



## Neurocirurgia de Emergência em Gestantes com Tumores Hipofisários.

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### RESUMO

**Introdução:** O tumor hipofisário consiste em um crescimento anormal da glândula pituitária e pode estar associado à hiperprolactinemia e à acromegalia. Este é um evento pouco comum, visto que, em gestantes com tumores hipofisários, o macroadenoma foi encontrado em cerca de 24% dos casos, e em relação à acromegalia, um estudo no Reino Unido revelou apenas 3 gestantes com essa condição, dentre as 71 estudadas com tumor hipofisário. Este estudo tem como objetivo relatar um caso de macroadenoma hipofisário associado à hiperprolactinemia e acromegalia em uma mulher que estava grávida. **Metodologia:** foi realizado um estudo observacional de braço único, no qual foram analisados o histórico da paciente e os resultados de exames complementares (laboratoriais e de imagem). **Relato do caso:** uma gestante de 24 anos com um macroadenoma pituitário concomitante. Ela foi submetida previamente à cirurgia transesfenoidal e tratada com cabergolina e octreotida, porém sem remissão completa dos sintomas. **Resultados e discussão:** a paciente desenvolveu diabetes e hipertensão durante a gestação, além de ruptura prematura de membranas. Sabe-se que a acromegalia pode levar ao desenvolvimento de diabetes e hipertensão gestacional, porém a ruptura prematura de membranas não está documentada como uma complicação direta da acromegalia ou hiperprolactinemia. **Conclusões:** é de extrema importância um diagnóstico precoce para um tratamento e acompanhamento adequados de pacientes com macroadenoma, visando melhorar a qualidade de vida, prevenir complicações e evitar intercorrências durante a gestação.

**Palavras-chave:** Ginecologia, alto risco, Neurologia.

# Emergency neurosurgery in pregnant women with pituitary tumors.

## SUMMARY

**Introduction:** Pituitary tumor consists of an abnormal growth of the pituitary gland and may be associated with hyperprolactinemia and acromegaly. This is an uncommon event, since, in pregnant women with pituitary tumors, macroadenoma was found in around 24% of cases, and in relation to acromegaly, a study in the United Kingdom revealed only 3 pregnant women with this condition, among the 71 studied with pituitary tumor. This study aims to report a case of pituitary macroadenoma associated with hyperprolactinemia and acromegaly in a pregnant woman. **Methodology:** a single-arm observational study was carried out, in which the patient's history and the results of complementary exams (laboratory and imaging) were analyzed. **Case report:** a 24-year-old pregnant woman with a concomitant pituitary macroadenoma. She previously underwent transsphenoidal surgery and was treated with cabergoline and octreotide, but without complete remission of symptoms. **Results and discussion:** the patient developed diabetes and hypertension during pregnancy, in addition to premature rupture of membranes. It is known that acromegaly can lead to the development of diabetes and gestational hypertension, but premature rupture of membranes is not documented as a direct complication of acromegaly or hyperprolactinemia. **Conclusions:** an early diagnosis is extremely important for adequate treatment and monitoring of patients with macroadenoma, aiming to improve quality of life, prevent complications and avoid complications during pregnancy. **Keywords:** Gynecology, high risk, Neurology.

## INTRODUÇÃO

A glândula pituitária se localiza na parte inferior do crânio e é formada por várias células que produzem diversos hormônios. O tumor pituitário ocorre quando há um crescimento anormal na glândula pituitária e os sinais e sintomas variam de acordo com a produção insuficiente ou excessiva de hormônios. Esses tumores podem ser classificados como macro ou microadenomas pituitários.<sup>1</sup> Tumores com diâmetro máximo de 10mm são chamados de microadenomas, enquanto aqueles com diâmetro maior ou igual a 10mm são chamados de macroadenomas (MAC). Macroadenomas gigantes são aqueles com diâmetro maior ou igual a 40 mm.<sup>2</sup>

Os prolactinomas são os tumores hipofisários mais frequentes, representando até 40% dos casos, com incidência de 1 a 6 casos por milhão/ano e prevalência de 500 casos / milhão de habitantes <sup>3,4,5</sup>. Este distúrbio tem uma grande predominância feminina (proporção mulher-homem de 8:1) e uma idade mediana ao diagnóstico de 30 anos<sup>6,7</sup>. Assim, espera-se que um prolactinoma esteja presente em cada 1.200 mulheres e, mais especificamente, em cada 500 mulheres em idade fértil<sup>8</sup>.

A Hiperprolactinemia é uma das disfunções mais comuns que afetam o funcionamento do sistema endócrino hipotalâmico-hipofisário. Sua ocorrência varia de 0,4% em adultos saudáveis não selecionados a até 9-17% em mulheres que apresentam problemas de fertilidade. Pacientes com macroprolactinomas geralmente apresentam níveis sanguíneos de PRL acima de 200ng/mL, enquanto aqueles com microprolactinomas costumam ter valores entre 100 e 200ng/mL, podendo ser inferiores a 100ng/mL em alguns casos.

O adenoma hipofisário é uma causa frequente de infertilidade em mulheres jovens devido à redução do funcionamento dos ovários causada pelo aumento da prolactina. Com o aumento constante dos níveis de prolactina, as pacientes podem apresentar problemas no ciclo menstrual, como períodos curtos, ausência de ovulação, pouca frequência menstrual e falta de menstruação, porque a prolactina inibe a produção de hormônios sexuais pela hipófise, diminui a produção de hormônios pelos ovários e também afeta a liberação do hormônio liberador de gonadotrofina pelo hipotálamo.(GnRH)<sup>11</sup>.

O tratamento clínico com agonista dopaminérgico (DA) é a opção de tratamento de primeira linha, levando a normoprolactinemia, eugonadismo e redução

tumoral em 80 a 90% dos casos<sup>16,17</sup>. Assim, a gravidez tornou-se possível para as mulheres portadoras de prolactinoma.

A gigantismo é uma condição clínica que surge devido à produção em excesso do hormônio do crescimento (GH) e, conseqüentemente, do fator de crescimento semelhante à insulina-1 (IGF-1), que é influenciado pelo GH. Um tumor somatotrófico é a causa mais frequente da gigantismo, abrangendo cerca de um terço de todos os tumores na hipófise que produzem hormônios; sua frequência anual é de seis a oito casos por milhão de indivíduos, com uma idade média de diagnóstico entre 40 e 45 anos.<sup>30</sup>.

Devido à sua progressão lenta dos adenomas, o intervalo médio do início dos sintomas até o diagnóstico é de aproximadamente 12 anos, dessa forma, quando diagnosticados, a maioria tem macroadenomas e alguns dos adenomas se estendem para as regiões paraselar ou supraselar<sup>30</sup>.

Em situações de macroadenomas somatotróficos, devido ao seu tamanho, é possível a ocorrência de uma diminuição na produção de outros hormônios pela glândula hipofisária, sendo os mais frequentes os hormônios gonadotrópicos. Isso pode resultar em amenorreia, oligomenorreia, galactorreia, e algumas mulheres podem experimentar ondas de calor e atrofia vaginal decorrentes da falta de estrogênio. Além disso, a acromegalia não controlada também está relacionada com o aumento da insulina, resistência à insulina e desenvolvimento de diabetes.<sup>30</sup>.

## • METODOLOGIA

Trata-se de estudo observacional descritivo de braço único em que foi analisado o prontuário da paciente e exames complementares laboratoriais e de imagem.

## • RESULTADOS E DISCUSSÃO

A hiperprolactinemia, alteração comum do eixo hipotalâmico-hipofisário, tem prevalência estimada de 0,4%, é comumente associada aos prolactinomas, tumores hipofisários relativamente frequentes que podem estar presentes em mulheres em idade fértil.<sup>3,4,5,8,9</sup>

Nossa descrição aborda o caso de uma paciente com gravidez de 34 semanas e 2 dias que possui um histórico de prolactinoma há 3 anos. Os resultados dos exames laboratoriais anteriores indicaram hiperprolactinemia e secreção de IGF-1, apontando

para a presença de um tumor lactotrófico e somatotrófico, identificado por ressonância magnética da sela túrcica. Durante o exame físico, a paciente apresentava características de acromegalia e relatava sintomas como galactorreia e amenorreia antes de engravidar. A acromegalia é frequentemente associada ao aumento do IGF-1, enquanto a galactorreia e a amenorreia são sintomas clássicos da hiperprolactinemia<sup>23</sup>, o que explica o quadro clínico apresentado por nossa paciente.

Os resultados da neuroimagem e dos exames laboratoriais estavam em concordância com a situação clínica, levando à necessidade de cirurgia para remover o tumor pela via transesfenoidal. Após o procedimento, o paciente ainda apresenta níveis altos de IGF-1 e dores nas articulações, indicando a possível volta do tumor, algo considerado raro para uma condição cuja taxa de recorrência varia entre 2 e 14%. No entanto, é frequente a persistência de hiperprolactinemia em mulheres com macroadenoma após o parto.<sup>24</sup>

É sabido que a gestação é uma condição que pode levar a piora do tumor pituitário devido à hiperplasia das células lactotróficas<sup>26</sup>. O IGF-1, por sua vez, é um hormônio que pode estar com níveis aumentados na gravidez<sup>27</sup>, contudo, essa alteração não é exclusiva da gestação nesse caso.

O aumento excessivo de hormônio de crescimento (GH) e fator de crescimento semelhante à insulina-1 (IGF-1) tem efeitos físicos, como o estímulo ao crescimento de diversos tecidos, incluindo pele, tecido conjuntivo, cartilagem, osso, órgãos e muitos tecidos epiteliais. Pode-se observar ao longo do tempo língua aumentada, voz mais grossa, formigamento nas mãos, espessamento da pele, mandíbula maior, mãos e pés inchados e maiores, resultando no aumento do tamanho dos sapatos, luvas e anéis.

A paciente apresentou um caso significativo de diabetes gestacional e hipertensão, que são complicações conhecidas da acromegalia durante a gravidez. Essas condições podem resultar em complicações tanto para a mãe quanto para o feto, no entanto a acromegalia em si não parece estar associada a resultados negativos. Além disso, há relatos de problemas de visão devido à compressão do quiasma óptico causada pelo tumor, levando a hemianopsia bitemporal (visão em túnel), mas esse não foi um sintoma apresentado por nossa paciente nem observado durante o exame neurológico. Ao investigar a relação do macroadenoma com a gestação, a paciente relatou que em 2016 buscou atendimento médico na Unidade básica de saúde (UBS) de Sobradinho II devido à infertilidade, pois já estava há 11 meses sem uso de

contracepção e não conseguia engravidar. Nessa ocasião foram solicitados exames laboratoriais, ultrassonografia transvaginal e espermograma para o esposo. Porém, houve demora na realização dos exames por problemas pessoais da paciente, e o diagnóstico de Hiperprolactinemia (prolactina [PRL] - fevereiro/2018: 121, 70) foi feito somente em 2018, período que já apresentava queixa de amenorreia e galactorreia, sendo solicitada tomografia computadorizada ( TC) de hipófise e encaminhamento ao serviço de endocrinologia.

Os medicamentos que agem na dopamina, como a cabergolina, são frequentemente prescritos para tratar os distúrbios de excesso de produção de prolactina. A pessoa em questão teve uma ruptura prematura das membranas que envolvem o feto, porém não existem indícios de que o uso da cabergolina durante a gravidez cause complicações durante a gestação ou no momento do parto. Mesmo assim, é recomendado que o uso desse medicamento seja interrompido durante a gravidez.<sup>25</sup>.

A cabergolina (CAB) é o DA de escolha devido à sua alta afinidade com o receptor de dopamina tipo 2, possui uma meia-vida mais longa, sendo sua posologia semanal, e ainda apresenta menor incidência de efeitos colaterais , como náuseas e hipotensão postural <sup>17,18,19</sup>. Na gravidez, a bromocriptina (BRC) tem sido a droga recomendada devido à sua meia-vida mais curta<sup>12</sup>. Ainda existe uma preocupação com a exposição fetal ao DA, pois mesmo que seja suspensa após a confirmação da gravidez, devido a vida mais longa da CAB, o feto ficará exposto a droga por pelo menos 30 dias<sup>15</sup>. Nesse caso, a paciente fez uso da CAB durante 8 semanas de gestação e o recém nascido não apresentou alterações.

Estudos em humanos já comprovaram que a BRC atravessa a barreira placentária, e apesar de não haver comprovação do efeito teratogênico em humanos e animais, a FDA (food and drug administration) recomenda a prescrição de DA com cautela e recomenda a sua suspensão após confirmação da gravidez.<sup>14,20</sup>

A eficácia do BRC na estimulação da gravidez foi examinada em mais de 6.000 situações até agora, sendo o BRC o único medicamento aprovado para esse fim. Apesar disso, as informações divulgadas não revelaram diferenças nos desfechos maternos e fetais (como aborto, parto prematuro e má formação) entre gestações estimuladas por CAB, BRC ou na população em geral dos Estados Unidos. As gestações estimuladas por cabergolina já alcançaram mais de 1.000 casos, no entanto,

mais dados são necessários para confirmar a eficácia do CAB e, principalmente, seu uso para estimular a gravidez, questão ainda em discussão.<sup>15,21</sup>.

Durante a gravidez, é possível que haja um aumento no número de células lactotróficas normais e das células tumorais devido ao alto nível de estrogênio, levando ao crescimento do tumor de forma sintomática em cerca de 3% dos casos com microadenoma e 21% com macroadenoma. Assim, os prolactinomas podem crescer durante a gestação, causando sintomas como dores de cabeça e alterações na visão.<sup>21,14</sup>.

## • CONCLUSÕES

É de extrema importância que a identificação dos sintomas apresentados seja feita rapidamente para um tratamento imediato e para melhorar a qualidade de vida das pacientes. A amamentação em livre demanda deve ser encorajada, pois não piora a situação da galactorreia<sup>8</sup>. Durante a gravidez, essa prática se torna ainda mais crucial devido à forte ligação entre o macroadenoma e a acromegalia, doença que aumenta o risco de diabetes e hipertensão gestacional, fatores presentes no caso descrito e que elevam consideravelmente as chances de complicações durante a gestação.

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