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PITUITARY ADENOMA APOPLEXY: PATHOPHYSIOLOGICAL MECHANISMS, CLINICAL HETEROGENEITY, DIAGNOSTIC PITFALLS, AND THERAPEUTIC OUTCOMES

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Abstract. Pituitary adenoma apoplexy is an acute neuroendocrine condition caused by hemorrhage or infarction within a pituitary adenoma and is associated with significant morbidity and potential mortality. Despite advances in neuroimaging and endocrine diagnostics, this complication remains underrecognized due to its polymorphic clinical presentation and frequent diagnostic misinterpretation. The present article analyzes the pathophysiological basis of pituitary adenoma apoplexy, emphasizing vascular insufficiency, metabolic imbalance of adenomatous tissue, and precipitating systemic factors such as pregnancy and pharmacological interventions. Clinical variability is illustrated by cases involving both microadenomas and macroadenomas, hormonally active and inactive tumors, with particular attention to prolactinomas. Diagnostic challenges, including frequent confusion with cerebrovascular events and pregnancy-related conditions, are critically discussed. Therapeutic strategies ranging from conservative management to dopamine agonist therapy and surgical decompression are evaluated in the context of neurological and endocrine outcomes. The analysis demonstrates that, in selected cases, pituitary apoplexy may result in spontaneous tumor regression and partial or complete endocrine remission. Early recognition and interdisciplinary management are essential for optimizing prognosis and preventing long-term complications.

Key words: pituitary adenoma apoplexy; prolactinoma; pituitary hemorrhage; hyperprolactinemia; pregnancy; magnetic resonance imaging; dopamine agonists; endocrine outcomes.

АПОПЛЕКСИЯ АДЕНОМЫ ГИПОФИЗА: ПАТОФИЗИОЛОГИЧЕСКИЕ МЕХАНИЗМЫ, КЛИНИЧЕСКАЯ ГЕТЕРОГЕННОСТЬ, ДИАГНОСТИЧЕСКИЕ ОШИБКИ И ТЕРАПЕВТИЧЕСКИЕ ИСХОДЫ

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Аннотация. Апоплексия аденомы гипофиза представляет собой острое нейроэндокринное состояние, обусловленное кровоизлиянием или ишемическим инфарктом опухолевой ткани гипофиза и сопровождающееся высоким риском тяжелых осложнений. Несмотря на развитие нейровизуализационных и гормональных методов диагностики, данное осложнение нередко остается нераспознанным вследствие клинического полиморфизма и диагностических ошибок. В статье рассматриваются патофизиологические механизмы апоплексии аденомы гипофиза, включая сосудистую недостаточность, несоответствие между метаболическими потребностями опухоли и кровоснабжением, а также роль провоцирующих факторов, таких как беременность и медикаментозная терапия.

Проанализированы клинические особенности апоплексии при микро- и макроаденомах, гормонально-активных и гормонально-неактивных опухолях, с акцентом на пролактиномы. Обсуждаются диагностические трудности и современные подходы к лечению, включая консервативную тактику, применение агонистов дофамина и нейрохирургическое вмешательство. Показано, что в ряде случаев апоплексия может приводить к регрессии опухоли и восстановлению эндокринной функции.

Ключевые слова: апоплексия аденомы гипофиза; пролактинома; кровоизлияние в гипофиз; гиперпролактинемия; беременность; магнитно-резонансная томография; агонисты дофамина; эндокринные исходы.

GIPOFIZ ADENOMASI APOPLEKSIYASI: PATOFIZIOLOGIK MEXANIZMLAR, KLINIK XILMA-XILLIK, DIAGNOSTIK XATOLAR VA DAVOLASH NATIJALARI

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Annotatsiya. Gipofiz adenomasi apopleksiyasi — bu gipofiz o'smasi ichida qon ketishi yoki ishemik infarkt natijasida yuzaga keladigan o'tkir neyroendokrin holat bo'lib, og'ir asoratlar va o'lim xavfi bilan kechadi. Zamonaviy neyroimaging va gormonal diagnostika usullariga qaramay, ushbu holat klinik belgilarning xilma-xilligi va noto'g'ri talqin qilinishi sababli ko'pincha kech aniqlanadi. Mazkur maqolada gipofiz adenomasi apopleksiyasining patofiziologik mexanizmlari, jumladan o'sma to'qimasining metabolik ehtiyoji bilan qon ta'minoti o'rtasidagi nomutanosiblik, tomir yetishmovchiligi va homiladorlik hamda dori vositalari kabi qo'zg'atuvchi omillar tahlil qilinadi. Mikro- va makroadenomalar, gormon-sekretor va gormon-sekretor bo'lmagan o'smalarda klinik kechish xususiyatlari ko'rib chiqilib, prolaktinomalar alohida e'tiborga olinadi. Diagnostik xatolar va davolashning konservativ, farmakologik hamda jarrohlik usullari baholanadi. Tadqiqot natijalari ayrim holatlarda apopleksiya o'smaning regressiyasi va endokrin funksiyaning tiklanishiga olib kelishi mumkinligini ko'rsatadi.

Kalit so'zlar: gipofiz adenomasi apopleksiyasi; prolaktinoma; gipofizga qon ketishi; giperprolaktinemiya; homiladorlik; magnit-rezonans tomografiya; dofamin agonistlari; endokrin natijalar.

Introduction. Pituitary adenoma apoplexy (PAA) represents a rare but potentially life-threatening neuroendocrine emergency characterized by acute hemorrhage or ischemic infarction within a pituitary adenoma. Despite advances in neuroimaging and endocrine diagnostics, PAA remains underdiagnosed due to its heterogeneous clinical presentation and frequent masquerading as other acute neurological or obstetric conditions. The reported incidence of pituitary apoplexy among patients with pituitary adenomas varies from 2% to 12%, although subclinical or misdiagnosed cases likely render this figure an underestimation [4,7]. Historically, pituitary apoplexy was thought to occur predominantly in large, hormonally inactive macroadenomas. However, with the widespread implementation of high-resolution magnetic resonance imaging (MRI), accumulating evidence indicates that microadenomas, particularly prolactin-secreting tumors, may also undergo apoplectic transformation [5,6]. The pathophysiological substrate of PAA involves a mismatch between the tumor's high metabolic demand and its relatively insufficient vascular supply, compounded by sudden fluctuations in systemic or local hemodynamics [4]. The clinical spectrum of PAA is remarkably broad, ranging from catastrophic presentations with acute visual loss, ophthalmoplegia, and adrenal crisis to mild or self-limiting episodes manifesting only as headache or transient endocrine dysfunction. Diagnostic delays are common, especially in young women, where symptoms may be incorrectly attributed to migraine, pregnancy-related complications, or cerebrovascular events [1,7]. The present article provides an expanded,

analytically reworked synthesis of clinical observations, pathophysiological mechanisms, diagnostic challenges, and therapeutic strategies in pituitary adenoma apoplexy. Special attention is paid to reproductive-age women, pregnancy-associated cases, and the long-term endocrine and radiological outcomes following conservative or medical management, based in part on previously published clinical material .

Materials and Methods. This study represents an integrative narrative and analytical review combined with structured reinterpretation of published clinical observations of pituitary adenoma apoplexy. The primary clinical dataset was derived from documented cases of pituitary adenoma apoplexy in young female patients, including both microadenomas and macroadenomas, with hormonally active and inactive tumor profiles. These cases were previously described in peer-reviewed Russian-language literature and served as the empirical foundation for further synthesis . Clinical data included demographic characteristics, reproductive history, precipitating factors, neurological and endocrine manifestations, laboratory hormone profiles, neuroimaging findings, treatment modalities, and outcomes. Hormonal assays encompassed prolactin, thyroid-stimulating hormone, gonadotropins, adrenocorticotropic hormone, cortisol, and growth hormone levels. MRI studies were evaluated for tumor size, signal heterogeneity, hemorrhagic or cystic components, suprasellar extension, and optic chiasm involvement. To ensure originality and analytical depth, the extracted clinical data were reorganized into comparative tables, pathophysiological models, and outcome matrices. Additional sources from English, Russian, and regional (post-Soviet) literature were incorporated to contextualize findings, explore mechanistic hypotheses, and compare management strategies [1,3,4,8]. Bibliographic references were arranged alphabetically, and in-text citations were numbered accordingly, resulting in non-sequential citation numbers consistent with international academic standards.

Results. Analysis of the reviewed cases revealed pronounced heterogeneity in both clinical presentation and disease trajectory. Acute onset headache was the most consistent symptom, present in all observed patients, although its intensity and associated neurological signs varied substantially. In one case involving a long-standing intrassellar prolactinoma, apoplexy served as the first event leading to definitive diagnosis after more than a decade of untreated hyperprolactinemic hypogonadism. In contrast, macroadenomas associated with pregnancy demonstrated abrupt symptom onset with nausea, visual disturbances, and rapid radiological evolution. Hormonal profiles immediately following apoplexy were notable for extreme prolactin elevations in prolactinomas, occasionally exceeding normal reference ranges by more than 30-fold, followed by precipitous declines during follow-up. This phenomenon likely reflects necrosis of prolactin-secreting lactotrophs with sudden release of stored hormone into systemic circulation. Importantly, other pituitary axes often remained preserved, suggesting selective vulnerability of tumor tissue rather than global hypopituitarism. Radiologically, MRI findings ranged from heterogeneous T1-hyperintense lesions consistent with acute hemorrhage to evolving cystic transformations during follow-up. In several patients, complete or near-complete radiological regression of the adenoma was observed, raising the concept of “auto-adenomectomy” following apoplexy.

Table 1. Comparative clinical characteristics of pituitary adenoma apoplexy

Parameter	Microadenoma-associated PAA	Macroadenoma-associated PAA
Typical tumor size	<10 mm	≥10 mm
Common hormonal profile	Hyperprolactinemia	Variable or non-functioning
Visual impairment	Rare	Frequent
Pregnancy association	Occasional	Common
Likelihood of spontaneous regression	Moderate	High
Need for urgent surgery	Rare	Conditional

Pregnancy emerged as a dominant precipitating factor. Physiological pituitary hyperplasia, estrogen-induced angiogenesis, and increased intrasellar pressure likely synergize to destabilize adenomatous tissue, predisposing it to infarction or hemorrhage. In several cases, symptoms initially misinterpreted as early gestosis resolved spontaneously, only later being recognized as manifestations of pituitary apoplexy.

Discussion. The findings underscore pituitary adenoma apoplexy as a multifactorial event arising from complex interactions between tumor biology, vascular supply, systemic hemodynamics, and endocrine milieu. Prolactinomas appear particularly susceptible, possibly due to their high metabolic activity and intrinsic vascular fragility [6,9]. The paradoxical observation that apoplexy may result in tumor regression and endocrine remission challenges traditional assumptions regarding its uniformly catastrophic nature. Diagnostic errors remain a critical issue. Neurologists, gynecologists, and general practitioners frequently encounter early manifestations of PAA but may lack awareness of its protean presentations. In reproductive-age women, the overlap with migraine, pregnancy-related disorders, or cerebrovascular syndromes contributes to delayed or incorrect diagnosis [1,7]. MRI of the sellar region with dedicated pituitary protocols should be considered mandatory in any patient with acute severe headache and endocrine abnormalities. Therapeutically, management strategies must be individualized. While classic teaching emphasizes urgent transsphenoidal decompression in cases with visual compromise or altered consciousness, accumulating evidence supports conservative or medical management in hemodynamically stable patients without progressive neuro-ophthalmic deficits [3,4]. Dopamine agonists, particularly cabergoline, play a dual role in prolactinomas by suppressing hormone secretion and potentially facilitating tumor involution.

Table 2. Pathophysiological mechanisms of pituitary adenoma apoplexy

Mechanism	Clinical implication
Vascular insufficiency	Ischemic necrosis
Sudden blood pressure changes	Hemorrhagic transformation
Estrogen-mediated hyperplasia	Pregnancy-related risk
Tumor metabolic demand	Selective lactotroph necrosis
Intrasellar pressure rise	Optic chiasm compression

Long-term prognosis is variable but often favorable in patients who survive the acute phase without major complications. Spontaneous tumor regression and normalization of pituitary function, as observed in several cases, suggest that apoplexy may paradoxically confer therapeutic benefit under certain conditions. Nevertheless, lifelong endocrine surveillance remains essential due to the risk of delayed hypopituitarism or tumor recurrence.

Conclusion. Pituitary adenoma apoplexy constitutes a diagnostically challenging and pathophysiologically complex condition at the intersection of neurology, endocrinology, and reproductive medicine. Its clinical manifestations range from subtle endocrine disturbances to fulminant neuro-ophthalmic emergencies. Modern neuroimaging has expanded recognition of apoplexy in both microadenomas and macroadenomas, particularly prolactinomas. Early recognition, interdisciplinary collaboration, and individualized management strategies are critical determinants of outcome. Pregnancy should be regarded as a major risk factor, warranting heightened vigilance among gynecologists and endocrinologists. Although pituitary apoplexy is traditionally viewed as a catastrophic event, emerging evidence indicates that, in selected cases, it may lead to spontaneous tumor regression and endocrine remission. Future prospective studies are required to refine risk stratification, optimize treatment algorithms, and elucidate the long-term natural history of this intriguing condition.

References.

1. Azizyan, V. N., Grigoriev, A. Y., Ivashchenko, O. V., & Molitvoslovova, N. N. (2011). Intraoperative hemorrhage in pituitary adenoma as a cause of acromegaly remission. *Endocrine Surgery*, 1, 39–44.

2. Dedov, I. I. (2010). *Clinical Neuroendocrinology*. Moscow: GEOTAR-Media.
3. Dedov, I. I., Melnichenko, G. A., Romantsova, T. I., Rozhinskaya, L. Y., Dzeranova, L. K., & Ilovayskaya, I. A. (2009). Hyperprolactinemia: modern approaches and old problems. *Bulletin of Reproductive Health*, 2, 2–8.
4. Kim, J. P., Park, B. J., Kim, S. B., & Lim, Y. J. (2008). Pituitary apoplexy due to pituitary adenoma infarction. *Journal of Korean Neurosurgical Society*, 43(5), 246–249.
5. Möller-Goede, D. L., Brändle, M., Landau, K., Bernays, R. L., & Schmid, C. (2011). Pituitary apoplexy: re-evaluation of risk factors and impact on outcome. *European Journal of Endocrinology*, 164(1), 37–43.
6. Oldfield, E. H., & Merrill, M. J. (2015). Apoplexy of pituitary adenomas: the perfect storm. *Journal of Neurosurgery*, 122(6), 1444–1449.
7. Ranabir, S., & Baruah, M. P. (2011). Pituitary apoplexy. *Indian Journal of Endocrinology and Metabolism*, 15(Suppl 3), 188–196.
8. Randall, B. R., & Couldwell, W. T. (2010). Apoplexy in pituitary microadenomas. *Acta Neurochirurgica*, 152(10), 1737–1740.
9. Tereshchenko, I. V. (2017). Pituitary adenoma apoplexy. *Clinical Medicine*, 95(2), 177–180.
10. Watt, A., Pobereskin, L., & Vaidya, B. (2008). Pituitary apoplexy within a macroprolactinoma. *Nature Clinical Practice Endocrinology & Metabolism*, 4, 635–641.