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The management of bilateral myelolipoma: Case report and review of the literature

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ABSTRACT

INTRODUCTION: Bilateral adrenal myelolipoma is a rare benign neoplasm. We presented the case of a young man affected by a bilateral myelolipoma and the analysis of the literature of bilateral cases of myelolipoma. Our purpose is to give a suggestion of clear terms of reference regarding the management of this kind of bilateral neoplasm.
PRESENTATION OF CASE: We reported the case of a 41-year-old healthy man complained of abdominal pain in the upper quadrants. No significant alterations were found in routine blood and endocrinological tests. The imaging (CT and MRI) showed a huge right adrenal mass and a smaller lesion at the left adrenal gland. The preoperative pathological characterization was suggestive for a myelolipoma. A right open adrenalectomy was performed, and a radiological surveillance was planned for the left tumor. The pathological exam confirmed the diagnosis.
DISCUSSION: In literature, there are 36 cases described. The clinical presentation consisted of symptomatic tumors, incidentally diagnosed lesions or myelolipomas in patients with an associated endocrinal disorder. Symptomatic tumors or those bigger than 7 cm, because of the potential risk of rupture, are usually treated surgically. In smaller (<7 cm) and asymptomatic ones the surgical treatment is not univocal.
CONCLUSION: In the setting of the surgical treatment, it is important to preserve in some way the hormonal function. For that reason, the bilateral adrenalectomy has to be reserved for symptomatic or sizeable (>7 cm) cases. As far as we know, this is the first review on bilateral myelolipomas.

1. Introduction

The adrenal myelolipoma is a rare benign tumor of the adrenal gland. The incidence in old autopsy-series is about 0.08–0.25%; however, nowadays it is being diagnosed more and more frequently because of the widespread use of ultrasound, computed tomography (CT) and Magnetic Resonance Imaging (MRI). It represents about 3–5% of primary tumors of the adrenal gland [1].

In general these tumors are asymptomatic, unilateral and small (on average less than 4 cm). Sometimes they can cause symptoms because of bulk effects or rupture and also reach impressive dimensions (biggest tumor described measured 31 × 24.5 × 11.5 cm and weighed 5900 g) [2]. In some cases, they can be found bilaterally.

So far, the pathogenesis of the myelolipoma is unknown, but an adrenocortical metaplasia in response to stimuli like necrosis, inflammation, infection or stress [3] is the most common theory. Another hypothesis identifies a stressful lifestyle and a messy diet as risk factors [4].

Histologically, it is composed of variable mixture of mature adipose tissue and hematopoietic elements. We describe the case of a young patient with bilateral myelolipoma and present an analysis of literature regarding the reported cases of bilateral myelolipoma. The goal of our study was to attempt to identify clinical features and treatment criteria in this setting. To the best of our knowledge, this is the first review on bilateral cases.

2. Case report

A 41-year-old healthy man complained of abdominal pain after eating in the upper quadrants from 6 months, without other symptoms. No significant alterations were found in a routine blood test. Endocrinological tests and assay of urinary catecholamines did not show significant alterations.

A CT (Fig. 1) highlighted a huge right adrenal mass sized about 17 × 12 cm (-20HU) and a similar lesion of 2.3 × 2.5 cm (-5HU) in the left adrenal gland. MRI (Fig. 2) confirmed the presence of

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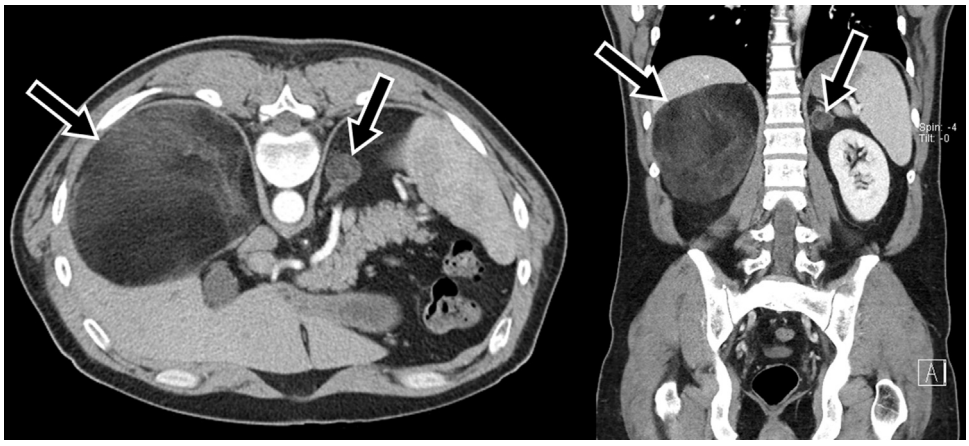


Fig. 1. CT scan.

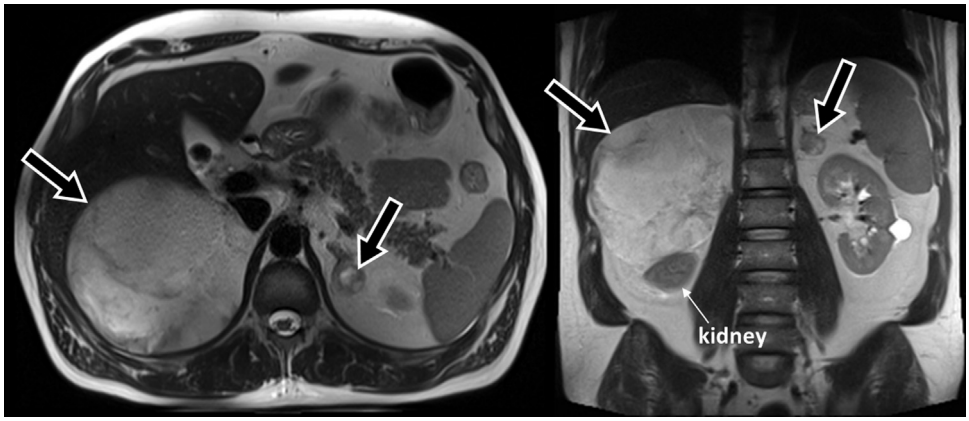


Fig. 2. MRI.

bilateral adrenal mass containing mainly fat with multiple septa, both consistent with myelolipomas.

A CT-guided biopsy of the major lesion showed the presence of fibroadipose tissue with focal hemosiderosis, without evidence of neoplastic cells or hematopoietic tissue.

In order to remove the huge symptomatic lesion, we performed a right open adrenalectomy (Fig. 3), using a Chevron incision. In order to safely and easily remove the main adrenal lesion (especially to achieve an adequate control of the adrenal vein), the Kocher maneuver have been required, together with the complete mobilization of the right liver and the right colic flexure, mainly because the mass being adherent to the right aspect and rear of the inferior vena cava (Fig. 4). Because of the asymptomatic feature and the small diameter, in order to preserve the adrenocortical function, we decided not to surgically remove the myelolipoma on the left side, monitoring over time its behavior by radiological surveillance.

The postoperative period was uneventful. After one-year follow-up with CT-scan, we did not find relapse on the right side, where the big myelolipoma was removed, and the left myelolipoma remained unchanged.

Macroscopically (Fig. 3), the specimen was a capsulated nodular lesion of 17 cm in diameter, weighing 1.170 kg. The color of the capsule was yellow mottled. To the cut, the tissue appeared fairly uniform, adipose and sallow, with hemorrhagic circumferential zones. The lesion seemed to be originated by the adrenal medulla with the capsule consisting of the cortex.

Microscopically (Fig. 5), the specimen showed a well-defined margins tumor, partly bounded by thin connective tissue capsule, largely consisting of mature adipose tissue with extensive hemosiderosis. Some areas of hematopoiesis have been identified, together with the presence of the three hematopoietic lineages. In peripheral areas have been discovered the presence of adrenal tissue with no significant histological changes.

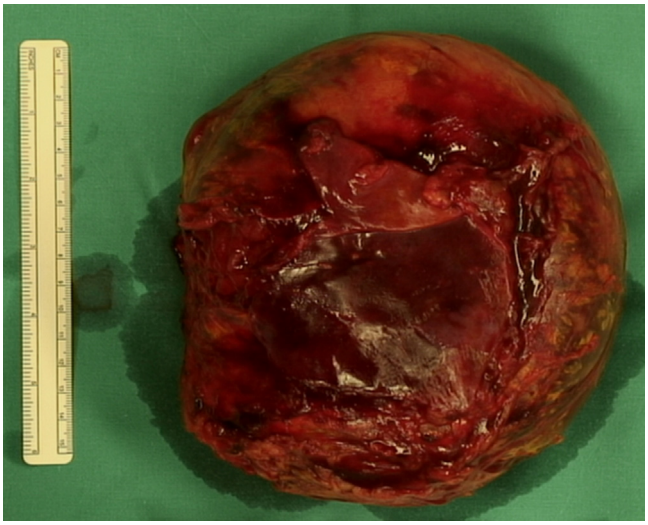


Fig. 3. Resected specimen.

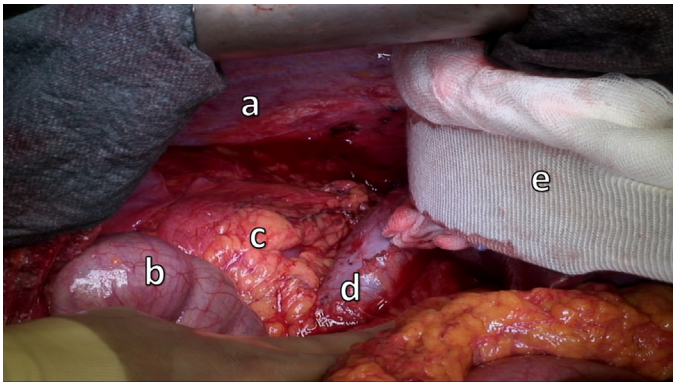


Fig. 4. Intraoperative picture showing the tumor bed after removal of the right myelolipoma. a: diaphragm, b: hepatic flexure, c: Gerota's fascia, d: inferior vena cava, e: right liver completely mobilized.

3. Method

We researched on PubMed myelolipoma cases described in the literature until 1st September 2014 using the following search criteria: myelolipoma, adrenal myelolipoma, adrenal tumor and adrenal incidentaloma. Moreover, we searched for the paper cited in the references of the articles about bilateral cases of myelolipoma.

We excluded monolateral and extra-adrenal myelolipoma cases. We also analyzed papers from some authors describing surgical series including bilateral cases.

We focused our attention on papers regarding the clinical and surgical management of these tumors. On the other side, we excluded from our analysis radiological articles describing only the radiological presentation of adrenal lesions, without any clinical description. Regarding the languages, English, Italian and Spanish articles were analyzed.

4. Discussion

4.1. Epidemiology

Adrenal myelolipoma is a rare benign tumor composed of mature adipose cells and hematopoietic tissue. Usually adrenal myelolipoma is a non-functioning, monolateral, small and asymptomatic tumor, and represents the 1.9% of adrenal incidentalomas [19]. However, bilateral cases of adrenal myelolipoma has been reported. In our literature search, we found 37 cases [5–23,25] of bilateral myelolipoma, excluding the case at hand, mostly described in case reports. We excluded from the analysis 18 patients among those mentioned above because of insufficient data. The average age of the 19 bilateral cases analyzed was 46 years (range 24–69) with an equal sex ratio (9 males e 10 females).

4.2. Clinical features and diagnosis

The most frequent clinical feature of bilateral cases described is monolateral symptoms [6,8,11,13–16,18,21] (9 patients), usually abdominal discomfort, with the concomitant radiologic finding of a contralateral myelolipoma, as in the case at hand.

Sometimes bilateral adrenal tumors were found incidentally [5,9,10,19] or because of nonspecific symptoms [23,24] during radiographic or sonographic exams.

Rarely bilateral myelolipomas were both symptomatic due to bulk effect (3 patients in our review [12,20,22]).

Routinely, an endocrinological examination was performed in order to find a congenital or secondary endocrinal disorder or a secreting neoplasm (plasma epinephrine, norepinephrine, ACTH, cortisol, renin, aldosterone, 17-OH-progesterone, 24 h urinary cortisol, free cortisol, metanephrine, vanillymandelic acid and homovanillic acid); in some case a screening test for congenital adrenal disorders was performed.

In our case, no significant endocrinological alterations were found, while in the literature we found 11 cases [19–25] of bilateral myelolipomas diagnosed in association with congenital or acquired endocrine disorders (Table 1). Three cases of eleven were excluded from our analysis because of missing data (there were one case of Cushing disease and two cases of adrenal hyperplasia). Five patients known to have an adrenal hyperplasia manifested symptoms related to bulk effect with the radiological finding of a bilateral adrenal lesion [11,20–23]. In two patients, the diagnosis of

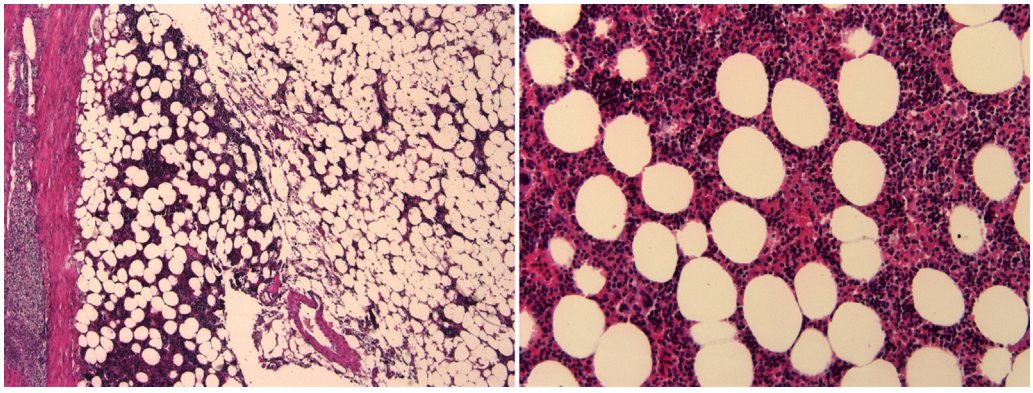


Fig. 5. Microscopical image.

Table 1
Bilateral adrenal myelolipomas with endocrine disorder.

	Kalidindi [11]	Ioannidis [20]	Mc Geoch [21]	Sakaki [23]	Jung [19]	Umpierrez [24]	Garduño García [22]	Kanj [25]
Sex	Female	Female	Male	Female	Male	Male	Female	Female
Age	42	34	34	69	44	47	64	24
Main dimension (cm) left–right	25 23	24 16	23 15	8 4	3.4 6	5 2.5	21 18	7 5.5
Bilateral symptoms	Yes			Yes				
Unilateral symptoms	Yes	Yes						
Nonspecific symptoms		Yes		Yes	yes			
Incidentaloma			Yes					
Endocrine disorder	Adrenal hyperplasia	Adrenal hyperplasia	Adrenal hyperplasia	Adrenal hyperplasia	Primary aldosteronism	Adrenal hyperplasia	Adrenal hyperplasia	Cushing's syndrome
Bilateral adrenalectomy	Yes	Yes	Yes		Yes (partial on the left one)	Yes	yes	
Unilateral adrenalectomy		Yes						
Partial adrenalectomy			Yes					
Follow-up			Yes					

Table 2
Clinical presentation and management of bilateral adrenal myelolipomas.

Clinical presentation	Management			
	Patients	Monolateral adrenalectomy	Bilateral adrenalectomy	Follow-up
Monolateral symptoms	9	5	4	0
Bilateral symptoms	4	0	4	0
Incidentaloma	6	1	3	2
Total	19	6	11	2

a bilateral myelolipoma was prior to the discovery of an endocrine disorder [19,24].

There are no cases reported of bilateral secreting myelolipoma as well as we did not find any case of bilateral myelolipoma with spontaneous or post-traumatic rupture.

The clinical features and the management of the 18 cases of bilateral myelolipomas analyzed are shown in Table 2.

As regards the micro-histological characterization, in the case at hand, a preoperative CT-guided biopsy of the major tumor was obtained and showed the presence of fibroadipose tissue with focal hemosiderosis. The minor one had the same radiological pattern. In the cases analyzed from the literature, the micro-histological evaluation was not routinely performed. Usually an adrenalectomy was performed precisely in order to achieve a histological confirmation. In most cases, the author reported typical radiological findings of myelolipoma, but sometimes the differential diagnosis with adenoma or liposarcoma may be unclear.

Only two authors reported a histological characterization of the tumors [5,18]. In four cases [8,14,15,18], the patients underwent monolateral adrenalectomy for the symptomatic tumor and, during surgery, a biopsy of the contralateral lesion was obtained, confirming the diagnosis of myelolipoma and, thus, allowing a planned follow-up for the lesion left in place. Eight patients [6,10–22] underwent bilateral adrenalectomy without a preoperative confirmation.

4.3. Treatment

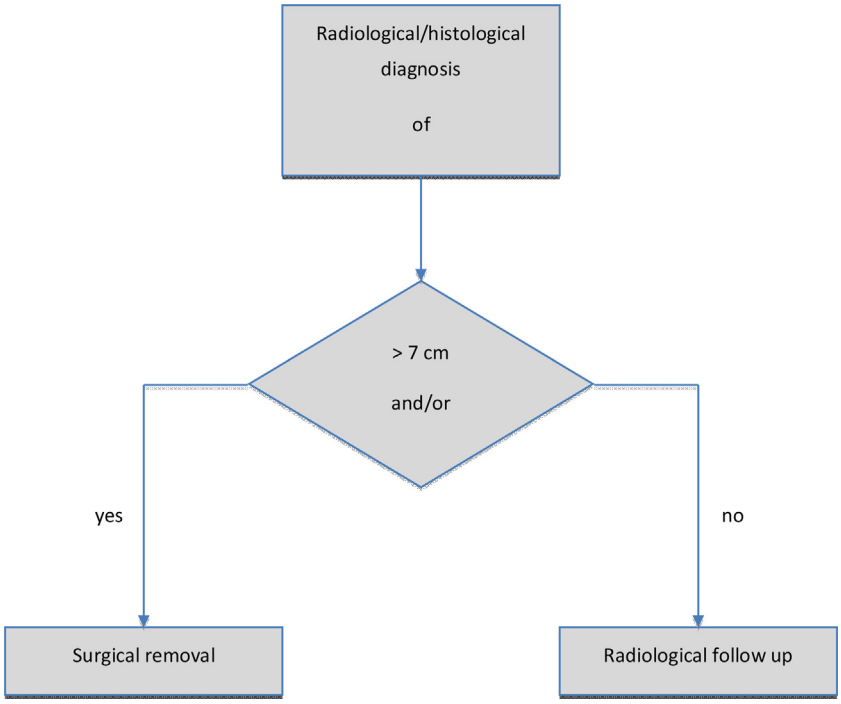
Generally, surgery is considered for symptomatic myelolipomas and also for asymptomatic ones bigger than 7 cm in diameter. Although bilateral adrenalectomy should be avoided to conserve the hormonal function, anyway it was performed even in patients with bilateral asymptomatic tumors because of the diameter larger than 7 cm and the resulting risk of rupture.

One exception is presented by Ketelsen et al. [5] with a patient being affected by huge bilateral asymptomatic myelolipoma ($12.3 \times 8.7 \times 19.3$ cm on the left and $19.1 \times 10.5 \times 22.6$ cm on the right side) in whom a wait-and-see strategy was adopted, after a fine-needle-aspiration proof of the benign nature of both lesions.

On the other hand, Jung et al. [19] reported a case of a patient affected by primary aldosteronism with bilateral myelolipoma of small dimensions (<7 cm) but with a significant growth (more than 30%) of both tumors after one-year follow-up. In this patient, a partial adrenalectomy was performed on the left side where the smaller tumor was located and a total one on the other side. The residual gland was sufficient to maintain the adrenal function, so a steroid replacement therapy could be avoided, while the aldosteronism was solved.

The surgical technique has not been detailed for all interventions. The surgical approach mostly described was a laparotomic one ($n = 9$), usually using Chevron incision, as in our case. In tumors less than 10 cm in diameter, successful laparoscopic interventions are described ($n = 4$). The surgical outcome was good for both

Table 3
If bilateral adrenalectomy → steroid replacement is required.



techniques, favoring the laparoscopic approach in terms of length of stay.

Shen et al. [6] described a new surgical technique, performing the bilateral myelolipoma excision (left asymptomatic, 8 cm and right symptomatic, 8.5 cm) with a laparoscopic retroperitoneal liposuction and subsequent adrenalectomy. No tumor recurrence was observed [6].

There are no bilateral cases described of emergency interventions for bleeding due to traumatic or spontaneous rupture. Conversely, there are 13 cases of unilateral myelolipoma with hemorrhage after spontaneous (11 cases) or post-traumatic (2 case) rupture. In all cases, the tumors were bigger than 7 cm [31–43]. In two cases of spontaneous hemorrhage, urgent embolization was performed, followed by delayed elective surgical excision of the myelolipomas [39,40]. In case of rupture, the adrenalectomy was always planned considering the lesion "symptomatic" in this setting; for that reason it is not clear the feasibility of an observational approach with or without embolization, because conservative strategy had never been used.

All patients submitted to a bilateral adrenal excision received a lifelong steroid replacement.

A conservative strategy for both bilateral tumors was described by Ketelsen et al. [5] (giant bilateral asymptomatic myelolipomas) as mentioned above and by Umpierrez et al. [24], who diagnosed incidentally two small adrenal lesions (3.5 × 5 cm on the left and 2 × 2.5 cm on the right side) with radiological typical characteristics of myelolipoma.

All asymptomatic tumors less than 7 cm in diameter [8,9,13–15,23,24] (except for the case reported by Jung et al., [19] with significant bilateral growth during follow-up) were managed conservatively, as we performed with the smaller asymptomatic myelolipoma (2.3 × 2.5 cm left side). The timing of follow-up was not always declared by the authors. Usually the follow-up plan consists in US or CT scan [8,16] or MRI after 12 and 24 months, but there is no uniformity. The tumor growth occurs in about half of the cases as reported by Han et al. [28], who carried out a surveillance for an average of 3.2 years (range 0.3–10.8 years) in a series of 12 patients with myelolipoma (only 1 bilateral case) and described a tumor growth in 6 patients, decrease in 2, and dimensional stability in 5.

5. Conclusion

Myelolipoma is a rare benign tumor consisting of a tissue mix of fat and myeloid cells, usually surrounded by a capsule. Adrenal myelolipoma can be diagnosed incidentally or can be revealed by symptoms caused by bulk effects (abdominal pain or distension, flank/back/lumbar/shoulder pain or discomfort, palpable abdominal mass, ileus, cardiac dyskinesia, cough) or spontaneous/post-traumatic rupture [1]. CT, ultrasound and MRI can all be used for diagnosis, CT having the advantage of the possibility of tissue density measurement [26]. In the differential diagnosis, we must consider teratoma, adenoma, lipoma, liposarcoma and angiomyelolipoma. In order to exclude malignancy and plan the management strategy, a fine-needle aspiration or a CT- or ultrasound- guided micro-biopsy are advised [27,28].

Bilateral myelolipomas are also described in association with endocrinal disorders: congenital adrenal hyperplasia caused by 21-hydroxylase deficiency, Cushing disease, primary aldosteronism. This may suggest a relationship between the pathogenesis of myelolipoma and the presence of endocrinal disease, but, as far as we found, this is still unknown. Only 3 cases of unilateral myelolipoma with catecholamine secretion [2,29,30] are described in the literature; no case of bilateral myelolipoma is reported in this setting.

Surgical intervention is required in symptomatic tumors and in tumors bigger than 7 cm, because of the potential risk of rupture [1,8]. Even if, unlike to the unilateral type, in the literature, there are no cases described of bilateral myelolipoma with tumor rupture. Myelolipoma can be treated with both conventional and laparoscopic surgery and in general do not relapse.

Asymptomatic lesions inferior to 7 cm can be left in place, as we planned in the case at hand. These neoplasms are benign and at low risk of rupture. This is why it is advised to be conservative, as soon

as possible, to preserve the hormonal function, on condition that histological nature is clarified. An annual follow up by CT or MRI is reasonable.

Finally, whenever possible, the endocrine function must be preserved; a partial adrenalectomy can be considered, as described by Jung et al. [19]. The surgical treatment of the asymptomatic lesions is not mandatory even if they are bigger than 7 cm, because of the very low risk of rupture, and a wait-and-see strategy could be adopted. Decision algorithm in bilateral myelolipoma is shown in Table 3.

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