REFACS

Original Article
Rev. Fam., Ciclos Vida Saúde Contexto Soc.
http://seer.uftm.edu.br/revistaeletronica/index.php/refacs/index
ISSN: 2318-8413 DOI*:* 10.18554/refacs.v12i4.7405

Macroprolactinomas in Adolescents and Young Adults

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Macroprolactinomas en Adolescentes y Adultos Jóvenes

Received: 21/02/2024 **Accepted:** 29/08/2024 **Published:** 29/12/2024

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Abstract:
Objective: to evaluate the degree of response to treatment based on reduction in tumor size, normalization of prolactin levels, restoration of pituitary function, and evolution of the neuro-ophthalmological condition. **Methods:** quantitative-retrospective review of medical records of adolescents and young adults treated at the Neuroendocrinology outpatient clinic of a teaching hospital in the state of Minas Gerais, Brazil, from March of 1991 to March of 2023. The diagnosed cases of macroprolactinoma and giant prolactinoma were confirmed by laboratory and imaging tests and analyzed intragroup. **Results:** six medical records were included, and among the cases, three were male and three were female. Amenorrhea and headache were the most common complaints in women, and neuro-ophthalmological in boys. After treatment, there was a reduction in tumor size, a drop in prolactin levels, reestablishment of some hormonal axes in some cases, and partial clinical improvement of neuro-ophthalmological symptoms. **Conclusion:** early diagnosis of prolactinomas in adolescents and young adults is challenging. The approach to macroprolactinomas in this age group represents a crucial piece in the understanding and effective management of this complex endocrine condition. In-depth discussion of these giant prolactinomas is essential to inform more effective clinical practices and direct personalized therapeutic interventions.
Keywords: Prolactinomas; Pituitary gland; Adolescent; Young adult.

Resumo:
Objetivo: avaliar o grau de resposta ao tratamento tendo como base a redução do tamanho tumoral, normalização dos níveis de prolactina, restauração da função hipofisária e evolução do quadro neuroftalmológico. **Método**: revisão quantitativa-retrospectiva de prontuários médicos de adolescentes e adultos jovens atendidos no ambulatório de Neuroendocrinologia de um hospital escola de Minas Gerais, considerando o período de março de 1991 a março de 2023. Os casos diagnosticados de macroprolactinoma e prolactinoma gigante foram confirmados por exames laboratoriais e de imagem e analisados intragrupo. **Resultados**: seis prontuários foram incluídos e, dentre os casos, três são do sexo masculino e três do sexo feminino. Nas mulheres, predominaram as queixas de amenorreia e cefaleia, e queixas neuroftalmológicas nos meninos. Após o tratamento, houve redução do tamanho tumoral, queda dos níveis de prolactina, restabelecimento de alguns eixos hormonais em alguns casos e melhora clínica parcial dos sintomas neuroftalmológicos. **Conclusão**: o diagnóstico precoce de prolactinomas em adolescentes e adultos jovens é um desafio. A abordagem dos macroprolactinomas nesta faixa etária representa uma peça fundamental na compreensão e gestão eficaz dessa condição endócrina complexa. A discussão aprofundada sobre esses prolactinomas gigantes é crucial para informar práticas clínicas mais eficazes e direcionar intervenções terapêuticas personalizadas.
Palavras-chave: Prolactinoma; Hipófise; Adolescente; Adulto jovem.

Resumen:
Objetivo: evaluar el grado de respuesta al tratamiento a partir de la reducción del tamaño tumoral, normalización de los niveles de prolactina, restauración de la función hipofisaria y evolución del cuadro neuroftalmológico. **Método**: Se realizó una revisión cuantitativa retrospectiva de las historias clínicas de adolescentes y adultos jóvenes atendidos en un ambulatorio de Neuroendocrinología de un hospital universitario de Minas Gerais, Brasil, en el período comprendido entre marzo de 1991 y marzo de 2023. Los casos diagnosticados de macroprolactinoma y prolactinoma gigante se confirmaron mediante pruebas de laboratorio e imagen y se analizaron por grupos. **Resultados**: Se incluyeron seis historias clínicas y, de los casos, tres eran hombres y tres mujeres. En las mujeres predominaban las quejas de amenorrea y cefalea, y en los hombres las quejas neuroftalmológicas. Tras el tratamiento, se produjo una reducción del tamaño del tumor, un descenso de los niveles de prolactina, el restablecimiento de algunos ejes hormonales en algunos casos y una mejoría clínica parcial de los síntomas neuroftalmológicos. **Conclusión**: El diagnóstico precoz de los prolactinomas en adolescentes y adultos jóvenes es un reto. El abordaje de los macroprolactinomas en este grupo de edad representa una parte fundamental de la comprensión y el tratamiento eficaz de esta compleja afección endocrina. Es crucial debatir en profundidad estos prolactinomas gigantes para informar sobre prácticas clínicas más eficaces y dirigir intervenciones terapéuticas personalizadas.
Palabras clave: Prolactinoma; Hipófisis; Adolescente; Adulto joven.

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INTRODUCTION

Prolactin-secreting pituitary tumors are the most common functional pituitary neoplasms, accounting for 30% to 60% of pituitary adenomas[1,2]. They are mainly microprolactinomas (<1 cm in diameter) and are more common in women. Macroprolactinomas (≥1 cm in diameter) are more common in men[2,3]. Giant prolactinomas are extremely rare, with a frequency of 2% to 3%, representing 0.5% of pituitary tumors[3-5]. They have a diameter ≥4 cm, extrasellar extension, are more prevalent in men (ratio 9:1), and have a mean age at diagnosis of 41 years[4-6]. In children and adolescents, prolactinomas account for 50% of all pituitary adenomas and 2% of all intracranial tumors. However, most of this population has macroadenomas, leading to neurological complications and pubertal delay. In this age group, familial endocrine neoplasias should be ruled out at diagnosis[1,7].

Prolactinomas arise from the monoclonal expansion of a single cell, which has presumably undergone somatic mutation. The mechanisms involved in this process are not yet well understood, but studies have shown a relationship with certain genes that act through fibroblast growth factors, in addition to the action of estrogens[8]. Most adenomas that secrete prolactin and cause hyperprolactinemia are composed of lactotrophic cells only. However, approximately 10% are composed of lactotrophic and somatotrophic or somatomammotrophic cells and, therefore, secrete growth hormone as well as prolactin. Most lactotrophic adenomas are sporadic, but they can rarely occur as part of multiple endocrine neoplasia syndrome type 1 (MEN1). Almost all lactotrophic tumors are benign; they can rarely be malignant and present metastasis[9].

Patients with prolactinomas may present symptoms resulting from hyperprolactinemia, pituitary hormone deficiency and/or the effect of the tumor mass. Hyperprolactinemia usually manifests with hypogonadism and galactorrhea, observed more frequently in women, associated with amenorrhea. The presence of neurological symptoms will vary depending on the direction of tumor growth; when in suprasellar extension, it can cause compression of the optic chiasm, resulting in decreased visual acuity. Tumor expansion can cause diplopia, due to damage to the oculomotor nerve, to serious conditions such as tumor apoplexy, with intense headache and eyelid ptosis[1].

Macroprolactinomas and giant prolactinomas, rare and more aggressive, present challenging diagnosis and management. Long-term monitoring of giant prolactinomas can contribute to a better understanding of the course of the disease and, thus, improve the management of these patients[3].

This article reports the cases of six adolescent and young adult patients treated at the Hospital de Clínicas of the Universidade Federal do Triângulo Mineiro (UFTM) with a diagnosis of macroprolactinoma and giant prolactinomas. This study aims to evaluate the degree of response to treatment based on reduction in tumor size, normalization of prolactin levels, restoration of pituitary function, and evolution of the neuro-ophthalmological condition.

METHODS

The study was conducted through a retrospective quantitative study with a review of medical records of six adolescent and young adult patients, aged between 16 and 22 years at the time of diagnosis, treated at the Neuroendocrinology outpatient clinic of the Endocrinology and Metabolism Department of the Hospital de Clínicas of the Universidade Federal do Triângulo Mineiro – UFTM, considering the period from March of 1991 to March of 2023. The analysis of medical records and data collection were carried out from January to February of 2024. This is an intragroup comparative analysis with data presented descriptively.

Patients within this age group who presented altered prolactin laboratory levels and evidence of pituitary adenoma larger than 1 cm on nuclear magnetic resonance imaging (NMRI) of the sella turcica, classified as macroprolactinoma or giant prolactinomas, were included in this analysis. Tumor types other than prolactinomas, tumors smaller than 1 cm and tumors diagnosed in patients outside this age range were excluded.

This study was submitted to the UFTM Research Ethics Committee and authorized under number 6,631,099, CAAE 75313523.8.0000.5154.

RESULTS

Six cases of macroprolactinomas were analyzed, four of which were giant, diagnosed between 1991 and 2023, with patient ages ranging from 16 to 22 years at diagnosis. Among these cases, three were female and three were male.

In females, the predominant symptoms were amenorrhea, galactorrhea, and headache, and in 2/3 of the cases, there was visual alteration with complaints of blurred vision in one case and temporal hemianopsia of the right eye in another. In male patients, the prevalent initial symptoms were headache and visual impairment, and there was intracranial hypertension in one case. Visual alteration reached almost total loss, bilaterally in two patients. Regarding pubertal development, it was observed that it was complete in females, but secondary amenorrhea occurred later in all three cases. In males, interruption of pubertal development was observed in all cases, at the specific Tanner stage in which the tumor manifested.

Initial prolactin levels ranged from 613 to 8000 ng/mL. Regarding initial tumor size, four cases exceeded 4 cm in diameter and were considered giant prolactinomas, three of which were male and one female. In addition to hyperprolactinemia, the patients presented panhypopituitarism with central hypothyroidism in cases 2, 5 and 6 and adrenal insufficiency in cases 2, 3, 5 and 6. Puberty was interrupted in case 5 at Tanner 3 and growth deficiency in case 6. Pituitary apoplexy was clinically suspected and radiologically confirmed in case 2. All cases received treatment according to the deficiency of the hormonal axis with levothyroxine, prednisone and testosterone, in the male cases.

Regarding treatment, cabergoline was the initial choice in all cases, with the exception of case 6, which required emergency surgery due to intracranial hypertension, followed by dopaminergic agonist. The outpatient follow-up of the patients ranged from one to 11 years. It was noted that the patients evolved with a satisfactory response, both in terms of decreasing serum prolactin levels and in reducing tumor size. In 2 patients (cases 4 and 5), MRI did not show any lesion in the pituitary region. Case 6 did not achieve normalization of prolactin levels, and a new surgery was proposed, but the patient refused and discontinued treatment at the service. The other cases are being followed up regularly.

Regarding the restoration of pituitary function in women, cases 1 and 4 had normal menstrual cycles spontaneously with treatment and did not present any pituitary deficiency. However, case 3 still has amenorrhea and continues to require glucocorticoid replacement. In men, case 2 recovered the gonadotropic and somatotropic axes, case 6 only the somatotropic axis, and case 5 maintained the panhypopituitarism.

The degree of neuro-ophthalmological impairment was not assessed with serial visual campimetry, but clinical evaluations showed partial improvement in the visual condition presented by cases 1, 2, and 5. However, case 3 is investigating involvement of the optic discs by the tumor, mainly on the right, and case 6 presents advanced papillary pallor.

The clinical, laboratory, and radiological data are represented in Chart 1.

Chart 1. Clinical, laboratory and radiological data of patients with macroprolactinoma and giant prolactinoma treated at the Neuroendocrinology outpatient clinic from March if 1991 to March of 2023. HC/UFTM, Uberaba/MG, Brazil, 2024.

Case	Sex	Age at Diagosis	Initial Symptoms	Initial Prolactin	Initila NMRI	Initial Treatment	Follow-up Time	Recent Prolactine	Recent NMRI
1	F	16 years	Secondary amenorrhea Galactorrhea Weight gain Holocranial headache Visual blurring	832.34 ng/mL	1.7X1.3X1.3 cm	Cabergoline	1 years	0.82 ng/mL	0.9x0.6x 0.3 cm
2	M	20 years	Holocranial headache Pituitary apoplexy Reduced visual acuity and scotomas	755.56 ng/mL	5.0x4.1x3.3 cm	Cabergoline	4 years	8.68 ng/ml	0.5x1.6x 1.9 cm
3	F	22 years	Galactorrhea Decreased libido Headache Progressive visual alteration with visual field with right temporal hemianopsia	8000 ng/mL	6.8x5.3x5.9 cm	Cabergoline	2 years	9.43 ng/mL	4.0x3.0x 1.5 cm
4	F	17 years	Amenorrhea Galactorrhea Headache No change in vision	1485 ng/mL	1.3x1.1x1.1 cm	Cabergoline	8 years	2.74 ng/mL	Absence of local injury
5	M	22 years	Low visual acuity with visual field in the right eye with absolute loss in all quadrants. Total loss of vision on left eye. Headache	3392 ng/mL	5.3x3.6x3 cm	Cabergoline	10 years	1.16 ng/mL	Absence of local injury
6	M	18 years	Intracranial hypertension Severe headache Sharp reduction in visual acuity	613.6 ng/mL	4.3x3.8 cm	Surgery	20 years	200 ng/mL	*CCT-1.4x1.6 cm

***CCT** - Cranial Computed Tomography Scan. **NMRI**- Nuclear Magnetic Resonance Imaging

DISCUSSÃO

Macroprolactinomas and giant prolactinomas are more common in the population between 20 and 50 years of age, and are rare in children and adolescents. This study describes six cases diagnosed between 16 and 22 years of age, four of which had giant prolactinomas. Regarding gender, all men presented tumors larger than 4 cm, while in women, one case was a giant prolactinoma and two cases were macroprolactinomas. Some authors argue that prolactinomas tend to be more aggressive in males, corroborating a higher prevalence of giant tumors in this gender[2-3].

Prolactinomas are common, but the cause is not yet well defined. These tumors can be sporadic or familial, and in these, a MEN1 mutation has been described, which, through its product menin, generates a negative effect on cell growth by inducing cell cycle inhibitor genes such as p27 and p18[8].

Prolactinomas in multiple endocrine neoplasia syndrome are more aggressive than sporadic ones due to loss of heterozygosity at the 11q13 locus and mutations in the menin gene.

Other mutations have been reported in the aryl hydrocarbon receptor-interacting protein (AIP) that are associated with familial pituitary adenomas. Mutations in the PRKAR1A (Carney complex-associated) and CDKN1B (MEN 4) genes have also been described in familial cases[8].

In sporadic cases, there are reports in the literature of genes that act through fibroblast growth factors (FGF-2 and FGF-4), such as the PTTG (pituitary tumor transforming gene) and HST (heparin-binding secretory transforming gene) genes. The PTTG gene is more associated with tumors that invade adjacent structures, since its expression is increased in tumors that invade the sphenoid bone. In other literature reviews, there is a description of genome-wide GWAS leading to aberrant splicing of several mRNAs including the estrogen-associated receptor γ gene (ERRγ) (ESRRG) and the splicing factor 3B1 gene (SF3B1), and these mutations can increase transcription of the prolactin gene[8,10,11].

The clinical manifestation in adolescents and young adults exhibits significant variability, depending on sex, age at diagnosis, tumor size, and prolactin levels. Signs and symptoms in girls, such as amenorrhea and galactorrhea, contrast with manifestations in boys, including delayed puberty and gynecomastia. Giant prolactinomas present with neuro-ophthalmological symptoms due to compression of surrounding structures with visual field alterations, diplopia, and headache. This complaint is more frequent in male patients[3,7].

Neuro-ophthalmological complaints were described in the four cases of giant prolactinomas, and in the three male cases, they were of marked reduction of vision and even total loss, and in one case, intracranial hypertension requiring urgent surgical intervention. In the female case of giant prolactinomas, there was also visual complaint in the right eye, in addition to headache, galactorrhea and secondary amenorrhea. Of the cases of giant prolactinomas, initial prolactin was elevated in two cases and in the other two cases prolactin was not elevated as expected in the literature in cases of giant prolactinomas, because in one case there was pituitary apoplexy and in the other the surgical approach for intracranial hypertension was performed prior to laboratory prolactin measurement.

Currently, dopamine agonists (DA) are the first-line treatment for giant prolactinomas. In reports in the literature, drug treatment has been long-term, even lifelong, and cure is rare[12]. In the cases presented, all patients were treated from the beginning with cabergoline, except for case 6, who was initially treated surgically due to intracranial hypertension, but was later prescribed DA. This treatment has been shown to be effective and well tolerated in children, adolescents, and adults. Treatment with cabergoline has been associated with uncommon short-term side effects, such as pituitary apoplexy.

However, the main concerns with the use of this medication would be its cumulative dose and potential long-term cardiac effects, such as aortic calcifications and tricuspid regurgitation. Periodic monitoring with echocardiography is recommended in patients using the medication in high doses for the long term[11].

Treatment for giant prolactinomas includes normalization of prolactin levels, restoration/maintenance of gonadal function, and reduction of tumor size. The therapeutic management of these tumors is challenging and there are few reports of long-term follow-up, since the diagnosis of giant prolactinomas is rare. The patients in the study presented significant reduction in prolactin levels, tumor size, restoration of some pituitary hormonal axes (mainly gonadotropic), and improvement in visual complaints. In case 6, a second surgery was proposed, but the patient did not agree and failed to attend appointments and was lost to follow-up.

The need for additional research becomes evident, especially with regard to adolescents, given the scarcity of available data. The identification of prognostic markers, the evaluation of combination therapies, and a deeper understanding of the genetic basis are promising areas of research. Furthermore, the lifelong continuity of treatment with dopamine agonists and the challenges associated with treatment withdrawal emphasize the importance of personalized therapeutic strategies and the role of surgery in extreme cases[2,13-15].

CONCLUSION

In summary, early diagnosis of prolactinomas in adolescents and young adults is challenging, given the variability of clinical presentation. The management of macroprolactinomas in this age group represents a key piece in the understanding and effective management of this complex endocrine condition.

In light of recent advances, it is clear that in-depth discussion of these giant prolactinomas is crucial to inform more effective clinical practices and direct personalized therapeutic interventions. The identification of gaps in knowledge highlights the need for further research dedicated to elucidating the underlying mechanisms, risk factors specific to this age group, and optimized management strategies. This improved understanding will allow not only a better quality of life for patients, but also the development of innovative therapeutic approaches.

A comprehensive understanding of these endocrine conditions in adolescents and young adults is essential to ensure a smooth transition from pediatric to adult care. Establishing well-defined transition protocols that take into account the specific characteristics of this population

is imperative to avoid gaps in care and ensure effective continuity in the management of giant prolactinomas. Healthcare professionals should be trained and educated on the clinical nuances of this transition, emphasizing the importance of an interdisciplinary approach to optimize clinical outcomes.

The ongoing study and discussion of macroprolactinomas and giant prolactinomas in adolescents and young adults provides a solid foundation for substantial improvements in clinical practice and research. By highlighting unresolved issues and pointing out directions for future studies, this article aims to catalyze significant advances in the understanding and management of these challenging endocrine conditions.

The study limitations were the loss to follow-up of one patient, the difficulties of serial visual perimetry examinations, and the fact that it was based on data from a retrospective and cross-sectional chart review, with data restricted to information collected during medical consultations. The ongoing pursuit of knowledge and collaboration between professionals from different specialties are crucial to advance the field of endocrinology and metabolism, aiming to improve the quality of life and prognosis of affected patients.

Considering the current scenario, this work highlights the continued relevance of research into giant prolactinomas in adolescents and young adults. Improving the understanding of these conditions will contribute not only to clinical practice but also to the quality of life and prognosis of these challenging patients.

REFERENCES

1. Tirosh A, Shimon I. Management of macroprolactinomas. Clin Diabetes Endocrinol. [Internet]. 2015 [cited in 25 Aug 2024]; 1:5. DOI: https://doi.org/10.1186/s40842-015-0006-4

2. Shimon I. Giant prolactinomas. Neuroendocrinology [Internet]. 2019 [cited in 25 Aug 2024]; 109(1):51-6. DOI: https://doi.org/10.1159/000495184

3. Fernandes V, Santos MJ, Almeida R, Marques O. Ten-year follow-up of a giant prolactinoma. BMJ Case Rep. [Internet]. 2015 [cited in 25 Aug 2024]; bcr2015212221. DOI: https://10.1136/bcr-2015-212221

4. Maiter D, Delgrange E. Therapy of endocrine disease: the challenges in managing giant prolactinomas. Eur J Endocrinol. [Internet]. 2014 [cited in 25 Aug 2024]; 170(6):R213-27. DOI: https://doi.org/10.1530/EJE-14-0013

5. Shrivastava RK, Arginteanu MS, King WA, Post KD. Giant prolactinomas: clinical management and long-term follow-up. J Neurosurg. [Internet]. 2002 [cited in 25 Aug 2024]; 97(2):299-306. DOI: https://doi.org/10.3171/jns.2002.97.2.0299

6. Wildemberg LE, Fialho C, Gadelha MR. Prolactinomas. Nouv Presse Med. [Internet]. 2021 [cited in 25 Aug 2024]; 50(4):104080. DOI: https://doi.org/10.1016/j.lpm.2021.104080

7. Fidelff HL, Boquete HR, Suárez MG, Azaretzky M. Prolactinoma in children and adolescents. Horm Res. [Internet]. 2009 [cited in 25 Aug 2024]; 72(4):197-205. DOI: https://doi.org/10.1159/000236081

8. Pinto EM, Bronstein MD. Aspectos moleculares da tumorigênese hipofisária. Arq Bras Endocrinol Metab. [Internet]. 2008 [cited in 25 Aug 2024]; 52(4):599-610. DOI: https://doi.org/10.1590/S0004-27302008000400005

9. Snyder PJ, Cooper DS, Martin KA. Causes of hyperprolactinemia. [Internet]. 2024 [cited in 20 Nov 2024] UpToDate. Available from: https://www.uptodate.com/contents/causes-of-hyperprolactinemia?search=causes%20of%20hyperprolactinemia&source=search_result&selectedTitle=1%7e110&usage_type=default&display_rank=1

10. Snyder PJ, Cooper DS, Martin KA. Causes, presentation, and evaluation of sellar masses. [Internet]; 2024 [cited in 20 Nov 2024]; UpToDate. Available from: https://www.uptodate.com/contents/causes-presentation-and-evaluation-of-sellar-masses?search=causes%2C%20presentation%2C%20and%20evaluation%20of%20sellar%20masses&source=search_result&selected-Title=2%7E150&usage_type=default&display_rank=2

11. Fukuhara N, Nishiyama M, Iwasaki Y. Update in pathogenesis, diagnosis, and therapy of prolactinoma. Cancers [Internet]. 2022 [cited in 25 Aug 2024]; 14(15):3604. DOI: https://doi.org/10.3390/cancers14153604

12. Maiter D, Delgrante E. Therapy of endocrine disease: the challenges in managing giant prolactinomas. Eur J Endocrinol. [Internet]. 2014 [cited in 25 Aug 2024]; 170(6):R213-R27. DOI: https://doi.org/10.1530/EJE-14-0013

13. Cozzi R, Ambrosio MR, Attanasio R, Battista C, Bozzao A, Caputo M, et al. Italian Association of Clinical Endocrinologists (AME) and International Chapter of Clinical Endocrinology (ICCE). Position statement for clinical practice: prolactin-secreting tumors. Eur J Endocrinol. [Internet]. 2022 [cited in 25 Aug 2024]; 186(3):P1-P33. DOI: https://doi.org/10.1530/EJE-21-0977

14. Fidelff HL, Boquete HR, Sequera A, Suárez M, Sobrado P, Giaccio A. Peripubertal prolactinomas: clinical presentation and long-term outcome with different therapeutic approaches. J Pediatr Endocrinol Metab. [Internet]. 2000 [cited in 25 Aug 2024]; 13(3):261-7. DOI: https://doi.org/10.1515/JPEM.2000.13.3.261

15. Auriemma RS, Pirchio R, Pivonello C, Garifalos F, Colao AM, Pivonelli R. Approach to the patiente with prolactinoma. J Clin Endocrinol Metab. [Internet]. 2023 [cited in 25 Aug 2024]; 108(9):2400-23. DOI: https://doi.org/10.1210/clinem/dgad174

Associated Publisher: Rafael Gomes Ditterich

Conflict of Interests: the authors declared there is no conflict of interest

Financing : none

Contributions:
Concept – Pereira NPAV
Investigation - Mamédio AS, Pereira NPAV
Writing – first draft - Mamédio AS, Pereira NPAV
Writing – revision and editing - Borges MF, Lara BHJ

How to cite this article (Vancouver)
Pereira NPAV, Mamédio AS, Borges MF, Lara BHJ, Ferreira BP. Macroprolactinomas in Adolescents and Young Adults. Rev Fam, Ciclos Vida Saúde Contexto Soc. [Internet]. 2024 [cited in *insert day, month and year of access*]; 12(4):e7405. DOI: https://doi.org/10.18554/refacs.v12i4.7405.

How to cite this article (ABNT)
PEREIRA, N. P. A. V.; MAMÉDIO, A. S.; BORGES, M. F.; LARA, B. H. J.; FERREIRA, B. P. Macroprolactinomas in Adolescents and Young Adults. **Revista Família, Ciclos de Vida e Saúde no Contexto Social**, Uberaba, MG, v. 12, n. 4, e7405, 2024. DOI: https://doi.org/10.18554/refacs.v12i4.7405. Access in: *insert day, month and year of access*.

How to cite this article (APA)
Pereira, N. P. A. V., Mamédio, A. S., Borges, M. F., Lara, B. H. J., & Ferreira, B. P. (2024). Macroprolactinomas in Adolescents and Young Adults. Rev. Fam., Ciclos Vida Saúde Contexto Soc., 12(4), e7405. Retrieved in *insert day, month and year of access* from https://doi.org/10.18554/refacs.v12i4.7405.