polymorphism in the diagnosis of nasopharyngeal angiofibroma.

Juvenile nasopharyngeal angiofibroma is a rare benign tumor that predominantly occurs in adolescent males, usually between the ages of 10 and 19 years. This disease is characterized by a high level of vascularization and a tendency to aggressive local spread, which makes it clinically significant and potentially dangerous [3,8]. Morphologically, angiofibroma consists of fibrous stroma permeated with multiple blood vessels of varying diameters, which provides its pronounced vascularity and explains its tendency to bleed. The clinical picture of the disease includes recurrent nosebleeds, nasal congestion, progressive airway obstruction, hearing loss, and, in more severe cases, facial deformity or exophthalmos. Symptoms depend on the degree of tumor invasion into adjacent anatomical structures, such as the paranasal sinuses, orbits, and even intracranial areas [7,9,10].

Diagnosis of angiofibroma usually involves imaging methods, among which CT and MRI play a key role, allowing to identify the extent of the tumor and its vascular structure. However, despite the fact that modern imaging methods and histological examination provide high diagnostic accuracy, timely detection and assessment of potential recurrences remain complex tasks [11].

Nasopharyngeal angiofibroma is a relatively rare disease, which accounts for about 0.05% of all head and neck tumors. This neoplasm has pronounced demographic features. It is almost exclusively found in adolescent males, which is due to hormonal and genetic factors affecting tumor growth and development. The average age of patients at the time of diagnosis is 15 years, with most cases recorded between the ages of 10 and 19 [12,13].

***Basic diagnostic methods and their limitations***

Diagnosis of nasopharyngeal angiofibroma involves a comprehensive approach that combines clinical, imaging, and histological methods. Visualization methods play a key role in the diagnostic process, among which computed tomography (CT) and magnetic resonance imaging (MRI) are of primary importance.

CT provides high accuracy in detecting bone destruction and allows determining the degree of tumor invasion into surrounding tissues, including the base of the skull. However, CT has limited capabilities in assessing soft tissue structures, which requires the additional use of other diagnostic methods [1,4].

Magnetic resonance imaging is considered more informative in assessing the soft tissue components of angiofibroma and the vascular characteristics of the tumor. MRI allows not only to clarify the boundaries of the neoplasm, but also to identify its connection with blood vessels, which is especially important when planning surgical intervention. The limitations of MRI are the high cost of the study and possible contraindications for patients with metal implants [8]. Angiography is used to assess the degree of tumor vascularization and to determine the sources of blood supply. This method is often used before surgery to perform embolization, which reduces the risk of intraoperative bleeding. However, the invasiveness of the procedure and the risks associated with vascular catheterization limit its use [12,14].

***Biological function of the GSTM1 gene and its significance***

The GSTM1 gene (Glutathione S-transferase mu 1) encodes an enzyme belonging to the glutathione S-transferase family. These enzymes play a key role in cell detoxification by catalyzing the bonding of glutathione with various electrophilic substrates. As a result of this reaction, potentially toxic compounds, including oxidative stress products and carcinogens, are neutralized, which helps protect cells from damage. The main biological function of the GSTM1 gene is associated with maintaining antioxidant protection and participating in the metabolism of various xenobiotics. Polymorphism of the GSTM1 gene, namely its deletion (the so-called "null" genotype), leads to the absence of production of this enzyme, which disrupts antioxidant processes in cells. People with the "null" genotype have an increased risk of accumulating oxidative damage, which can contribute to the development of various diseases, including tumor processes [16]. The importance of the GSTM1 gene is particularly relevant in the context of nasopharyngeal angiofibroma, since changes in antioxidant defense may affect the aggressiveness of tumor growth and its response to therapy. Studies show that GSTM1 gene polymorphism may be associated with a predisposition to tumors characterized by a high level of vascularization and active metabolism. This makes the analysis of this genetic marker a promising direction for studying the pathogenesis of angiofibroma and developing new diagnostic and prognostic approaches [19]. The GSTM1 gene plays a central role in the body's detoxification system, participating in the metabolism of xenobiotics - external chemical compounds that can have a toxic effect on the body. The expression product of this gene, the enzyme glutathione S-transferase class μ (GSTμ), catalyzes the conjugation of glutathione with electrophilic molecules, which makes them water-soluble and facilitates their elimination from the body. This process significantly reduces the levels of potentially harmful compounds and protects cells from oxidative damage [11,20].

The association of GSTM1 polymorphism with gastric cancer has also been the subject of a number of studies. For example, studies have shown that GSTM1 deficiency was associated with an increased risk of developing gastritis and, subsequently, gastric cancer. Such patients have a disruption in the metabolism of carcinogens, which can cause inflammation of the gastric mucosa and contribute to the development of tumors [17].

Specificity of the effect of polymorphism on nasopharyngeal tissues

Nasopharyngeal tissues are a special area of the body exposed to various factors, such as infections, chronic inflammation, as well as carcinogenic agents, including tobacco smoke and polluted environment. Polymorphism of the GSTM1 gene, especially its deletion, can have a

specific effect on nasopharyngeal tissues, predisposing them to the development of tumor diseases, such as nasopharyngeal angiofibroma, as well as other tumors of the head and neck. The tissues of the nasopharynx, due to their anatomical location, are regularly in contact with the external environment and are exposed to various toxins and carcinogens, such as combustion products, viruses and bacterial agents. The GSTM1 gene encodes an enzyme that is involved in the neutralization of these toxic substances by binding them to glutathione. In the presence of GSTM1 polymorphism, especially when it is deleted, the ability of nasopharyngeal cells to cope with these toxins is weakened, which increases the risk of their accumulation and tissue damage [5,16,19]. The absence of a functional GSTM1 enzyme contributes to an increase in the level of oxidative molecules in cells, which causes oxidative stress. Nasopharyngeal tissues, especially the mucous membrane, are subject to chronic inflammation and inflammatory processes, which can be aggravated by insufficient antioxidant protection. The accumulation of free radicals can disrupt cell membranes, DNA and RNA, which contributes to mutations and carcinogenesis. These changes can lead to the development of tumors such as nasopharyngeal angiofibroma, which is characterized by rapid growth, increased vascularity, and a tendency to metastasize.

***Methods for studying GSTM1 polymorphism***

To study the polymorphism of the GSTM1 gene, especially its deletion, several methods of molecular genetic analysis are used, the most common of which are polymerase chain reaction (PCR) and DNA sequencing. Both methods allow for accurate and reliable determination of the presence or absence of certain genetic variants, including the deletion of the GSTM1 gene. PCR is a method of amplifying specific regions of DNA, which allows for obtaining a large number of copies of the target fragment, even if the DNA is initially present in very small quantities. PCR is the gold standard for detecting polymorphisms, including the deletion of the GSTM1 gene. To detect the polymorphism of GSTM1, specific primers are used that amplify the DNA fragment containing this gene. In the presence of the GSTM1 gene, PCR amplifies the corresponding fragment, while in the case of a deletion of this gene, amplification does not occur or the fragment is smaller. This allows for precise determination of the gene status: homozygous normal (two copies of the gene), heterozygous (one copy of the gene and a deletion of one of the alleles), or homozygous with a deletion (absence of both copies of the gene) [14]. Sequencing is a method for determining the exact sequence of nucleotides in a DNA fragment. Sequencing can be used to analyze the GSTM1 gene to accurately determine the presence or absence of deletions, as well as other possible variations in its structure. During DNA sequencing, the amplified fragment of the GSTM1 gene is analyzed at the nucleotide sequence level. Sequencing allows detection of not only the deletion, but also other mutations that may be important for the functional activity of the gene. Capillary electrophoresis sequencing or the latest next-generation sequencing (NGS) technologies, which allow multiple samples to be analyzed simultaneously with high accuracy, are often used to analyze GSTM1 polymorphisms.

**Conclusions.** The use of genetic markers, in particular GSTM1 polymorphism, is crucial for the diagnosis and treatment of nasopharyngeal angiofibroma. Genetic testing can improve diagnostic accuracy, develop an individual treatment plan, and predict the outcome of the disease based on individual genetic characteristics.

GSTM1 polymorphism can identify a predisposition to angiofibroma, which enables early detection and appropriate medical tactics. This information can also be used to adapt therapeutic methods, increase treatment effectiveness, and reduce side effects. In addition, genetic markers play an important role in predicting the risk of recurrence and tumor aggressiveness, helping in the choice of treatment and patient monitoring. It is recommended to continue research on the association of GSTM1 gene polymorphism with various clinical characteristics and its interaction with other genetic markers to identify complex genetic predisposition.

Implementation into clinical practice requires the development of standards and recommendations for genetic testing, as well as educational programs for doctors. It is also recommended to conduct interdisciplinary studies to better understand the pathogenesis of angiofibroma and develop new treatment strategies.

In conclusion, it should be noted that genetic markers, in particular GSTM1 polymorphism, have the potential to improve the diagnosis, prognosis and individualization of treatment of nasopharyngeal angiofibroma.

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