original article

Prevalence and characteristics of sellar masses in the city of Al Ain, United Arab Emirates: 2011 to 2016

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BACKGROUND: The prevalence of sellar masses (SMs) is reported in Europe and North America but only limited data are available from the Middle East and North Africa (MENA) region.

OBJECTIVES: Assess the prevalence and characteristics of SMs in Al Ain city, United Arab Emirates.

DESIGN: Retrospective, descriptive multicenter study.

SETTING: Three endocrine centers in Al Ain.

PATIENTS AND METHODS: All patients diagnosed with SMs in the city of Al Ain, Emirate of Abu Dhabi, between 2011 and 2016 were evaluated. Cases were identified using ICD 9 and 10 codes and demographic and clinical data were collected. The prevalence rate was calculated for patients alive and residing in Al Ain city until 31 December 2016.

MAIN OUTCOME MEASURES: Clinical presentations and prevalence rate.

SAMPLE SIZE: 272.

RESULTS: The mean (SD) age on presentation was 40.8 (14.3) years (range: 6-114 years, median: 40.0). The 170 (61.8%) females and 128 (46.5%) were native citizens of the United Arab Emirates. Two hundred and forty five (90%) patients had pituitary adenomas (PAs) while 27 (10%) had non-pituitary sellar lesions. The four most common SMs were prolactinoma (n=139, 51.1%), nonfunctioning adenoma (NFA) (n= 69, 25.4%), somatotroph adenoma (n=32, 11.8%) and craniopharyngioma (n=15, 5.5%). Patients with prolactinoma, corticotroph adenoma, and Rathke's cleft cyst had small sellar masses (<1 centimeter) while the majority of patients with other SMs had macroadenomas. Hypogonadism and growth hormone deficiency was present in 41.8% and 20.5% of the patients, respectively. Of 268 patients with available data, 82 patients underwent surgery while 25 patients received radiotherapy. At the end of 2016, 197 patients were residing in Al Ain city. The overall prevalence of SMs was 25.7/100 000 with PAs constituting most of these masses (n=177) for a prevalence of 23.1/100 000.

CONCLUSIONS: This is the first study of SMs in the United Arab Emirates and the MENA region. Prolactinoma and NFA were the two most common SMs. Further studies are needed to explore the reasons for the lower prevalence of SMs in our region compared with other countries.

LIMITATIONS: Retrospective design, relatively small sample size.

CONFLICT OF INTEREST: None.

Sellar masses (SMs) comprise lesions that arise from the pituitary gland or its surrounding structures. According to their size, extension and function, patients with SMs may have variable presentations including symptoms of mass effect such as headache or vision loss as well as features of hormonal dysfunction.[1] While several studies have reported the epidemiological characteristics of SMs from Europe[2-6] and North America,[7] no information on the epidemiology of SMs from the Middle East and North Africa (MENA) region has been reported except for small studies describing the experience from tertiary referral centers.[8-12] The aim of this study was to assess the prevalence and characteristics of SMs in the city of Al Ain in the United Arab Emirates.

PATIENTS AND METHODS

Al Ain is one of the largest cities of Abu Dhabi emirate. The population has increased from 585 900 in 2010 to 766 900, including non-native persons, in 2016 based on Abu Dhabi Emirate statistics.[13] Healthcare is provided through governmental and private hospitals as well as primary health care centers across the city. Tawam Hospital in affiliation with John Hopkins Medicine and Al Ain Hospital are the only two governmental hospitals providing endocrine service in the city. In addition, two centers in the private sector were providing endocrine service during the study period. Furthermore, one semi-governmental center, opened in 2011, provides primarily outpatient-based diabetes care. Tawam Hospital was the only center for pituitary surgeries in Al Ain during the study period.

We conducted a multicenter retrospective study of all patients with SMs evaluated in Al Ain between January 2011 to December 2016. All centers were informed about the study (verbally and by email) by the principal investigator. While all five centers agreed to participate initially, three centers were included in the study, which included the two governmental hospitals (Tawam Hospital, Al Ain Hospital) and one from the private sector (New Medical Center). The other two centers did not participate in the study due to time limitations. As in a study from Canada,[7] the following diagnoses were included: prolactinoma, nonfunctioning pituitary adenoma (NFA), somatotroph adenoma, corticotroph adenoma, thyroid stimulating hormone-secreting adenoma or any of the nonpituitary tumors including craniopharyngioma, Rathke's cleft cyst (RCC), pituitary cyst, meningioma, and lipoma. The patients were identified using International Classification of Diseases (ICD) 9 and 10 codes pertaining to the above diagnoses. Charts of all patients were reviewed and data on demographics, clinical presentation, hormonal status, tumor size and treatment modalities were collected. Duplicate entries from patients who attended more than one hospital were removed to avoid overestimation. Patients who were alive and residing in the city on 31 December 2016 were selected for prevalence assessment.

PAs were categorized based on their size into macroadenomas (≥10 mm) or microadenomas (<10 mm).[1] Prolactinoma was diagnosed based on symptoms, elevated serum prolactin (>17.6 ng/mL in males, >29.2 ng/mL in females) and magnetic resonance image (MRI) evidence of adenoma. Somatotroph adenoma was diagnosed in patients with typical clinical features, elevated age and gender-specific serum insulin-like growth factor-1 (IGF-1) and inability to suppress GH following a 75g oral glucose load less than <0.4 ng/mL (when performed).[14] Corticotroph adenoma was diagnosed based on clinical and biochemical features of hypercortisolism in the presence of pituitary adenoma. NFA was diagnosed in the absence of hormonal overproduction (clinical and/or biochemical). For macroadenomas, prolactin level of <200 ng/mL (normal range 2.1 to 17.7 ng/mL in males and 2.8 to 29.2 ng/mL in females) was considered suggestive of NFA.[1] For other sellar and parasellar masses, the diagnosis was based on typical radiological features judged either by an experienced neurosurgeon (WA) or obtained directly from the radiology report.[7] For all patients who underwent surgery, tissue diagnosis was the primary method to establish the diagnosis. Secondary hormonal deficiency either isolated or combined was diagnosed as per current guidelines.[15] The study was approved by Al Ain Medical District Ethical Committee (AAMDEC CRD 19/2017).

Data were entered into Microsoft Excel 2011 and analyzed in Stata SE 15.1. Qualitative variables were tabulated as frequencies and percentages (%) and quantitative variables as means and standard deviations (SD) or median with minimum and maximum as appropriate. The Z-test was used to test the difference of two means and the chi-square test was used to test association between nominal variables.

RESULTS

A total of 272 patients were diagnosed with SMs (**Table 1**). The mean (SD) age on presentation was 40.8 (14.3) years (range: 6-114, median 40.0 years). There were 170 (62.5%) females and 128 (47.1%) and all were native and citizens of the United Arab Emirates. Two hundred and forty five (90.1%) patients had PAs while 27 (9.9%) had non-pituitary SMs. The four most common SMs were prolactinoma (n=139, 51.1%), NFA (n=69, 25.4%), so-

Table 1. Characteristics of patients with sellar masses in the city of Al Ain, United Arab Emirates from 2011 to 2016.

	Males (n=102)	Females (n=170)	All patients
Age (years)	43.8 (12.8)	38.6 (14.1)	40.6 (13.8)
Native citizens	26 (25.5)	102 (60.0)	128 (46.5)
Diagnosis			
Prolactinoma	33 (32.4)	106 (62.4)	139 (51.1)
Nonfunctioning pituitary adenoma	35 (34.3)	34 (20.0)	69 (25.4)
Somatotroph adenoma	21 (20.6)	11 (6.5)	32 (11.8)
Craniopharyngioma	10 (9.8)	5 (2.9)	15 (5.5)
Corticotroph adenoma	--	5 (2.9)	5 (1.8)
Rathkeys cleft cyst	--	4 (2.4)	4 (1.5)
Others[a]	3 (2.9)	5 (2.9)	8 (2.9)
Clinical manifestations[b]			
Headache	52/82 (63.4)	46/101 (45.5)	98/183 (53.6)
Menstrual disorders	-	51/92 (55.4)	51/92 (55.4)
Visual loss	34/82 (41.5)	6/98 (6.1)	40/180 (22.2)
Incidental	16/80 (20)	18/100 (18)	34/180 (18.9)
Decreased libido	14/59 (23.7)	-	14/59 (23.7)
Secondary hormonal dysfunction[b]			
Growth hormone deficiency	11/42 (26.2)	6/40 (15)	17/82 (20.7)
Hypogonadism	30/54 (55.6)	15/54 (27.8)	45/108 (41.7)
Hypothyroidism	17/65 (26.2)	7/80 (8.8)	24/145 (16.6)
Adrenal insufficiency	15/64 (23.4)	2/81 (2.5)	17/145 (11.7)
Diabetes Insipidus	--	--	--
Mode of therapy[b]			
Surgery	49/99 (49.5)	33/167 (19.8)	82/266 (30.8)
Radiation therapy	14/100 (14)	10/166 (6)	24/266 (9)

Data are number (%) or mean (SD). [a]Others: Meningioma (5), hypophysitis (1), arachnoid cyst (1) and pinecytoma (1) [b]Denominator is less than 272 as only those with available data were included.

matotroph adenoma (n=32, 11.8%) and craniopharyngioma (n=15, 5.5%). Common symptoms at presentation in men were headache (63.4%), visual loss (41.5%) and decreased libido (23.7%) in men and menstrual disorders (54.8 %) in women, headache (45.5%) and vision loss (6.1%). Of the 180 patients with full presenting features, 34 (18.9%) presented as incidental findings on imaging studies done for unrelated reasons. Family history was obtained in 169 patients: 10 (5.9%) had a family history of SMs. The size at presentation was reordered in 257 patients and of those, 147 (57.2%) presented with macroadenomas. Patients with prolactinoma, corticotroph adenoma and RCC were more likely to have sellar masses of <1 cm (64.4%, 66.7% and 100% respectively) while those with NFA, somatotroph adenoma and craniopharyngioma mostly presented with larger masses (>1 cm) (79.4%, 86.2%, 92.2% respectively). Hypogonadism and growth hormone deficiency (GHD) were present in 41.8% and 20.5% of the patients, respectively. Follow-up data were available for 268 patients and of those, 82 underwent surgery while 24 had radiotherapy. At the end of 2016, 197 patients were residing in Al Ain city.

The overall prevalence of SMs was 25.7/100 000 with PAs constituting most of these masses (n=177) with a prevalence of 23.1/100 000 (**Table 2**). Except for somatotroph adenoma, the prevalence of all SMs were higher in females. The details of the three most common SMs are discussed below.

Prolactinoma

Prolactinoma was the most common type of SM constituting 56.7% of all PAs and 51.1% of all SMs with a prevalence of 15.0/100000. There were more women (n=106, 76.3%) in the prolactinoma group and the mean (SD) age at diagnosis was 28 (9.7) years with most (n=96, 69.1%) being diagnosed between the ages of 21 and 40 years. Men were diagnosed at an older age compared to women (33 yrs vs 27; *P*<.01). Data on tumor size at presentation were available in 132 patients, of whom 85 (64.4%) presented with microadenomas and 47 (35.6%) had macroadenomas. Men had higher rates of macroadenomas compared to women (58% vs 28%; *P*<.01). At presentation, hypogonadism was the most common hormonal dysfunction, being diagnosed in 23 of 68 patients with available data (51.1%) followed by GHD in 7 of 30 (23.3 %), hypothyroidism in 10 of 68 (14.7%) and adrenal insufficiency (AI) in 3 of 71 (4.4%). None of the patients had diabetes insipidus (DI) at diagnosis. Twelve of 125 (9.6%) patients with available data underwent surgery while only one patient received radiation therapy.

Nonfunctioning adenomas

NFA was the second most frequent type of SMs, accounting for 25.4% of all SMs. The prevalence of NFAs was 5.1/100000. The gender distribution of NFA was similar in men and women (35 vs 34). The mean (SD) age of diagnosis was 42 (17.9) years with women being diagnosed at a younger age (36.6 [17.9] years) than men (47.3 [16.6] years) (*P*<.05). The size of NFA on presentation was recorded in 68 patients, of which 54 (79.4%) presented with macroadenomas. Almost all men (n=34, 97.1%) had presented with macroadenoma compared to 60.1% (n=20) in women. Among those with available data, the three most common modes of presentation were headache (35/58, 60.3%), incidental finding (23/57, 40.4%), and vision loss (21/59, 36.2%). Similarly, the commonest hormonal dysfunction was hypogonadism (5/20, 34.3%) followed by hypothyroidism (11/41, 26.8%), GHD (6/22, 23.8 %) and AI (1/23, 17.4%). None of the patients had DI at diagnosis. Data on surgery and radiotherapy was available for 68 patients. Of those, 26 (38.2%) underwent surgery and 6 (8.8%) had radiotherapy.

Somatotroph adenoma

Following prolactinoma, somatotroph adenoma constituted the second most common functioning adenomas, representing 13.1% of PAs, with a prevalence of 2.6/100000. The mean (SD) age at diagnosis was 38 (10.1) years. Males constituted 65.5% (21/32) of all acromegaly patients. At presentation, 25 (71%) had macroadenoma, 4 (19%) had microadenoma and no data were available in 3 (10%) patients. Of those with available data, hypogonadism was the most common hormonal deficiency (5/20, 25%), followed by hypothyroidism (1/21, 4.8%) and AI (1/23, 4.3%). None of the patients had DI at diagnosis. Twenty-three of 31 (74.2%)

Table 2. Prevalence of sellar masses by gender for all patients diagnosed from 2011 to 2016.

Disease	n	Male		Female		Total
		Rate/100000	n	Rate/100000	n	Rate/100000
Pituitary adenomas	54	12.0	123	39.1	177	23.1
Prolactinoma	23	5.1	92	29.2	115	15.0
Nonfunctioning pituitary adenoma	19	4.2	20	6.4	39	5.1
Somatotroph adenoma	12	2.7	8	2.5	20	2.6
Corticotroph adenoma	--	--	3	1.0	3	0.4
Craniopharyngioma	7	1.5	5	1.6	12	1.6
Rathke's cleft cyst	--	--	3	1.0	3	0.4
Others	1	0.02	4	1.3	5	0.1
All sellar masses	62	13	135	42.8	197	25.7

Population of Al Ain in 2016: 766 936 (males 451 754 , females 315 182)

and 9 of 29 (31 %) patients with available data underwent pituitary surgery and radiotherapy, respectively.

Pituitary incidentalomas

Thirty-four patients were diagnosed with pituitary incidentalomas. Of those, 23 patients had NFA, 4 prolactinomas, 3 craniopharyngiomas, 2 RCC, 1 meningioma and 1 arachnoid cyst. Only 3 patients had required surgery while the rest were under surveillance. Patients with pituitary incidentalomas compared to those with clinically manifesting sellar masses (CMSMs) were older at diagnosis (42.9 yrs vs 34.4, *P*<.05), had higher frequency of macroadenomas (82.4% vs 56.3%, *P*<.05) but lower visual field defect (2.9% vs 24.1%, *P*<.01) (**Table 3**).

DISCUSSION

To the best of our knowledge, this is the first population-based study to evaluate the epidemiology of SMs in the United Arab Emirates and the MENA region. The overall prevalence of SMs in our study was 25.7 per 100 000 which is about 4-fold lower compared to a similar study from Canada.[7] Similarly, the prevalence of PAs (23.1 per 100 000) was remarkably lower compared to other reports from across the globe (**Figure 1**).[2,3,5-7,16] The reasons for the lower than expected prevalence rates for all types of SMs in our study are not entirely

Table 3. Comparison between pituitary incidentalomas and clinically manifesting sellar masses (CMSM) from 2011 to 2016).

	Pituitary incidentalomas (n=34)	CMSM (n=148)	*P* value
Age (years)[a]	42.9 (22.4)	34.4 (12.4)	.002
Female gender[b]	18 (52.9)	82 (56.2)	.733
Diagnosis[c]			
Prolactinoma	4 (11.8)	78 (52.7)	
NFA	23 (67.6)	34 (23.0)	
Somatotroph adenoma	--	24 (16.2)	
Rathkes cleft cyst	2 (5.9)	1 (0.7)	
Craniopharyngioma	3 (8.8)	5 (3.4)	
Corticotroph adenoma	--	3 (2.0)	
Others[d]	2 (5.9)	3 (2.0)	
Presentation			
Headache (yes)[b]	21 (61.8)	68 (48.6)	NS
Vision loss (yes)[e]	1 (2.9)	34 (24.1)	<.01
Tumor size[b]			
Macro	28 (82.4)	81 (56.3)	<0.01
Micro	6 (17.6)	63 (43.8)	
Hormonal loss			
GH deficiency[e]	4 (28.6)	13 (21.7)	NS
Hypogonadism[e]	4 (25.0)	37 (45.7)	NS
Hypothyroidism[b]	6 (25.0)	15 (14.4)	NS
Adrenal insufficiency[e]	3 (12.0)	14 (13.2)	NS
Treatment			
Surgery[b]	6 (18.2)	48 (34.5)	NS
Radiation[e]	2 (6.1)	(9.6)	NS

Data are number (%) or mean (SD). [a]Z- test for two means; [b]Chi-Square test; [c]Cell value not sufficient to calculate the *P* value; [d]Meningioma (1) and arachnoid cyst (1) for incidental finding; meningioma (2) and hypophysitis (1) for clinically manifesting cases; [e]Fisher Exact test. CMSM: clinically manifesting sellar masses.

clear, but could be largely attributed to under-diagnosis of SMs in our population. Moreover, incorrect use of ICD codes may have impacted our results. One of the solutions to overcoming under-diagnosis of SMs is to enhance the awareness of health care provider with the clinical presentation and the importance of early diagnosis of SMs.

Prolactinomas constituted the most commonly detected SMs in our study followed by NFA and GH-producing adenomas. Similar distribution has been reported in other studies.[2,3] Also, we showed that men with prolactinomas were diagnosed at an older age and had higher rate of macroadenomas compared to women. This is consistent with previously published data demonstrating a gender difference in the presentation of prolactinoma.[17] Recently, Paepegay et al showed that even among the group of macroprolactinomas, men had a higher mean tumor size and higher prevalence of visual dysfunction compared to women.[18] These findings support the notion that prolactinomas in men could have an aggressive course.

In our study, patients with NFA were diagnosed at an older age compared to prolactinoma patients. This finding is not surprising as hyperprolactinemia suppresses gonadotropin-releasing hormone and results in hypogonadism, the symptoms (menstrual disorders and infertility) of which are specific and of concerns to the young patients in the reproductive age group. In contrast, NFA is slowly growing tumors and patients tend to have nonspecific symptoms. These tumors are usually discovered when patients present with a mass effect or are evaluated for other unrelated complaints. This pattern of presentation is in line with the published literature suggesting that age could serve as a clue in the differential diagnosis of SMs.[6]

Hypopituitarism is common in patients with SMs.[15] In our study, hypogonadism and GH deficiency were the two most common hormonal deficiencies present at diagnosis. Of note, none of our patients had DI at presentation. Similarly, other studies showed a very low risk of DI in patients with SMs in general; especially in PAs because of the slower rate of adenoma progression in

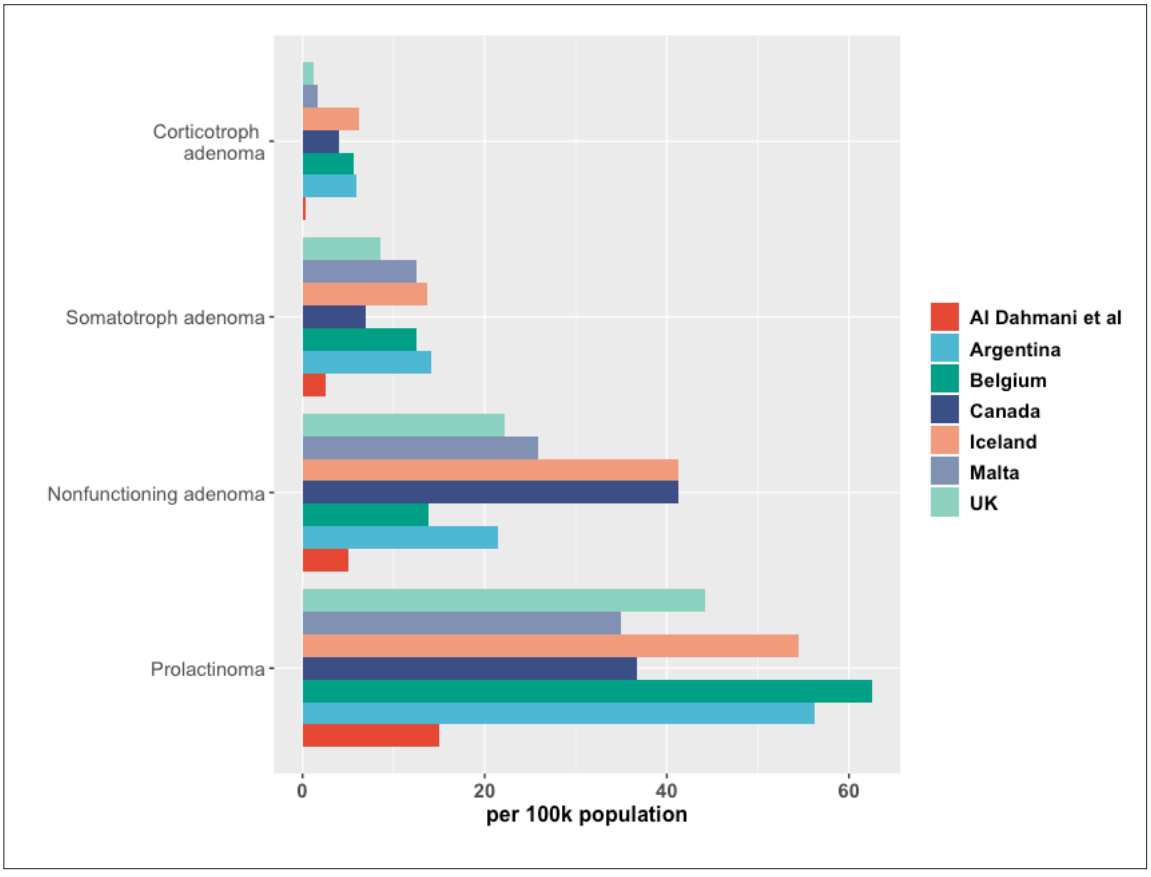

Figure 1. Prevalence of sellar masses in the present study compared to prevalence in other studies in other countries.

such patients.[6] Hence, the presence of DI should alert the physician to consider other sellar pathologies in the differential diagnosis such as craniopharyngioma, hypophysitis or rarely metastasis to the pituitary.

Pituitary incidentalomas are usually diagnosed after the fourth decade of life with the majority of patients having NFAs.[19] Similarly, most of our patients had NFAs and were diagnosed at an older age compared to CMSMs. Also, the majority of the patients had macroadenomas at diagnosis, which is in line with other studies.[19,20] Interestingly, however, the rate of vision loss was much lower in the pituitary incidentalomas cohort compared to CMSMs (2.9 vs 24.1%, $P<.01$). This could be due to the difference in the actual size of macroadenomas between the two groups. Also, pituitary incidentalomas may have a slow pace of tumor growth and therefore were detected before the occurrence of significant suprasellar extension and optic chiasm compression. However, data on the mean tumor size, pattern of sellar extension and mean change in tumor size on follow up is lacking and this hypothesis remains to be proven. One similar study did not report any significant difference in the prevalence of visual field abnormalities in patients with pituitary incidentalomas at diagnosis compared to CMSMs.[21] However, in the same study, the risk of apoplexy on follow up was much lower in the pituitary incidentalomas cohort suggesting that these adenomas might have indolent behavior in comparison to CMSMs.

The strength of the study stems from being the first in the MENA and Gulf region to investigate the prevalence of PA and SMs. Also, data from the three main hospitals in the city were collected. However, two private and semiprivate medical centers providing endocrine services in the city did not participate in the study and their patients were not included. This limitation is minimized because none of these centers perform pituitary surgeries and amongst them, one primarily provides diabetes outpatient care. It is also very likely that some of the patients from the excluded medical centers may have been evaluated at one of the study sites for reasons of a medical second opinion, quite common in the country. Furthermore, the difference between the prevalence of SMs/PAs in our study and previous studies is substantial and points out to under diagnosis rather than missing a number of patients in other smaller centers. Additionally, data were collected retrospectively and therefore clinical presentation and hormonal dysfunction data were not consistently available.

In conclusion, the prevalence of SMs and PAs were much lower than the reported rates in other studies suggesting that SMs are probably underdiagnosed and underreported in our city. Our data also confirms distinct age, gender and tumor size differences in the presentation of prolactinomas and pituitary incidentalomas. Further studies are needed to explore the reasons for the low prevalence of SMs in our region.

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