



# Prolactinoma in males: a single center experience in Northern Africa

Nada El Yamani<sup>1</sup>, Anouar Jamal<sup>1</sup>, Nissrine Bouichrat<sup>1,2</sup>, Siham Rouf<sup>1,2</sup>, Hanane Latrech<sup>1,2</sup>

1) Department of Endocrinology-Diabetology and Nutrition, Mohammed VI University Hospital Center, Faculty of Medicine and Pharmacy, University of Mohammed 1st, Oujda, Morocco

2) Laboratory of Epidemiology, Clinical Research and Public Health, Mohammed VI University Hospital Center, Faculty of Medicine and Pharmacy, University of Mohammed 1st, Oujda, Morocco

## Abstract

**Background and aims.** Male prolactinoma remains a singular entity. Our study represents the first reported experience of male prolactinoma in Northern Africa. Our work aimed to characterize prolactinomas in the male population, an entity known for its aggressive features, and also to highlight the specific challenges encountered in a North African clinical context.

**Methods.** This is a retrospective descriptive study of male patients presenting with prolactinoma at the endocrinology, diabetology and nutrition department of a university hospital center over a 10-year period.

**Results.** The mean age at diagnosis was  $37 \pm 11$  years. Mass effect related symptoms were present in 83% of cases. Decreased visual acuity was found in 60% of cases. Galactorrhea was found in 13% of cases, decreased libido in 60% of cases, and gynecomastia in 20% of cases. At the time of diagnosis, the mean prolactin level was 4,685 ng/ml (79-33,000). All patients had hypogonadotropic hypogonadism. Among our patients, 66% had undergone dopaminergic agonists as monotherapy, and pituitary surgery was performed in 33% of cases in conjunction with dopaminergic agonists. After a 30-month average follow-up, medical treatment achieved prolactin control in 83% of cases and tumor shrinkage in 70%, while surgery achieved prolactin control in 85% and tumor shrinkage in 70% of cases.

**Conclusion.** Prolactinoma in men is usually invasive and of considerable volume, putting patients at risk of mass effect related symptoms, especially ophthalmologic complications. Hence the importance of early, multidisciplinary and personalized management.

**Keywords:** prolactinoma, prolactin, testosterone, hypogonadism, visual impairment, dopaminergic agonist, pituitary surgery

## Background and aims

Prolactinomas are prolactin (PRL) secreting adenomas derived from pituitary lactotrophs, and they are typically benign, rarely malignant [1]. Prolactinomas are the most prevalent form of pituitary adenomas, both in women and men, accounting for 40-66% of cases in epidemiological studies [2,3]. Recent epidemiological studies indicate that the standardized incidence rates for prolactinomas are 3 to 4 per 100,000 per year in women, but only 0.8 to 1 per 100,000 per year in men, underscoring

their rarity in the male population [4,5].

While the majority of prolactin-secreting tumors in women (90%) are microadenomas, men typically present with macroadenomas or giant prolactinomas in around 75% of cases [3].

In men, clinical symptoms usually arise from the tumor's local mass effect or from symptoms related to hyperprolactinemia, including erectile dysfunction, decreased libido, oligospermia, and gynecomastia [6].

The treatment goals are to normalize serum prolactin levels, restore

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Address for correspondence:

Hanane Latrech

hlatrech@hotmail.fr

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pituitary function, and achieve tumor shrinkage on magnetic resonance imaging (MRI). Dopaminergic agonists are considered the first-line treatment. Pituitary surgery may be considered in emergency situations or if there is intolerance or resistance to dopamine agonists [6,7].

Research on prolactinoma characteristics in males is quite limited in developing countries. This study presents the first reported experience with prolactinoma in a male population in Northern Africa. Our work aimed to characterize prolactinomas in the male population, an entity known for its aggressive features, and also to highlight the specific challenges encountered in a North African clinical context.

## Methods

### Study design

This was a retrospective and descriptive study. It was conducted over a period of 10 years in the Endocrinology-Diabetology and Nutrition Department of a University Hospital Center, from 2015 to 2025. All patients have complete medical records.

### Study population

The study involved data from 15 male patients followed up for prolactinoma. All these patients were admitted to the Endocrinology-Diabetology and Nutrition Department, and fulfilled the diagnosis criteria of prolactinoma. Therapeutic decisions were made in a multidisciplinary staff meeting involving endocrinologists, radiologists, ophthalmologists, and neurosurgeons.

#### Inclusion criteria

- Male patients fulfilling prolactinoma diagnosis criteria
- Complete medical records including clinical observations, biochemical analyses, and radiological assessments.

#### Exclusion criteria

- Incomplete medical records.
- Prolactinoma in women.

### Study protocol

Our study included only men patients presenting with prolactinoma. The clinical data that were collected included: age at diagnosis, diagnosis timeframe, main complaint at presentation especially hyperprolactinemia related symptoms (such as galactorrhea, gynecomastia, infertility, decreased libido, erectile dysfunction); and tumor mass effect related symptoms (such as headaches and decreased visual acuity). For each patient, we assessed prolactin level using Chemiluminescent-Microparticle-Immuno-Assay (CMIA), considering values between 5 to 25 ng/mL as normal. Tumor size and extension were evaluated by magnetic resonance imaging (MRI). Tumor volume was calculated using the formula:  $0.5 \times \text{width} \times \text{length} \times \text{height}$ . Prolactinoma diagnosis was based on hyperprolactinemia with exclusion of any secondary non tumoral cause, combined with the presence of a pituitary

tumor identified through MRI, and according to the tumor size, patients were classified into microprolactinoma when the tumor maximum diameter was less than 1 cm, and macroprolactinoma when the tumor maximum diameter was over 1 cm. Giant prolactinoma was considered when the maximal tumor diameter was over 40 mm, or when the tumor suprasellar extension exceeded 20 mm. A serum prolactin level  $>200$  ng/mL was generally considered highly suggestive of a macroprolactinoma, meanwhile lower levels may be observed for microprolactinoma, typically between 25–200 ng/mL, but diagnosis requires correlation with clinical and radiological findings [6,8-10].

Screening for complications was conducted for all patients, including radiological, ophthalmological, and biological assessments. Extrasellar location and invasive features were assessed in every patient, especially optic chiasm compression. Fundoscopic examination was also conducted in every patient presenting with macroprolactinoma or giant prolactinoma. Moreover, baseline hormonal measurements (ultra-sensitive Thyroid stimulating hormone TSHus, Free Thyroxine-4 FT4, Follicle stimulating hormone FSH, luteinizing hormone LH, testosterone, morning cortisol and Insulin-Growth-Factor-1 IGF1) were performed in all cases at diagnosis, and again at clinical visits. Gonadotropin deficiency was mentioned when serum testosterone was low, and gonadotropins levels were low or normal-low according to age and pubertal staging. Thyrotropic insufficiency was mentioned when FT4 was low and TSHus was low or normal-low, and corticotropic deficiency was mentioned when morning baseline cortisol was low, whereas somatotropin insufficiency was mentioned when IGF1 was low [11].

Type of dopaminergic agonist was mentioned for each patient, with the treatment dose and duration. When surgery was performed: its indication, type, and complications were noted, and also post operative evolution. Hormonal replacement therapy was documented in cases where hypopituitarism was identified.

Treatment response was evaluated based on three parameters: clinical examination especially ophthalmologic symptoms, decrease of prolactin levels, and tumor shrinkage screened on MRI [12]. Prolactin control was defined as normalization of serum prolactin levels below 25 ng/mL [8].

### Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 21. Qualitative variables were expressed as frequencies and percentages, and for continuous variables data were expressed using means with their standard deviations ( $\text{mean} \pm \text{SD}$ ) or ranges, and median with 95% confidence intervals.

The normality of continuous variables intended for correlation analysis was assessed using the Shapiro–Wilk

test. Since the data did not follow a normal distribution ( $p < 0.05$ ), Spearman's rank correlation coefficient was used to assess the associations between variables. A  $p$ -value  $< 0.05$  was considered statistically significant. No statistical comparisons were performed between subgroups (e.g., micro vs. macro/giant prolactinomas), due to the limited sample size ( $n=15$ ) which may increase the risk of error.

### Ethics

The ethical review committee approved the study design and protocol. Considering the retrospective type of the study, we worked on clinical records, and all involved patients provided oral consent to the use of their medical data. The ethical review committee "CERBO" (Comité d'éthique pour la Recherche Biomédicale d'Oujda) approved the study design and protocol under the reference number 22/2020 and number project 7745.

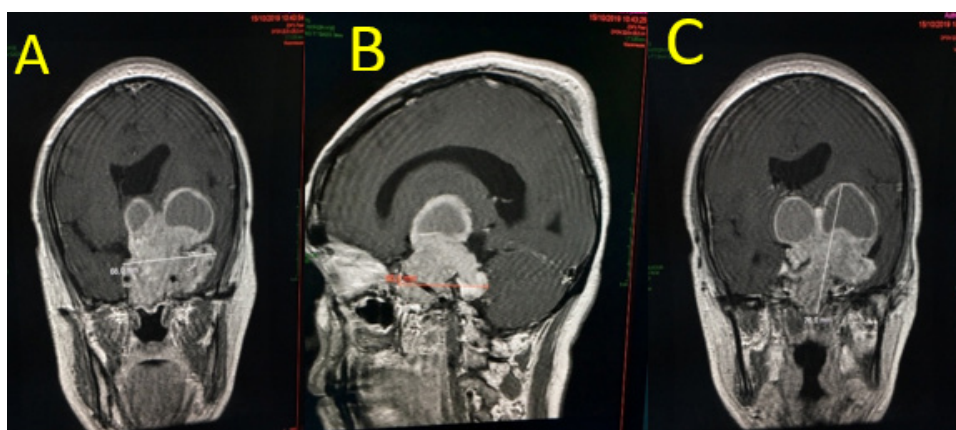
### Results

We enrolled 15 patients in our study. The mean age at diagnosis was  $37 \pm 11$  years (range: 19–55), and the median age was 31 years, with a 95% confidence interval of 27 to 48 years. Main complaint at diagnosis was predominantly headaches (80%) followed by decreased libido (60%) and decreased visual acuity (60%). According to the tumor size, patients were classified into micro prolactinoma (6%), macro prolactinoma (40%) and giant prolactinoma (53.33%). Hypogonadotropic hypogonadism was reported in all patients, whereas thyrotropic deficiency was reported in 40% of cases, and corticotropic deficiency in 26% of cases. The mean prolactin level was 4685 ng/mL, with values ranging from 79 to 33,000 ng/mL. The median was 200 ng/mL, with a 95% confidence interval of 79.80 to 2,000 ng/mL. A significant positive correlation (Spearman's  $\rho = 0.802$ ,  $p = 0.030$ ) was observed between prolactin levels and the tumor maximum diameter. The general characteristics of our patients are summarized in table I.

**Table I.** Clinical, biological, and radiological features at presentation.

	Male patients with prolactinoma (n=15)
Age at diagnosis (years)	$37 \pm 11$ (19-55)
Age at diagnosis n, (%) :	
< 40 years	9 (60%)
>40 years	6 (40%)
Diagnosis timeframe (months)	13 (3-36)
Main complaint at first visit n, (%) :	
- Decreased visual acuity	9 (60%)
- Headaches	12 (80%)
- Galactorrhea	2 (13.33%)
- Gynecomastia	3 (20%)
- Infertility	1 (6%)
- Decreased libido	9 (60%)
- Erectile dysfunction	5 (33.33%)
Prolactin level (ng/ml)	4685 (79-33,000)
Affected pituitary axis : n,(%)	
- Gonadal	15 (100%)
- Corticotropic	4 (26.66%)
- Thyrotropic	6 (40%)
- Somatotroph	3 (20%)
Radiological classification n,(%) :	
- Microprolactinomas	1 (6%)
- Macroprolactinomas	6 (40%)
- Giant prolactinomas	8 (53.33%)

The mean tumor diameter was 44.9 mm ranging from 8 mm to 82 mm. The median was 38 mm, with a 95% confidence interval of 25–65 mm. The mean tumor volume was 69 cm<sup>3</sup> (range: 0.2–163 cm<sup>3</sup>), and the median was 33 cm<sup>3</sup>, with a 95% confidence interval of 15–70 cm<sup>3</sup>. Figure 1 illustrates a radiological example of an invasive prolactinoma in a 27 years old patient. Most of our patients presented with giant prolactinoma as invasive features were observed in 8 patients (60%), with suprasellar extension affecting the optic chiasm in 46% of patients. Indeed, 54% of our patients presented with ophthalmologic symptoms at diagnosis.



**Figure 1.** Invasive macroprolactinoma in a 27 years old patient admitted first for intracranial hypertension; A,C: Frontal plane; B: Sagittal plane.

Decreased visual acuity was noted in 66% of patients, 30% of them were at risk of blindness, and fundoscopic abnormalities were found in 59.3% of patients. Radiological features are summarized in table II, and ophthalmologic complications are summarized in table III.

**Table II.** Radiological characteristics at presentation.

	Male patients with prolactinoma (n=15)
Maximum tumor diameter (mm)	44.9 (8 mm-82 mm)
Tumor volume (cm <sup>3</sup> )	69 (0.2-163)
Component (n,%) :	
- Glandular	11 (73.33%)
- Cystic	1 (6%)
- Hemorrhagic and necrosis	3 (20%)
Location (n,%) :	
- Intrasellar	6 (40%)
- Invasive	9 (60%)
Invasion type (n,%) :	
- Suprasellar with optic chiasm involvement	7 (46.66%)
- Lateral with cavernous sinus involvement	5 (33.33%)
- Infrassellar with sphenoidal sinus involvement	4 (26.66%)

**Table III.** Ophthalmologic complications.

	Male patients with prolactinoma (n=15)
Decreased visual acuity (%)	10 (66.66%)
Fundoscopic abnormalities	
- Papillary pallor	5 (33.33%)
- Papilledema	3 (20%)
- Optic nerve cupping	1 (6%)
Visual field defects	
- Scotoma	3 (20%)
- Bitemporal hemianopsia	1 (6%)

In our series, all patients were started on dopaminergic agonists; 66.66% (n=10) of them were treated with DA as monotherapy, and 33% (n=5) patients underwent combination therapy with DA and neurosurgery. None of our patients underwent radiotherapy. Surgical decisions for our patients were reached in multidisciplinary meetings involving endocrinologists, radiologists, neurosurgeons and ophthalmologists. Cabergoline was the dopaminergic agonist administered to all patients, with an average dose of 1 mg per week (range 0.5-1 mg/week). Pre-therapeutic assessment for valvulopathy using transthoracic echocardiography was negative in all cases.

Regarding patients who underwent surgery alongside dopaminergic agonist treatment, the surgical indications were visual impairment in 26% (n=4) of cases and pituitary apoplexy in one case. An endoscopic trans-sphenoidal endonasal approach was used in 26% (n=4) of patients, while a temporal approach was used in one patient. This latter patient first underwent ventriculo-peritoneal shunting for intracranial hypertension, then underwent surgery for apoplexy in the six following months of cabergoline treatment. Tumor resection was performed in all patients. Postoperative complications included the onset of corticotrophic insufficiency in one patient, thyrotrophic insufficiency in another, and antidiuretic hormone (ADH) insufficiency in one case; these patients were subsequently treated with hydrocortisone, L-thyroxine, and vasopressin. No patients reported infectious symptoms, meningitis, or rhinorrhea.

During follow-up, mass effect related symptoms resolved in all patients; 73.33% (n=11) of patients showed visual function improvement. No DA adverse effects were reported. MRI follow-up was conducted on all patients 3 to 6 months post-surgery, one year after medical treatment initiation, then annually thereafter, except in emergency situations.

**Table IV.** Hormonal and tumor size response to monotherapy (dopaminergic agonist), and to combination therapy (dopaminergic agonist + surgery).

	DA as monotherapy (n=10)	DA with pituitary surgery (n=5)
Prolactin (ng/ml):	Mean : 1181±430 Median : 1000 95% CI : [300–2,000]	Mean : 1264±451 Median : 1,100 95% CI : [500–2000]
- Baseline		
- At last visit	Mean : 93±30 Median : 60 95% CI : [35–90]	Mean : 116±40 Median : 70 95% CI : [40–100]
Prolactin control (%)	83%	85%
Tumor volume (cm <sup>3</sup> ):	Mean : 64±20 Median : 33 95% CI : [10–70]	Mean : 83±25 Median : 70 95% CI : [50–130]
- Baseline		
- At last visit	Mean : 29±12 Median : 15 95% CI : [5–35]	Mean : 44±10 Median : 35 95% CI : [30–45]



No patient showed radiological remission. Three patients required revision surgery regarding residual tumor with visual impairment. Pituitary function improved in 26.66% (n=4) of cases. Corticotrophic function restored in one patient and hydrocortisone dosage was reduced in two others. Prolactin control was achieved in 80% of cases undergoing DA as monotherapy. The mean prolactin level at last visit was 93 ng/ml (ranging from 5 to 430 ng/ml) with tumor shrinkage in 70% of cases. Meanwhile, prolactin control was achieved in 80% of cases undergoing DA alongside surgery, with a mean prolactin level at last visit at 116 ng/ml (ranging from 5 to 470 ng/ml). Tumor shrinkage was achieved in 70% of cases. Biological and radiological progressive features are summarized in table IV.

### Discussion

Our study highlighted prolactinoma features in the male population at a single center in Northern Africa, which is not often reported in literature. Headaches (80%), impaired visual acuity (60%), and decreased libido (60%) were the main complaints at first presentation. Most of our patients were classified as giant prolactinomas (53.33%) and only one case of microprolactinoma (6%). A significant positive correlation was noted between prolactin levels and tumor size. All patients presented with hypopituitarism, while fundoscopic abnormalities were present in 59.3% of cases. Regarding treatment, prolactin control was achieved in most of patients, whether treated with dopaminergic agonists alone (83%) or in combination with surgery (85%); tumor shrinkage was noted in 70% of cases in both groups.

In accordance with numerous studies, the median age in our population was  $37 \pm 11$  years, ranging from 19 to 55 years, as Colao et al. [13] and Khare et al. [14] reported a mean age of  $35 \pm 14$  years and  $35 \pm 10$  years, respectively.

Unlike women, who typically present with hyperprolactinemia related symptoms, over half of men initially report symptoms related to local mass effects [13,15-17]. This entity was quite obvious in our study, as most of our patients reported headaches (83%) and visual impairment (63%) as initial symptoms. Of particular interest, all our patients reported hypogonadism symptoms; decreased libido was the most common one (60%). Still, galactorrhea was relatively rare, occurring in only 2 patients (13%), which was consistent with literature data suggesting this condition requires both low testosterone and high estrogen level, which are not always present. It is important to mention that the average consultation timeframe was 13 months (ranging from 3 to 36 months). This suggests that patients may often overlook symptoms, particularly those associated with hypogonadism, which aligns with the findings of A.-L. Hulting et al [18]. Consequently, both patients and physicians should pay attention to decreased libido as a potential sign of underlying somatic diseases in order to prevent tumor diagnosis at a larger size.

As expected, hypopituitarism was observed in all patients. Gonadal axis was the most commonly affected (100%), followed by thyrotropic axis (40%), then corticotrophic axis (26%). These data are consistent with literature findings which indicates that hypogonadotropic hypogonadism and thyrotropic insufficiency are more prevalent than corticotrophic insufficiency [19,20]. All those cases involved either macroprolactinomas or giant prolactinomas [13,19,21,22], in which these findings indicate that hypopituitarism is due not only to hyperprolactinemia but also to pituitary cell damage resulting from the tumor mass effect. This differs with microprolactinomas, where hyperprolactinemia alone is the contributing factor [20].

Hyperprolactinemia is a well-established cause of hypogonadotropic hypogonadism in our patients [6]. Our study found an average prolactin level of 4,685 ng/ml ( $79-33,000$ ), which is notably higher than the level reported by Delgrange et al ( $2,789 \pm 573$  ng/ml) [16], yet lower than that reported by Khare et al ( $7,927 \pm 16,748$  ng/ml) [14]. According to literature data, there is a correlation between serum prolactin levels and adenoma size: larger prolactinomas are associated with higher prolactin levels [6,19,23,24]. This aligns with our findings, as we observed a significant positive correlation between serum prolactin levels and tumor size.

Prolactinomas in male patients are typically larger and often invasive [13,14,25]. Delgrange et al. reported that 18% of their cases were giant prolactinomas, while 88% were macroprolactinomas, of which 53% were invasive [16]. Likewise, Papegaey et al. found that all their cases were macroprolactinomas, 50% of them were invasive [17]. Khare et al. also reported that all cases were macroprolactinomas, with 80% being invasive and 41% classified as giant prolactinomas [14]. These data are consistent with our results, where 84% of cases were macroprolactinomas, 53% of which were giant prolactinomas. With a focus on the extent of adenoma invasion in our series, it was found to be invasive in 9 patients (60%), indicating a comparable rate to the existing literature [14,16,17]. This finding supports the fact that prolactinomas may have different characteristics and biological behaviors in men compared to women [14,25].

In a recent review of 12 studies involving macroprolactinoma patients undergoing cabergoline treatment (61% were men), normalization of prolactin levels was observed in 80% of cases, with a significant shrinkage of tumor volume in 87% of cases [26]. This was consistent with our findings, as prolactin control was achieved in 83% of cases undergoing DA as monotherapy, with tumor shrinkage in 70% of cases. Meanwhile, prolactin control was achieved in 85% of cases undergoing DA as well as surgery, and tumor shrinkage in 70% of cases which was consistent with literature data suggesting surgical recovery rate up to 45% for macroprolactinomas. Although

male prolactinomas tend to be larger and more invasive, we noted significant improvements in biological markers and imaging findings. This reinforces the theory that dopaminergic agonist treatment can normalize prolactin levels, regardless of tumor size [26].

Despite significant hormonal control and tumor shrinkage in the majority of our patients, complete radiological remission was not achieved in any case. This may be attributed to the invasive features of prolactinomas in our series, which often fail to achieve complete radiological resolution, despite combined medical and surgical treatment. Tumor invasion into the suprasellar region or cavernous sinus often makes full removal challenging, limiting the chances of radiological remission. However, our data show that clinical improvement and hormonal control are achievable therapeutic goals, even in the absence of full radiological remission.

## Conclusion

The particular strength of our study is that it is the first to report the features of prolactinoma in the male population at a single center in North Africa. In line with the literature, our study underscored the invasive aspect of prolactinomas in males. It also underlined the importance of early consideration of hypogonadism symptoms in the male population, which are often overlooked, in order to avoid diagnosis at an advanced stage.

Although our findings provide valuable insights, our study is not without limitations, which should be considered. It is limited by its small sample size and retrospective, single-center design, which may affect data generalizability. However, this reflects the known lower prevalence of prolactinomas in male patients. Future studies should involve larger, prospective multicenter series to validate these findings and to investigate factors delaying diagnosis.

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