Adrenal and Extra-adrenal Myelolipomas - A Comparative Case Report

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ABSTRACT

Myelolipoma is an uncommon benign tumour composed of mature fat tissue and haematopoietic elements and is most commonly found in the adrenal gland. We report a case, which was discovered incidentally on chest X-ray, of a rare occurrence of multifocal extra-adrenal myelolipoma in the thoracic paravertebral region. This was further investigated with multi-detector computed tomography and magnetic resonance imaging. The presumed diagnosis, of extra-adrenal myelolipoma, was histologically confirmed via tissue sample obtained by computed tomography guided biopsy. We compare the adrenal and extra-adrenal entities from the perspective of published literature and also review the cases, published in Pubmed, of extra-adrenal myelolipomas in order to summarize the different locations of this lesion.

CASE REPORT

CASE REPORT

An asymptomatic 70-year-old European male presented with a right paravertebral mass, that had been detected incidentally on routine chest x-ray (fig 1). The patient underwent a computed tomography of the chest with intravenous contrast media, revealing 7 paravertebral lesions: 5 lesions on the right side and 2 lesions on the left (fig 2). The largest lesion, visible on the chest x-ray, was located at the level of T 5/6 with 45x26x56 mm in diameter (fig 2e), and the smallest lesion was located on the right side at the level of T11, with a diameter of 10x7x11mm. Some of these lesions were slightly lobulated and all lesions were encapsulated with well-defined borders and no infiltration of the neighbouring tissue. Lesions showed predominantly mixed densities, ranging from soft tissue, isodense to muscle; to fat-equivalent densities of about -70 Hounsfield units (fig 2b). Neither calcification nor active bleeding was found and there was no splenomegaly or evidence of bone marrow expansion. The patient then underwent a magnetic resonance imaging of the thoracic spine (fig 3). Lesions were partially hyperintense on T1 and T2 weighted images, with signal drop-out on fat suppression technique; and partially hypointense on T1 WI and isointense on T2 WI, with moderate enhancement after intravenous injection of gadolinium. No invasion of the neighbouring structures, no extension to the spinal canal or the neuroforamina was observed. CT-guided biopsy was performed under CT-fluoroscopy guidance, in prone position (fig 4). In the sample tube, the cylinders of tissue taken had a fat like appearance; being pale yellowish in colour and were floating over the formalin surface. Pathological examination revealed bone marrow elements and megakaryocytes (fig 4b). The final diagnosis was bilateral myelolipoma with location in the paravertebral region. Due to the benign nature and the asymptomatic presentation of these multiple tumours no further treatment was required.

A comparative case with adrenal myelolipoma is provided in the figures section (fig 5).

DISCUSSION

Myelolipoma is an uncommon benign tumour, composed of mature fat tissue and haematopoietic elements (myeloid and erythroid cells) [1]. The German pathologist Edgar von Gierke first described it in 1905 when he noticed such a lesion in the adrenal gland, but it was not until 1929, that the lesion

was given its name, "myelolipoma", by the French pathologist Charles Oberling [2,3]. Generally, myelolipomas are adrenal lesions and extra-adrenal myelolipomas (EAMLs) are a very rare entity.

Epidemiology:

The incidence of myelolipoma is less than 1% on post-mortem and accounts for 7-15% of adrenal masses [1,4]. Nowadays it is incidentally discovered at ultrasound or computed tomography [4]. In the future, the incidence of these lesions may increase due to the expanding use of radiological investigation. The incidence of EAMLs is not exactly known but in an autopsy series, of 67 cases with myelolipomas, submitted to the archives of the Armed Forces Institute of Pathology (AFIP) between 1981 and 1997, only 10 cases (about 14% of the cases in this study) were observed with extra-adrenal location [4]. In our search in Pubmed, over 100 cases of EAMLs were identified (table 1). Myelolipomas are usually found between the sixth and eighth decade, although, EAMLs have also been described in younger patients [1,5,6].

Etiology:

Although several theories have been discussed, the origin of myelolipoma remains unclear. Theories include remnants of fetal bone marrow, embolism of bone marrow cells, and hyperplasia of heterotopic reticulum cells [7,8]. Chang et al. described a case of adrenal myelolipoma with a translocation t(3;21)(q25;p11). A similar change, t(3;21)(q26;p11), is found in haematopoietic neoplasms, such as myelodysplastic syndromes and chronic myeloid leukaemia. This finding suggests that myelolipoma is a derivative from misplaced haematopoietic cells [9]. A study performed by Bishop et al. showed myelolipomas which display X-chromosome inactivation in both fat and haematopoietic elements, which suggests clonal origin of myelolipoma [10].

Pathology:

Myelolipomas are usually unilateral, and very rarely bilateral [1]. EAMLs are very rare, about half of which occur at the presacral region and retroperitoneal space. Other, uncommon, locations have been described and Table 1 summarizes all locations of EAMLs that have been found to date in our search in Pubmed. According to this summary, based on Pubmed cases, ours is the fourth published case, representing multifocal EAML in the posterior mediastinum [11,12,13].

Adrenal myelolipomas vary in size, from several millimetres to more than 30 cm, and usually in the range of 2-10 cm in diameter [14,1]. The mean diameter of the EAML, in the series of the AFIP, was 8.2 cm; ranging from 4-15 cm. The largest documented EAML, recorded in the studied literature, was 26x15x11cm in diameter [15]. Most myelolipomas are well circumscribed; a true capsule is not seen, rather, compressed connective tissue surrounding the lesions represents a pseudocapsule [16]. The cut sections show fat and soft tissue components. Fat amount is variable, ranging from almost complete fat to a few tiny foci in the soft tissue mass [17]. Haemorrhage is more common in larger lesions of more than 10 cm in diameter, with male predominance of 89% [16]. Calcification may also be found. Microscopically, myelolipomas contain mature fat cells and megakaryocytes (fig 4b) [1,14]. They are different from true bone marrow in that they contain no reticular sinusoids or bone spicules [16]. Adrenal myelolipomas may be found coincidentally with other lesions in the adrenal glands, such as adenomas and less commonly with pheochromocytoma or metastases. These cases are described as "collision tumours" [18]. Pathological features of EAMLs are very similar to adrenal myelolipomas, except that haemorrhage and calcifications are very rare.

Clinical issue:

Myelolipomas are usually asymptomatic and discovered incidentally on routine radiological examination. About 10% become large and can cause vague symptoms, such as pain [1,17]. EAMLs are usually asymptomatic, although symptoms may occur due to mass effect according to localization. For example; renal failure in the case of compression from perirenal lesions, sciatic pain or urinary retention in presacral lesions or numbness and gait disturbance in case of intraspinal lesions [19,20,21,22]. The most significant complication that could occur with large myelolipomas is acute haemorrhage, which can be present with pain and that localizes in the back or flanks, with nausea, vomiting, hypotension and anaemia [16]. Haemorrhage in EAMLs is a very rare complication; no reported case in the studied literature records a clinical picture of acute haemorrhage. Myelolipomas are hormonally inactive. About 10% only are associated with endocrine disorders, such as Cushing's syndrome, congenital adrenal hyperplasia, Conn's syndrome, pheochromocytoma, hyperparathyroidism or adrenogenital syndrome [17,23,24,25,26]. No case of a hormonally active EAML was found.

Imaging

General features:

Due to the identical tissue composition of adrenal and extra-adrenal myelolipomas pathologically, imaging features are the same.

Conventional radiology:

Adrenal myelolipomas are difficult or even impossible to detect on plain radiography, except in cases of very large lesions with fat predominance where a lucent mass may be seen [4]. They can also be seen if calcified [14]. EAMLs may be seen depending on their location, as in our case of a paravertebral thoracic lesion (fig 1).

Ultrasound:

The well-defined fatty masses in myelolipomas appear echogenic in ultrasound [27]. Myeloid tissue is heterogeneous in appearance [1]. Haemorrhage and calcification change the sonographic pattern. Haemorrhage appears usually as low-echo areas compared to fat, and calcification appears as hyperechoic areas with acoustic shadowing [4]. According to location endosonography can be applied in the work up [28].

Cross sectional imaging:

Cross sectional imaging is necessary to confirm the origin of myelolipoma and crucial to differentiate these rare lesions from other, more common, tumours. Multiplanar

reconstruction (MPR) may be helpful in determining the exact location of the lesion.

Computed Tomography:

Understanding the histological tissue composition helps in understanding the CT appearance. The fatty part of the tumour has a negative attenuation value (between -30 and -90 Hounsfield units) (fig 2b & 5b) [1]. Myeloid component of the tumour appear higher in attenuation than the fatty part or other surrounding fat, for example retroperitoneal fat (fig 5). Enhancement is seen in the myeloid tissue after injection of contrast media [14]. When fat and myeloid tissue is diffusely mixed, the attenuation value will be between fat and water [17]. Myelolipomas usually show a recognizable pseudocapsule (fig 5a, c & d) [1,16,14]. CT is superior in detecting haemorrhage, which appears as areas of high densities. It is useful in detecting the size of haemorrhage and also the causative mass in cases of acute abdomen [4]. Calcification is seen in about 20% of adrenal myelolipomas, and only in very few cases of EAMLs [1,29,30]. Calcification is hyperdense and often punctate [17]. It may be related to previous haemorrhage.

Magnetic Resonance Imaging:

The key feature on MRI is the hyperintense signal of fat on both T1WI and T2 WI (fig 3a &b). The myeloid elements have low signal intensity on T1WI and moderate signal on T2 WI (fig 3a &b). According to the admixture of fat and myeloid tissue, MRI imaging features can be categorized in 3 groups: Group 1, where fat predominates, so lesions will be homogenous hyperintense on T1WI. Group 2, where there is mixed fatty and myeloid components, so lesions will be heterogeneous with contrast enhancement. Group 3, where myeloid cells predominate, so lesions will show nodules with hypointense T1 signal and moderate T2 signal with enhancement after contrast injection [31]. Macroscopic fat is easily detected on MRI using fat suppression techniques (fig 3c &e) or on Short-Tau Inversion Recovery (STIR) (fig 3f), by loss of signal in the fatty parts of the mass [1,14]. Fat will also show chemical shift artefacts, or loss of signal in the out-of-phase sequence in voxels containing both fat and water, resulting in an appearance called "Indian ink" or "etching artefacts" [32]. In case of haemorrhage, MRI features vary widely, according to the age and size of haemorrhage [4].

Nuclear medicine:

Nuclear medicine examinations can play a role in the diagnosis of myelolipoma, such as bone marrow scintigraphy using Technetium-labelled monoclonal antibodies directed against myeloid elements [33].

Angiography:

In cases of unclear origin of the tumour, angiography can help in defining the blood supply [1]. It may also help in delineating the vasculature of the mass prior to surgery. The morphology of adrenal myelolipoma in angiography is predominantly avascular with a peripheral rim of vascularity from branching vessels [14].

Differential diagnosis

Adrenal myelolipoma:

Adrenal myelolipomas must be differentiated from other fat containing lesions of the adrenal glands, such as adenomas, which lack myeloid components and also lack true fat density even in the presence of intracytoplasmic lipid, which can be detected by chemical shift imaging. Adrenal adenomas classically show a washout of contrast on the delayed imaging phase.

Adrenal myelolipomas with low fat content need to be differentiated from other adrenal lesions, such as: Pheochromocytomas, which are usually highly vascular; adrenal carcinoma and metastases, which usually have a higher intensity than myelolipomas; adrenal lymphomas, which are usually of a homogenous soft tissue-density, and lastly, from ganglioneuroma and neuroblastoma which are seen in children and young adults and are commonly associated with syndromes like neurofibromatosis, multiple endocrine neoplasia, von Hippel-Lindau disease or paraganglioma-syndromes [1].

Extra-adrenal lesions from neighbouring structures can be confused with adrenal myelolipomas, such as retroperitoneal lipomas, liposarcomas and renal angiomyolipomas [34].

Extra-adrenal myelolipoma:

Generally EAMLs should be differentiated from extra-medullary haematopoiesis (EMH), as there are similar morphological aspects between these two entities, the differences will be discussed later. Otherwise the differential diagnosis of EAMLs depends on the anatomic localization of the lesions. Many other lesions in the retroperitoneal space, being the most common location of EAMLs, should be easily to differentiate: Lipomas lack the myeloid tissue; well-differentiated liposarcoma are poorly marginated with infiltrative growth pattern and teratomas are usually detected in a younger age group and may be associated with vertebral anomalies.

In our case the two main differential diagnoses are EMH and neurogenic tumours; both of which are typically located in the paraspinal region and can also show multiplicity. Therefore a comprehensive discussion of this differential diagnosis is warranted (table 3).

EMH is a compensatory mechanism in chronic anaemia by formation of blood elements outside the bone marrow cavity, due to marrow failure or ineffective circulating mature blood cells. This is encountered in the liver and spleen, occasionally, forming paravertebral masses [35]. Any other mesenchymal tissue can be involved. In the pathological specimen, it is a non-capsulated mass with discrete flesh colour. Histologically, it is best described as marrow elements obtained from outside the bone marrow [36]. It is seen between the third and fourth decades in patients with chronic anaemia such as thalassaemia (common in the Mediterranean region), or sickle cell anaemia (common in Africa) [37]. Patients have usually received repeated blood transfusions. The lesion itself is asymptomatic, and it rarely compresses the

spinal cord. Patients suffer from signs and symptoms of chronic anaemia. Various lines of treatment are described, for example: Blood transfusion, hydroxyurea which increases the production of haemoglobin F, Irradiation in cases of cord compression, and excision, which, has a high risk of recurrence and may cause anaemic crisis [36]. On imaging, EMH-lesions appear well circumscribed, usually more than 5 cm in diameter. Fatty deposition occurs only in long standing lesions so they are usually homogenous and iso- to mildly hyperintense to muscles on both T1 and T2 WI. They show homogenous enhancement, only in cases of fatty deposition they show heterogeneity. Technetium 99m sulfur colloid can detect EMH-lesions. Other helpful findings on imaging include hepatosplenomegaly and signs of intramedullary hyperplasia, like thickened trabeculae and widened ribs.

The second differential diagnosis of our case is the neurogenic tumours. These include nerve sheath tumours (schwannomas, neurofibromas, and their malignant counterparts) and ganglion cell tumours (neuroblastoma, ganglioneuromas and ganglioneuroblastomas).

For simplicity we will discuss only the neurofibroma (NF) as an example. NF is a benign nerve sheath tumour, and is the most common cause of posterior mediastinal tumours [38]. It can also be found along any peripheral nerve. 10% of these tumours are multiple [39]. Macroscopically it is a non-encapsulated, solid tumour of variable appearance and may show cystic degeneration [39,40]. Microscopically it is formed of nerve sheath cells and collagen bundles [41]. NFs may be associated with von Recklinghausen's disease (neurofibromatosis I) with increased incidence of other neurogenic tumours such as optic glioma [42]. Malignant transformation may occur especially in cases of neurofibromatosis. Peak manifestation age is 20-30 years [39]. The lesion may be asymptomatic or may cause pain due to nerve entrapment or malignant transformation [40]. Patients may show other signs of von Recklinghausen's disease such as café au lait spots and neurofibromatous nodules. Surgical excision of the localized lesion may be advised. Recurrence rate is higher in cases of multiple or plexiform lesions [39,40]. On imaging, it may be localized, diffuse or plexiform [39]. Neurofibromas are typically smooth round tumours, which may show cystic degeneration or calcification. Extension into neuroforamina may give the dumbbell shape appearance [40]. On CT they are homogenously hypodense. On T1 WI the centre of the lesion may have higher signal than the periphery in contrary to T2 WI where the periphery has a higher signal [40]. After contrast injection, they show mild to moderate homogenous enhancement or a target appearance [40]. FDG-PET can differentiate malignant transformation by the higher standardized uptake value (SUV) in malignant lesions [39]. Other manifestations of neurofibromatosis may be visible in imaging such as cutaneous nodules, bone deformities, remodelling, erosions and scalloping as well as widened neuroforamina [40].

Other entities, with paravertebral location, should be easy to differentiate. Malignant pleural lesions, such as pleural mesothelioma, have an infiltrative nature and volume reducing effect on the lung. Secondary lymphoma is more common than primary lymphoma of the chest wall, usually accompanied by mediastinal lymph node enlargement and sclerosis of the adjacent ribs. Subpleural lipomas, as well as fibrin bodies lack myeloid elements. Intrathoracic splenic tissue occurs only on the left side with other signs of previous trauma, such as rib fractures or diaphragmatic rupture.

Diagnosis, prognosis & treatment:

The key to the diagnosis of adrenal and EAMLs is the presence of fat intermingled with myeloid elements and also the benign nature of the tumour. In most cases, diagnosis of adrenal myelolipomas can be confidently based on CT or MRI features alone [17]. Due to the rarity of EAMLs, it may occasionally be difficult to establish the diagnosis from imaging features only. In cases where diagnosis is uncertain and in those with low fat content, a histological sample will be helpful. Percutaneous fine needle biopsy (FNA) is simple, safe and effective. It will demonstrate numerous trilineage haematopoietic cells and a variable proportion of mature adipose cells. The presence of megakaryocytes is also an important feature [17,43,44]. Intraoperative cytodiagnosis, on touch preparation, can also be used in diagnosis. This is an important adjunct to frozen sections of fresh tissues, especially when tissue is technically unsuitable for cryostat section [45].

The prognosis is excellent, and therefore when diagnosis is certain, surgery is not necessary for small non-haemorrhagic myelolipomas [1,23]. In some cases a follow up, with CT or MRI, is appropriate [6]. Surgery is recommended in symptomatic patients, or when there is progressive growth with mass effect [6]. Some surgeons recommend surgery for large tumours (over 9 cm in diameter) due to the increased risk of haemorrhage with consecutive acute abdomen [27]. Other surgeons recommend laparoscopic adrenalectomy for tumours larger than 4 cm [46]. In fact, less than 40 published cases of myelolipomas have presented with signs and symptoms that required surgical resection [6].

Due to the rare incidence of EAMLs, no general surgical guidelines are mentioned in the studied literature and most surgical excisions were performed because of the uncertainty regarding the nature of the tumour or because of mass effect, for example in the case of intraspinal myelolipoma [21]. Risk of recurrence after excision is minimal due to the benign nature of these tumours, so there is usually no need for postoperative follow up [47]. Interventional radiology and embolization can play a role in the treatment of haemorrhage [47,48].

TEACHING POINT

Extra-adrenal myelolipomas are rare lesions, but the likelihood of detecting such lesions may increase with the increasing use of radiological investigations, therefore awareness of the typical location and appearance of these benign tumours is important in the differential diagnosis of fat-containing lesions. Fine needle biopsy is helpful in confirming the diagnosis in uncertain cases so that an asymptomatic patient will avoid unnecessary surgery.

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FIGURES

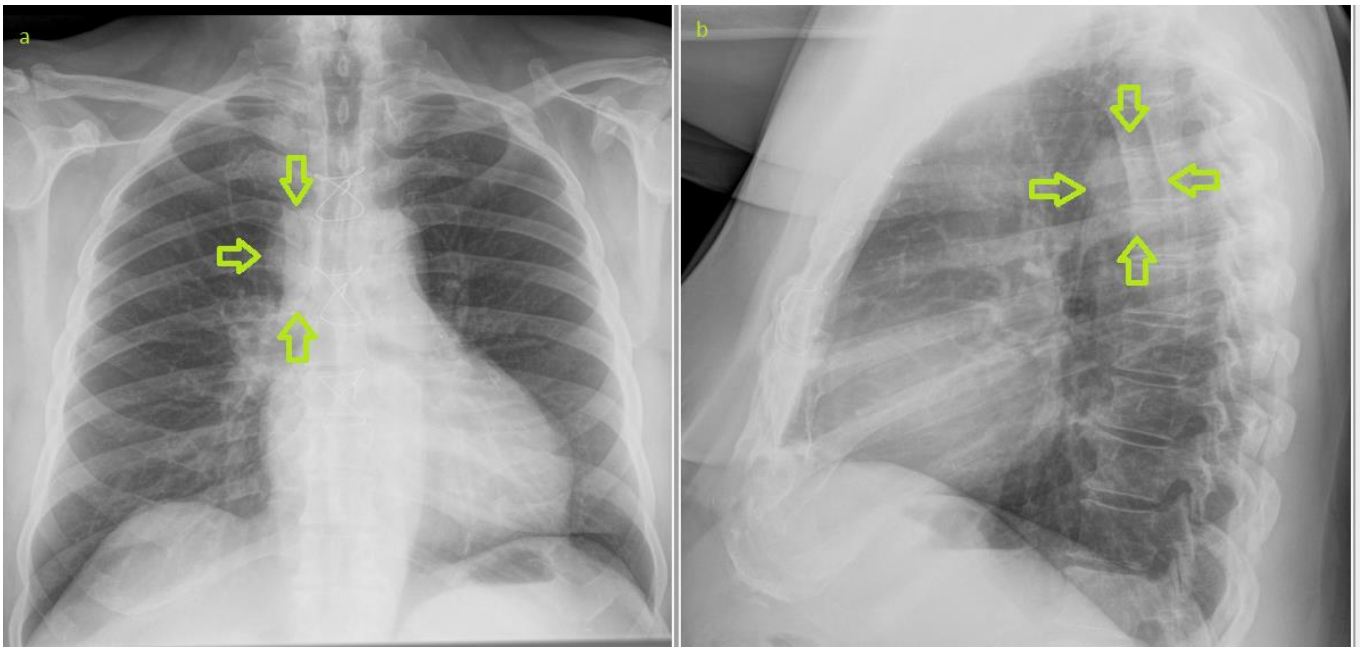

Figure 1: 70-year-old male with bilateral multifocal paravertebral extra-adrenal myelolipoma. Chest X-ray showing incidentally detected right paravertebral mass (arrows). Plain chest radiography, posteranterior (a) and lateral (b), erect posture.

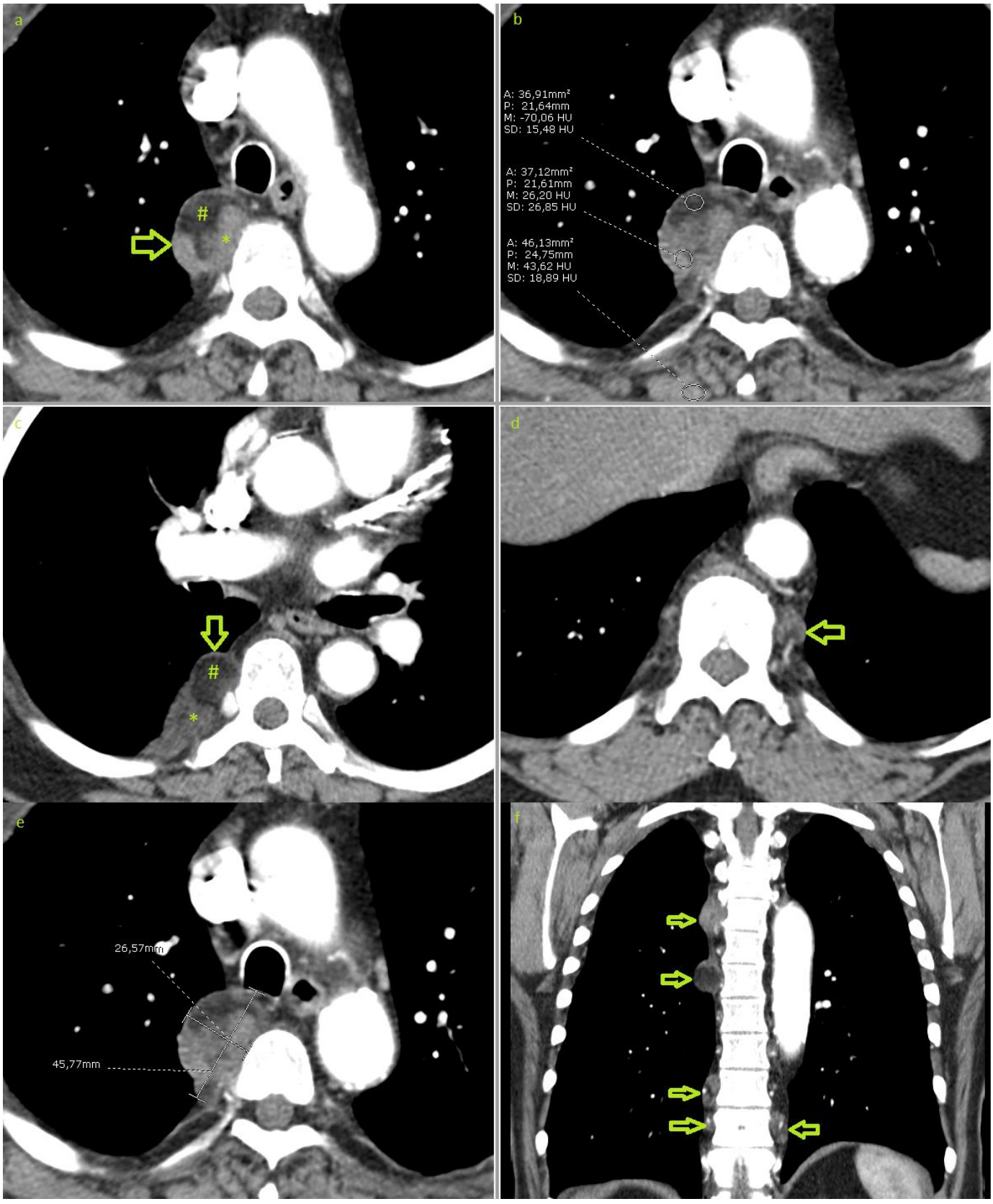

Figure 2: 70-year-old male with bilateral multifocal extra-adrenal myelolipoma. Contrast enhanced CT of the chest in an arterial phase demonstrating a well-circumscribed right paravertebral mass at the level of the aortic arch measuring 45x26x56mm(a & e). The mass shows mixed density, partially hypodense with -70 hounsfield units (b) due to fat content (#) and partially hyperdense due to myeloid tissue (*). Multiple smaller lesions are shown bilaterally (arrows in c, d & f). No infiltration of the neighbouring tissues. (Technique: 16-MDCT scanner, Automatic tube current modulation ranging between 131 and 250 mA, 120KVp. 5mm slice thickness. Soft tissue window, level/width: 15/350. i.v. injection of 60ml of 300mg/ml iodine concentration non-ionic contrast. a)- e) axial plane, (f) coronal reformation).

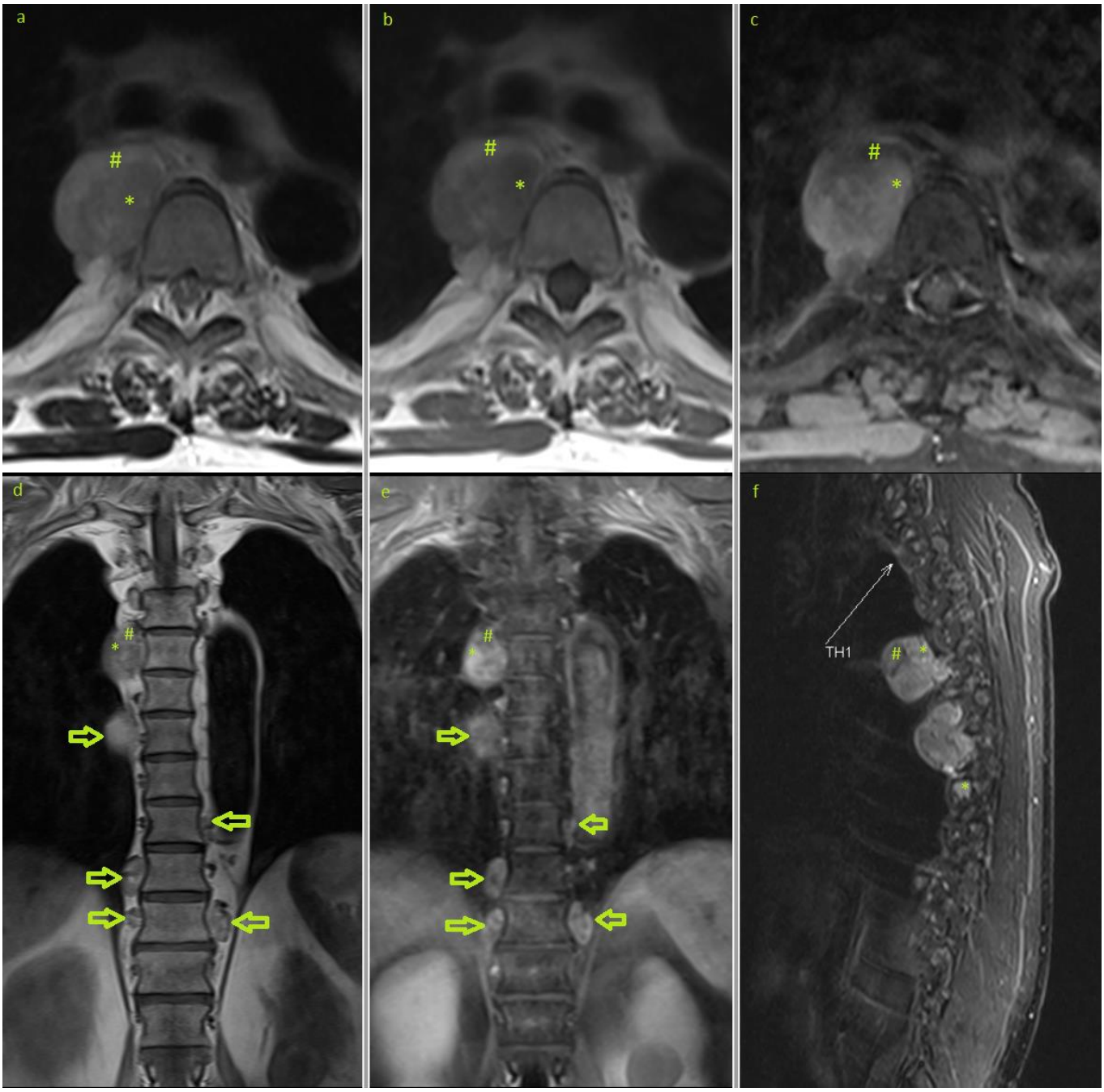

Figure 3: 70-year-old male with bilateral multifocal paravertebral extra-adrenal myelolipoma. MRI of the thoracic spine showing a right paravertebral mass with mixed signal intensity, partially hyperintense on T2 (a) and T1WI (b) due to the fat content of the mass (#) which shows signal drop-out on the fat suppression images (c & e) and on STIR sequence (f), and partially isointense on T2 (a) and hypointense on T1WI (b) due to the myeloid component (*) which shows hyperintensity on STIR (f), and moderate enhancement (c & e). Other similar lesions (arrows) are shown on the coronal plane (d). (Technique: 1.0 T scanner. a) axial T2WI: TR/TE: 3990/105, slice thickness 8, spacing 11.20, acquisition matrix: 256x205. b) axial T1WI: TR/TE: 509/11, slice thickness: 8, spacing 11.20, acquisition matric: 256x205. c) axial contrast enhanced T1WI with fat suppression: TR/TE: 742/12, slice thickness: 8, spacing: 11.20, acquisition matrix: 256x205. Administration of 15ml gadolinium based contrast agent. d) coronal non-enhanced T1WI: TR/TE: 863/13, slice thickness: 6, spacing 7.20, acquisition matrix: 187x512. e) coronal contrast enhanced T1WI with fat suppression: TR/TE: 1020/11, slice thickness: 6, spacing 7.20, acquisition matrix: 205x256. f) Sagittal Short tau inversion recovery (STIR): TR/TE: 3330/63, slice thickness: 3, spacing 3.60, acquisition matrix: 256x205)

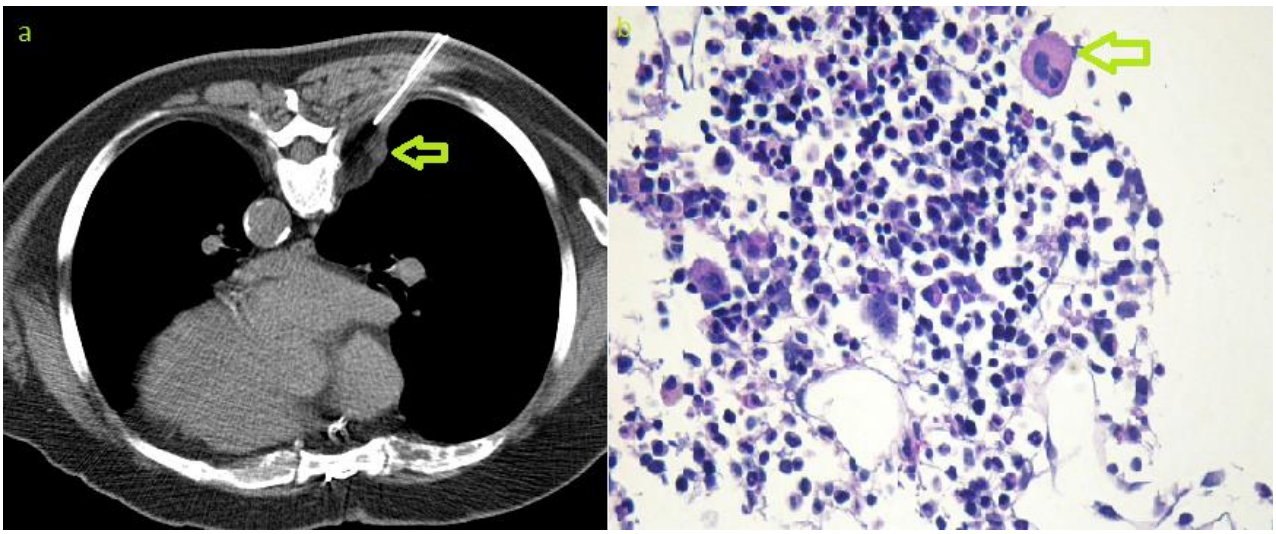

Figure 4: 70-year-old male with bilateral multifocal paravertebral extra-adrenal myelolipoma. CT-guided biopsy. a) axial non-enhanced CT obtained during biopsy procedure showing the needle that was advanced in a dorsal approach for biopsy of the paravertebral lesion (arrow). b) Photomicrography (Periodic acid Schiff stain, magnification 200x) showing bone marrow cells and megakaryocyte (arrow). Photomicrograph image courtesy of Prof. Alexander Tzankov, pathology department, University Hospital Basel, Switzerland)

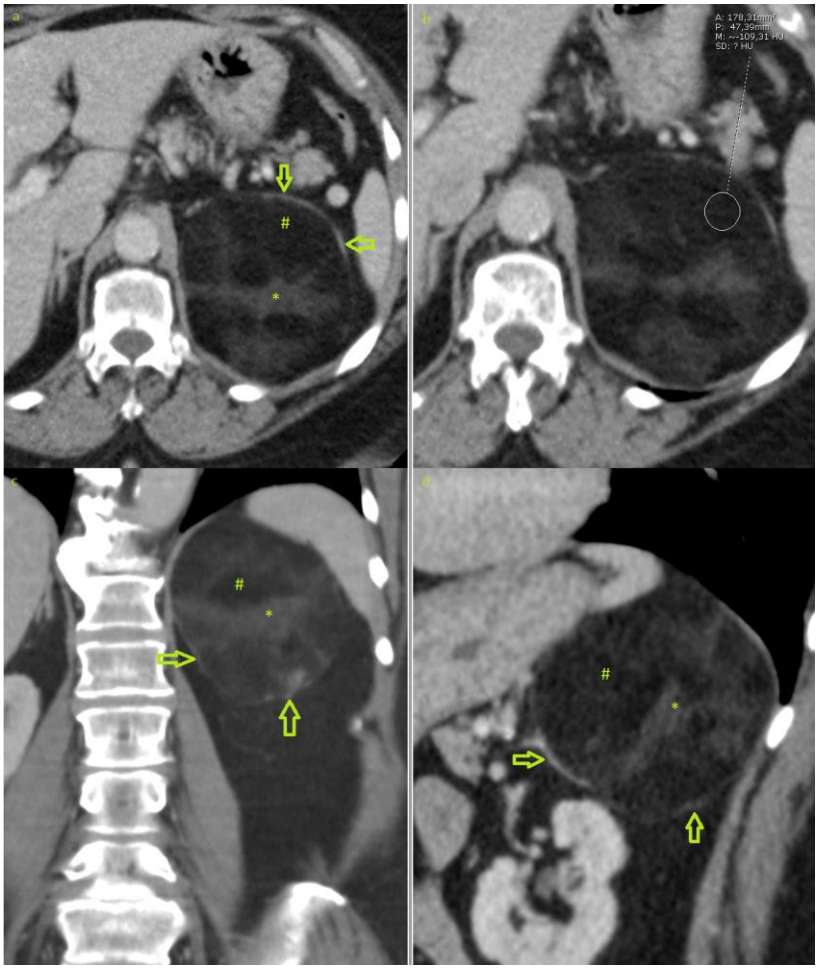

Figure 5: (comparative case) 68-year-old female with left adrenal myelolipoma. Contrast enhanced CT of the abdomen in a venous phase showing a well-circumscribed mass in the region of the left adrenal gland measuring 86x99x95mm. The mass is composed of fat cells (#) with density of -109 HU(b) and myeloid tissue with relatively higher attenuation. The mass shows a pseudocapsule (arrows in a, c &d). No infiltration of the neighboring structures. (Technique: 16-MDCT scanner. Automatic tube current modulation ranging between 300 and 440 mA, 120 KVp, 5mm slice thickness. Soft tissue window, level/width: 40/400. i.v. injection of 100 ml Imeron 300. Coronal and sagittal reformatted CT with 5mm slice thickness. a) &b) axial planes, c) coronal reformation and d) sagittal reformation).

Single EAML	No. of cases	Multiple EAML	No. of cases
Head and Neck			
-Mandible	**1**		
-Nasal Cavity	**1**		
Chest			
-Chest wall	**1**	**-Thoracic**	**2**
-Endobronchial	**1**	**-Posterior mediastinum**	**2**
-Mediastinum	**8**		
-Pleural	**2**		
-Pulmonary	**2**		
-Thoracic	**1**		
Abdomen and Pelvis			
-Hepatic	**13**	**-Bilateral renal**	**2**
-Presplenic	**1**	**-Retroperitoneal**	**1**
-Stomach	**1**	**-Greater omentum**	**1**
-Mesentery	**2**		
-Perirenal	**8**		
-Renal hilum	**2**		
-Renal sinus	**3**		
-Retroperitoneal	**10**		
-Presacral	**33**		
-Lower pelvis	**1**		
-Ovarian	**1**		
-Prevesical	**2**		
Intralymphonodular	**1**		
Intraspinal	**1**		
EAML with simultaneous involvement of multiple organs			
-Retroperitoneal and intrathoracic			**2**
-Renal and posterior mediastinum			**1**
-Generalized (retroorbital, chest, abdomen and pelvis)			**1**
-Adrenal and EAML (retroperitoneal)			**1**

Table 1: Summary of different locations and number of corresponding cases of Extra-adrenal myelolipomas (EAMLs) found on PubMed.

Facts and figures about myelolipomas:
- <1% of autopsies
- 7-15% of incidental adrenal masses
- 6^{th}- 8^{th} decade
- 14% of myelolipomas are extra-adrenal
- 50% of Extra-adrenal Myelolipomas (EAMLs) are presacral & retroperitoneal
- Hemorrhage is common in larger lesions (>10cm) with male predominance 89%
- 20% of adrenal myelolipomas show calcifications
- 10% of myelolipomas are symptomatic
- 10% associated with endocrine disorders
- Surgery is indicated in lesion more than 9 cm

Table 2: Facts and figures about myelolipoma

	Extra-adrenal myelolipoma	**Extra-medullary haematopoiesis**	**Neurofibroma (Example of neurogenic tumors)**
Definition	Benign tumour composed of fat and myeloid tissues	Formation of blood elements outside the bone marrow cavity	Benign nerve sheath tumour
Etiology	Still unclear	-Marrow failure -Ineffective circulating mature blood elements	Unknown or syndromic
Incidence	Extremely rare	Rare	Uncommon
Pathological features			
Site	-Presacral -Retroperitoneal -Other rare sites	-Spleen/ liver -Paraspinal -Other sites: (any mesenchymal tissue)	-Posterior mediastinum -May occur along any peripheral nerve
Multiplicity	Usually single	Multiple	10% multiple
Capsule	Pseudocapsule	Non capsulated	Non capsulated
Macroscopic	Yellow fat areas on cut section	Discrete flesh coloured mass	-Solid tumour -Cystic degeneration
Microscopic	Megakaryocytes	Marrow elements outside the bone marrow	-Nerve sheath cells -Collagen bundles -Myxoid degeneration
Associated (Related) conditions	Usually non	-Haemoglobinopathies (thalassemia, sickle cell anaemia) -Haemosiderosis (in case of repeated transfusions)	-Neurofibromatosis I -other neurogenic tumours (e.g. optic glioma) -Malignant transformation
Clinical features			
Age peak	6^{th}-8^{th} decade	3^{rd}-4^{th} decade	3^{rd} -4^{th} decade
Demographics	--	-Thalassemia: Mediterranean countries -Sickle cell anaemia: African Americans	--
Symptoms	-Asymptomatic -Depending on the location symptoms from mass-effect possible	-EMH itself is asymptomatic -May cause symptoms in case of spinal compression	-Asymptomatic -Mass-effect -Nerve entrapment -Pain (due to malignant transformation)
Symptoms of associated conditions	--	-Signs and symptoms of chronic anaemia -Hepatosplenomegaly	-Von Recklinghausen's disease: .Café au lait spots .Neurofibromatosis nodules
Treatment	Asymptomatic lesions (confidently diagnosed by imaging) should be left alone	-Blood transfusion -Hydroxyurea -Irradiation -Excision	Surgical excision in localized lesions.
Prognosis	Very good	Excision is associated with high recurrence rate and may cause anaemic crisis	Recurrence in case of multiple or plexiform lesions
Imaging features			
General features	Well marginated Fat & myeloid tissues	Well marginated (Fatty deposition may occur in long standing lesions) (Usually >5cm)	-Localized, diffuse, plexiform -Dumbbell shape -Smooth round appearance -Cystic degeneration -Calcification
X-ray (depending on site & size)	Well demarcated mass	Well demarcated mass	Well demarcated mass
CT	-Fat: negative attenuation -Myeloid: higher attenuation	-Homogenous hypodense -Heterogeneous in case of fatty deposition	Homogeneous hypodense
T1 WI	-Fat: hyperintense -Myeloid: low signal	Iso to mildly hyperintense to muscles	Centre of the lesion have higher signal than periphery
T2 WI	-Fat: hyperintense -Myeloid: moderate signal	Iso- to mildly hyperintense to muscle	Periphery has higher signal than the centre
Contrast	Enhancement of myeloid components	-Homogenous mild enhancement -Heterogeneous in case of fatty deposition	-Homogenous mild/moderate enhancement -Target appearance
Scintigraphy	Monoclonal antibodies directed against myeloid elements	Technetium 99m sulfur colloid marrow scan	FDG-PET Higher SUV in malignant transformation
Other findings	---	-Hepatosplenomegaly -Intramedullary hyperplasia: .Thickened trabeculae .Widened ribs.	Neurofibromatosis: .Cutaneous nodules .Bone remodelling, deformities, erosions and scalloping .Widened neuroforamina

Table 3: Comparison between extra-adrenal myelolipoma (EAML), extra-medullary haematopoiesis (EMH) and Neurofibroma (as an example of neurogenic tumour)

	Adrenal	**Extra-adrenal**
Incidence	-<1% of autopsy -7-15% of incidental adrenal masses	-Very rare -About 14% of all myelolipomas
Age predilection	6^{th}-8^{th} decades	Younger patients may be also involved
Etiology	Not quite understood	
Multiplicity	-Unilateral -Rarely bilateral (10%)	Multiple lesions are extremely rare
Site	Adrenal glands	-Presacral -Retroperitoneal -Other rare sites
Size	Usually 2-10cm	Usually 4-15cm
Gross pathology	-Pseudocapsule -Fat and soft tissue	
Hemorrhage	In larger lesions (>10cm)	Extremely rare
Calcification	20 % usually due to hemorrhage	Extremely rare
Microscopic picture	Mature fat cells & megakaryocytes	
Clinical Picture	-Usually asymptomatic -10% causing vague symptoms	-Usually asymptomatic -Symptoms according to location & size
Imaging key findings	-Fat: low attenuation in CT & high in both T1 & T2 WI -Myeloid tissue: higher density, low signal on T1 WI, moderate on T2 WI, moderate enhancement	
Differential diagnosis	Adenoma	-According to location -Extra-medullary hematopoiesis -Lipoma/Liposarcoma
Prognosis	Excellent	Excellent
Indication for surgery	-Symptomatic lesions -Larger tumors (risk of hemorrhage)	-Uncertainty of diagnosis -Mass effect

Table 4: Comparison between adrenal and extra-adrenal myelolipomas

ABBREVIATIONS

AFIP - Armed Forces Institute of Pathology
CECT - Contrast material Enhanced Computed Tomography
CT - Computed tomography
EAML - Extra-adrenal myelolipoma
EMH - Extra-medullary Hematopoiesis
FDG-PET - Fluordeoxyglucose Positron Emission Tomography
FNA - Fine Needle Biopsy
HU - Hounsfield Units
MPR - Multiplanar reconstruction
MRI - Magnetic resonance imaging
NF - Neurofibroma
STIR - Short-Tau Inversion Recovery
SUV - Standardized Uptake Value
WI - Weighted Images

KEYWORDS

Extra-adrenal; adrenal; paravertebral; myelolipoma; incidental; CT; MRI; fat

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