GEORGIAN MEDICAL NEWS

ISSN 1512-0112

N0 9 (330) Сентябрь 2022

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

GEORGIAN MEDICAL NEWS
No 9 (330) 2022

HETEROGENEITY OF CLINICAL MANIFESTATIONS OF HYPERPROLACTINEMIA (REVIEW AND OWN OBSERVATIONS)

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Abstract.

Objective The article is devoted to the features of the clinical picture of hyperprolactinemia, which can be partially determined by both gender and age of patients. Along with the well-known "classic" manifestations of hyperprolactinemic syndrome, such as clinical signs of hypogonadism and mechanical pressure of the pituitary tumor on adjacent anatomical structures, there are others that are poorly known to a wide range of practicing physicians. Less frequent manifestations of hyperprolactinemia include the development of hypopituitarism, osteoporosis or osteopenia, alopecia. The analysis of literature data is illustrated with clinical examples from our own practice. It is noted that the pronounced heterogeneity of the clinical manifestations of hyperprolactinemia determines the need to develop continuity and consistency between doctors of different specialties for timely diagnosis and adequate treatment of this pathology.

Key words. Hyperprolactinemia, clinical manifestations, hypogonadism, alopecia, galactorrhea, prolactinoma.

Introduction.

Hyperprolactinaemia, defined as an increase in serum prolactin (PRL) above the upper limit of the reference values, on the one hand, is characterized by heterogeneity and diversity of clinical manifestations, on the other hand is considered the most common cause of hypogonadotropic hypogonadism with the appearance of hormonal and metabolic disorders [1,2].

Increased PRL levels decrease gonadotropin pulsatile secretion through inhibition of hypothalamic gonadotropin releasing hormone production. In addition, there may be direct effects of hyperprolactinemia on testes and ovaries.

Typical clinical signs of hyperprolactinemia in women include different types of menstrual disorders (more often amenorrhea or oligomenorrhea), infertility, galactorrhea. Decreased libido and dyspareunia may also be present. Long term estrogen deficiency may lead to osteoporosis or osteopenia [3]. In young women presenting with infertility PRL concentration should be determined accurately, whether or not the patient has other symptoms suggestive of excess PRL such as galactorrhea or menstrual cycle disorder [4].

In men, manifestations of hyperprolactinemia can be various sexual disorders in a form of decreased libido independently of testosterone levels, impotence, erectile dysfunction, oligo-azoospermia which lead to infertility, gynecomastia, galactorrhea (rare) and also low bone mass as a result of prolonged hypogonadism [3,5]. At the same time in a large series with 1370 participants presenting with erectile dysfunction, hyperprolactinemia was present only in 1.5% [6].

Hyperprolactinemia is more common in women. The prevalence of hyperprolactinemia ranges from 0.4% in an unselected normal adult population to as high as 9 to 17% in women with reproductive disorders. Its prevalence was found to be as high as 17% among women with polycystic ovary syndrome [7]. In each case, the clinical manifestations due to hyperprolactinemia differ in a certain variety, and in some patients the clinical signs of this hormonal disorder are generally nonspecific. The latter point may be the cause of untimely establishment of a correct diagnosis, as well as diagnostic errors. Thus, it is relevant to analyze the variants of clinical manifestations of hyperprolactinemia, taking into account literature data and our own experience.

Clinical manifestations of hyperprolactinemia and their analysis.

Galactorrhea and breast diseases in hyperprolactinemia

One of the most characteristic manifestations of hyperprolactinemia in women is galactorrhea, because the breast is a target organ for PRL. Galactorrhea is milk production from the breast unrelated to pregnancy or lactation. Milk production one year after cessation of breastfeeding is non-lactational and is considered as galactorrhea. According to various authors, galactorrhea is diagnosed in 20-80% of cases of hyperprolactinemia [8]. The absence of this symptom in some patients is due to the fact that a necessary condition for the development of galactorrhea is an elevated level of PRL on the background of sufficient levels of estrogen in the blood. It is important to note that the degree of galactorrhea does not always correlate with the level of PRL and the duration of the disease [9]. In 50% of women with secretions of milk-like fluid from the nipples PRL may be normal and, conversely, in 60% of cases of hyperprolactinemia galactorrhea may be absent [10]. The galactorrhea is usually bilateral and can be white or rarely green. It must be remembered that bloody discharge from the nipples can be a sign of breast tumors. So, it needs further workup in oncological direction. A Sudan IV stain for fat droplets can confirm whether the discharge is milk or not [11,12].

Some women can have non-puerperal galactorrhea along with regular menstrual cycles and normal PRL levels. This so-called “idiopathic galactorrhea” is estimated to be present in up to 40-50% of all women with non-puerperal galactorrhea [3]. In contrast, the finding of galactorrhea in men is highly suggestive of a prolactinoma and is reported in ~10% of cases in such patients [2,13].

Hyperprolactinemia can be detected in 30% of women with galactorrhea or infertility, in 10–25% of women with secondary amenorrhea or oligomenorrhea and in 75% of those with both amenorrhea and galactorrhea [14]. This should be taken into account by gynecologists when working with patients with menstrual disorders.

Hyperprolactinemia also plays a leading role in the pathogenesis of disharmonic breast diseases. An increased level of PRL leads to hypergastrinemia, enlarges the number of estradiol receptors in the breast tissue, enhances sensitivity to the action of estradiol, accelerates the growth of epithelial cells in the mammary gland, having a direct stimulating effect on the development of proliferative processes in them. This forces patients to come to an appointment with a mammologist, the examination plan of whom should include a mandatory study of the level of PRL. It has also been proven that hyperprolactinemia can have a carcinogenic effect on breast tissue [15].

Prolactinoma as a cause of hyperprolactinemia.

Among the causes of hyperprolactinemia, a special place is occupied by the presence of hormonally active pituitary tumor, which produces PRL. This tumor is the most common of all possible variants of pituitary adenoma and accounts for about 40% of cases [16]. Approximately 90% of pituitary tumors are microadenomas (less than 10 mm in diameter) [17]. Prolactinoma is less common in men than in women, typically presenting as an incidental finding on a brain computed tomography scan or magnetic resonance imaging (MRI), or with symptoms of tumor mass effect. This is most evident as a complaint of headache, visual field defects, external ophthalmoplegia [18]. In premenopausal women, signs and symptoms of hyperprolactinemia predominate, whereas in men, tumoral effects are more important [5]. By the time of diagnosis in men, approximately 60% have macroprolactinomas.

In patients harboring macroprolactinomas, more rare tumor mass effect symptoms include cerebrospinal fluid rhinorrhea, hydrocephalus, and seizures. Such symptoms force patients to visit doctors of different specialties (otolaryngologist, neurologist, psychiatrist etc.), and only high experience of them helps to make correct diagnosis and prescribe an appropriate treatment.

Hypopituitarism beyond hypogonadism can occur if there is compression of the pituitary stalk or destruction of normal pituitary tissue [1,2,19,20]. Such a variant of the disease manifestation is quite clearly demonstrated by our own clinical observation, which is given below.

Clinical observation demonstrated symptoms of hypogonadism and mass effects of the macroadenoma in man.

Patient P., male, 58 years old. Due to short-term loss of consciousness, hyperprolactinemia was detected on the background of pituitary macroadenoma, after which the patient's hearing deteriorated and a "veil" appeared in front of his left eye. These symptoms were manifestations of the mass effect of a pituitary tumor measuring 18.3 * 12.0 * 15.4 mm. Noteworthy was the level of PRL - 112.17 ng / ml (at a rate of 5-25 ng / ml), which, according to the literature, is not very typical for macroprolactinoma, namely - too low [17,21]. Meanwhile, the question of the relationship between the level of PRL and the size of the prolactinoma remains debatable. In addition to the above symptoms, the patient suffered from erectile dysfunction as a manifestation of hypogonadotropic hyperprolactinemic hypogonadism, which he regarded as "age-related". It should also be noted that in this clinical case, compression of structures adjacent to the tumor also led to the development of secondary adrenal and thyroid insufficiency, which had been confirmed in this case by the results of relevant hormonal studies and required hormonal replacement therapy. Note that for some time the patient was disturbed by some possible manifestations of hyperprolactinemia. However, erectile dysfunction and recurrent headaches were not considered by the patient as a reason to visit a doctor but were perceived as "natural" symptoms of aging. As a result of the prescribed suppressive treatment with cabergoline along with hormonal replacement therapy with levothyroxine and prednisone the patient's state of health improved significantly. Headaches became very rare, there was no visual changes, in 6 months of such treatment positive dynamics of the tumor size was noted. But unfortunately, there was no effect of therapy on erectile dysfunction. It is possible that with timely access to a doctor (for example, an andrologist for erectile dysfunction or a neurologist for headaches), timely diagnosis and adequate treatment would lead to better results.

Thus, prolactinomas in men are usually large and invasive, presenting with signs and symptoms of hypogonadism and mass effects, including visual disturbances. Increased PRL level is associated with low testosterone, sometimes with anemia, metabolic syndrome and if long-standing also osteoporosis.

Prolactinomas in women.

Unlike men, women have hyperprolactinemia diagnosed, usually at the stage of

microadenoma or even without the detection of organic pathology of the pituitary gland according to MRI. This is due to the manifestation of a number of fairly pronounced symptoms, some of which have been listed above.

The relationship of hyperprolactinemia with oligo-amenorrhea and irregular menstrual cycles has been well-known. Eftekhari N. with co-authors found out that among patients with vaginal bleeding of unknown cause, hyperprolactinemia was present in more than 50% of cases and in 46% it was associated with galactorrhea [22].

An illustration of the above from our own clinical practice is the case history of patient D., woman, 23 years old, who consulted a gynecologist about recurrent menorrhagia. MRI of the pituitary gland revealed a microadenoma 5 * 6 mm in size. Evidence that uterine bleeding was associated with an increase in PRL is that it stopped after normalization of hormone levels on the background of suppressive therapy with dopamine agonists.

Hair loss in patients with hyperprolactinemia.

One of the symptoms that occur in patients with hyperprolactinemia is hair loss, the appearance of which forces patients to come to a dermatologist or trichologist. This symptom is more common in women, possibly due to the fact that women pay attention to it more often than men.

Recently, many studies concentrated on exploring new functions of PRL, and now PRL is recognized as playing a role in the hair growth [23]. The effect of PRL on hair growth has been extensively studied in mammals [24]. In human scalp skin, PRL and PRL receptors were identified for the first time in 2006 by Foitzik et al. The protein luteotropin was found in a thin layer of keratinocytes, while PRL receptors were found in the outer root sheath and in the proximal part of the inner root sheath, as

well as in the matrix keratinocytes.

The mechanism by which PRL directly regulates hair growth is due to its inhibitory effect on hair shaft elongation and premature induction of the catagen phase. In addition, luteotropin also plays a significant role in the proliferation and apoptosis of keratinocytes in hair follicles by decreasing the number of Ki-67-positive cells and increasing the quantity of TUNEL + cells [23].The luteotropic hormone seems to increase the level of free testosterone and dehydroepiandrosterone sulfate, decreasing at the same time the level of serum testosterone-estradiol-binding globulin [25].

Speaking of hair loss, it should be borne in mind that this symptom is quite characteristic of uncompensated hypothyroidism and often allows this diagnosis. At the same time, a combination of hypothyroidism and hyperprolactinemia is not uncommon. It is connected with physiological regulation of PRL secretion. It is controlled by hypothalamic PRL inhibitor factor, other factors like vasoactive inhibitory peptide and also thyroid releasing hormone which cause to increase PRL secretion [26]. So, in patients with primary hypothyroidism, increased levels of thyroid releasing hormone according to the negative feedback can lead to rise PRL levels. In this case, there is a clear algorithm for patient management. First, hypothyroidism is compensated, and then the level of PRL is assessed again on the background of normal thyroid stimulating hormone [12]. We will illustrate this scenario with the medical history of patient X, 23 years old, who consulted a trichologist with complaints of hair loss. The examination revealed hyperprolactinemia of 35.97 ng / ml, in connection with which the patient was referred to an endocrinologist, who, along with hyperprolactinemia, diagnosed hypothyroidism. After compensation of hypothyroidism with hormone replacement therapy with levothyroxine, the level of PRL also returned to reference values, indicating the secondary nature of hyperprolactinemia. Over time, against the background of adequate treatment of hypothyroidism, hair loss stopped.

Peculiarities of the course of hyperprolactinemia.

The heterogeneity of clinical manifestations of hyperprolactinemia lies not only in the variety of manifestations of the disease, but also in the peculiarities of the course. To illustrate, we present the clinical case of a 42-year-old woman M., who received dopamine agonist therapy for microprolactinoma for 15 years. The course of the disease was aggravated by the development of secondary dopamine resistance, which was manifested by the inability to maintain normal levels of PRL on the background of the maximum tolerated dose of the drug (2 mg of cabergoline per week). Due to the fact that the treatment was not effective because of the development of secondary resistance to the dopamine agonists and the patient felt better when she was not receiving dopamine agonists which can be explained by side effects of the drugs, patient refused any therapy on her own. Along with changes in different receptors in tissues, described in the literary sources [12], we consider prolonged inadequate therapy with dopamine agonists as one of the possible mechanisms of resistance to dopamine agonists in our patient. In control measurements, the level of PRL ranged from 75.6 to 51.1 ng / ml. After about 3 years without therapy on the background of hyperprolactinemia, the patient became pregnant and gave birth to a healthy girl in time.

The unusualness of this clinical case is due to the fact that the main features of pregnancy in untreated patients with hyperprolactinemia are the frequent threat of abortion (about 32%), which in more than half of cases ends in involuntary termination. In addition, reproductive losses in pregnant women who did not receive suppressive therapy with dopamine agonists before conception are significantly higher than in those whose pregnancies occurred with appropriate treatment [27]. In addition, it should be noted that pregnancy, which is accompanied by hyperprolactinemia because of pituitary adenoma, can lead to an increase in tumor size. Thus, tumor growth due to pregnancy was identified in 2.5% of 800 macroprolactinomas, 18% of 288 macroprolactinomas without previous surgery or radiotherapy and 4.7% of 148 macroprolactinomas submitted to surgery and/or radiotherapy [28]. It is unclear whether tumor growth is secondary to the high estrogen levels or to dopamine agonists withdrawal due to pregnancy.

Osteopenia in patients with hyperprolactinemia.

Hyperprolactinemic patients have high bone turnover, impairing bone mineral density and leading to skeletal fragility [29]. Along with-it hypogonadotropic hypogonadism associated with persistent high PRL level may be a cause of secondary osteoporosis [30-32]. In some studies subjects with hyperprolactinemia and low bone density do not demonstrate increased fractures [33]. Other authors report a higher prevalence of vertebral fractures in particular in postmenopausal women with untreated prolactinomas, compared to patients treated with dopamine agonists [34]. Simultaneously there is a lack of evidence that normalization of PRL levels improves bone mineral density or reduces the risk of fractures [35]. A retrospective cohort study has shown that the prevalence of bone impairment is significantly higher in men with prolactinomas than in women. Impaired bone mineral density reflects the severity of long-term hyperprolactinemia and associated hypogonadism [30,36]. Treatment of hyperprolactinemic patients with osteopenia and osteoporosis is carried out according to generally accepted standards. However, without treatment of the underlying disease and reduction of PRL levels, the standard accepted method of managing osteoporosis, in our opinion, will be ineffective.

Hyperprolactinemia in children.

In children the clinical manifestations of hyperprolactinemia vary mainly according to gender, age of onset, PRL levels and pituitary tumor size if it is present. According to the literature, headache is the commonest complaint in case of prolactinoma in children [37]. In adolescents it is more common to have menstruation related problems, including primary amenorrhea than galactorrhea [38,39].

Conclusion.

So, doctors of various specialties may suspect hyperprolactinemia. Thus, gynecologists are approached by women with complaints of menstrual irregularities and / or infertility. Patients of andrologists often complain of erectile

dysfunction or decreased libido. Mammologists deal with galactorrhea in women and hyperplastic processes in the breast in patients of both sexes. Dermatologists and trichologists are approached by patients with complaints of hair loss. Patients turn to ophthalmologists not only with complaints of lateral vision impairment, but also with a blurred image in front of the eyes in the form of blurring, "veils". Rheumatologists and orthopedic traumatologists should add PRL to the screening plan for patients with osteoporosis or osteopenia, as hyperprolactinemia is one of the possible factors in reducing bone mineral density. In this regard, it is especially important continuity and consistency between doctors of different specialties, when the correct diagnosis will allow the patient to come to the appointment of a specialist - endocrinologist and conduct adequate therapy.

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Резюме

Статья посвящена особенностям клинической картины гиперпролактинемии, которая частично может определяться как полом, так и возрастом пациентов. Наряду с общеизвестными «классическими» проявлениями синдрома гиперпролактинемии, такими, как клинические признаки гипогонадизма и механического давления опухоли гипофиза на расположенные рядом анатомические структуры, приводятся другие, плохо известные широкому кругу практикующих врачей. К менее распространенным вариантам проявления гиперпролактинемии относят развитие гипопитуитаризма, остеопороза или остеопении, алопеции. Анализ литературных данных иллюстрирован клиническими примерами из собственной практики. Отмечается, что выраженная гетерогенность клинических проявлений гиперпролактинемии, определяет необходимость выработки преемственности и согласованности между врачами разных специальностей для своевременной диагностики и адекватного лечения данной патологии.

Ключевые слова: гиперпролактинемия, клинические проявления, гипогонадизм, алопеция, галакторея, пролактинома.