Bilateral Adrenal Myelolipoma Associated with Thalassemia: A Case Report and Literature Review


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Abstract

Myelolipomas are rare benign tumors composed of mature fat and bone marrow elements, typically found in the adrenal gland, but have been reported in extra-adrenal locations. Adrenal myelolipoma seldom produces symptoms unless it attains considerable size or hemorrhage into itself. The origin of adrenal myelolipoma remains obscure, various theories have been proposed. Here, we present a case of giant bilateral adrenal myelolipoma associated with thalassemia. In this case, hematopoietic stimulus of chronic anemia might have been associated with the development of adrenal myelolipoma. In patients with incidental finding of adrenal myelolipoma, underling red cell disorders causing extramedullary hematopoiesis should be excluded. ( J Intern Med Taiwan 2003;14:190-195 )

Key Words: Adrenal Myelolipoma, Thalassemia, Adrenalectomy

Introduction

Adrenal myelolipomas are relatively rare tumors, usually originate from the adrenal cortex and histologically consisting of mature fat and hematopoietic tissue 1. In the past, a myelolipoma was usually found incidentally at autopsy 2. As noninvasive imaging techniques improved, premortem diagnosis of adrenal tumors is increasing 3. Adrenal myelolipomas are usually asymptomatic, seldom produces symptoms unless it attains considerable size or hemorrhages into itself 2,4. The etiology of myelolipoma is not fully understood 5,6. Adrenal myelolipoma are not extramedullary hematopoiesis and usually not associated with any specific hematological disorder 6,7.
However, in patients with severe anemia, concomitant with adrenal myelolipoma has been sporadically reported. We present this case of nonfunctioning bilateral adrenal myelolipoma of very large dimensions in a patient with thalassemia. Whether such association was merely by chance or related to some etiologic factors remained unclear.

Case Report
A 38 year-old male patient complained of left side chest pain and flank pain after a traffic accident. He had history of anemia since childhood but without transfusion or further treatment. Abdominal CT scan revealed a well-encapsulated soft tissue mass, 12x10x8 cm, in the left suprarenal area with internal bleeding, and another 9x8x7 cm mass, composed of fat, soft tissue and calcification, is present in the right suprarenal area, splenomegaly and increased hepatic density which was compatible with chronic hemosiderosis. Laboratory tests showed Hb 8.3 g/dL, Hct 29.3%, RBC 3.93 x 106/uL, WBC 5400/uL, MCV 74.6 fL, MCH 21.1 pg, MCHC 28.3 g/dL, Platelet 143x103 /uL, PT 17.1 sec, APTT 55.0 sec, TIBC 207 ug/dL (260-420 ug/dL) and Ferritin 185 ug/L (55-200 ug/L). Biochemistry showed blood sugar 82.9 mg/dL, GOT 105.7 IU/L, GPT 121.1 IU/L, BUN 5.6 mg/dL, creatinine 0.71 mg/dL, K 4.59 mEq/L. He was a hepatitis B carrier, since the liver biopsy had not been performed, the abnormal liver function test may due to either chronic viral hepatitis or hemochromatosis.

A hemoglobin electrophoresis showed Hb A 87.5%, Hb Barts 10.4%, Hb A2 0.9%, Hb CS (Hb constant spring) 1.2%, which was compatible with alpha thalassemia with Hb constant spring heterozygosity. Endocrine studies showed normal adrenal function with cortisol level 13.4 ug/dL at 8 am (6-25 ug/dL) and 10.6 ug/dL at 4 pm respectively, plasma aldosterone concentration 115 pg/mL (37-240 pg/dL), plasma renin activity 2.5 ng/mL/hr (0.15-3.9 ng/mL/hr). Urine metanephrines appeared metanephrine 107 ug/day (52-341 ug/day), normetanephrine 88.4 ug/day (88-444 ug/day) and methoxytyramine 195 ug/day (10-296 ug/day). Secondary hypogonadism due to hemochromatosis was noted with low serum FSH < 0.3 mIU/mL (1.4-1.8 mIU/mL), LH 0.7 mIU/mL (1.5-9.3 mIU/mL) and low testosterone level, 50 ng/dL (241-827 ng/dL). Sella MRI showed atrophic adenohypophysis.

He underwent exploratory laparotomy with left adrenectomy and splenectomy. The tumor was a 585 gram well-capsulated hemorrhagic mass, pathohistological study revealed a myelolipoma composed of mature adipose tissue and large amount of hematopoietic elements. Followed up 30 months later, enlargement of the right adrenal tumor, 11.5 x10x7.5 cm, was showed by MRI study, the adrenal function still remained normal, and hemoglobin level was 10.2 g/dL without blood transfusion. Discussion
Myelolipomas are benign tumors composed of variable amounts of mature fat and bone marrow like hematopoietic cells, typically found in the adrenal gland, but have been reported in extra-adrenal locations 1,9. Myelolipoma is distinct from true bone marrow without presence of reticular sinusoids, and also distinct from extramedullary hematopoietic tissue, which does not contain fat tissue 9. Advances in diagnostic imaging have resulted in an increasing recognition of adrenal myelolipoma 1,10,11, which accounts for 7-15% of all adrenal incidentalomas 3. Adrenal myelolipoma were first described by Gierke in 1905 and named by Oberling in 1929 9,12. With the introduction of new diagnostic tools, the surgical removal of myelolipomas occurred more frequently 11,13. In 1985 deBlois and DeMay reported the first case of a myelolipomas based solely on radiographic findings and pathologic findings by CT-guided fine needle aspiration 14. Numerous reports of this entity have been published in the literature, and more than half of cases have been reported since 1980.

Prevalence of adrenal myelolipoma at autopsy was 0.08-0.8% 1,4. Male and female patients are affected equally and there is no laterality preference 4,7,15. Most adrenal myelolipomas are small (diameter < 4cm) and asymptomatic (70%) 16. Several giant forms weighting up to 5.5 kg have been reported 17. Large tumors may cause acute hemorrhage and local symptoms secondary to mechanical compression. Majority of tumors are unilateral, however, a few cases with bilateral adrenal myelolipomas have been reported 2. Very large bilateral adrenal myelolipomas, such as ours, are exceedingly rare 6,16,18.

The diagnosis of myelolipomas made by demonstrating the presence of fat, very low CT attenuation values ( – 30 to –100 Hounsfield Units), within an adrenal mass on CT scan. The size and lipoma characteristic appearance usually make diagnosis accurately, and the presence of hematopoietic tissue allowing differentiation from other tumors 1,12. Proportion of fat detected on CT is variable. On MRI, the presence of fat is best demonstrated on T1-weighted images, the fat containing area in a myelolipoma should be equal in signal intensity to that of subcutaneous and retroperitoneal fat at all pulse sequences 12,17,19.

Generally, adrenal myelolipomas require no treatment however if symptomatic or if diagnosis is in doubt, surgery is needed. Usually only monolateral adrenalectomy is performed, even in the presence of bilateral tumors, to preserve adrenal function 18. The etiology and pathogenesis of myelolipoma remains obscure, various theories have been proposed including hyperplasia of embryologically displaced myeloid cells which developed from embryonic rests of mesenchymal stem cells located in the adrenal gland 5,7,20; embolism of hematopoietic stem cells lodging in the adrenal gland 7,9
and adrenocortical cells metaplasia of the reticuloendothelial cells of blood capillaries in response to stimuli, such as necrosis, infection or stress. The latter theory is most widely accepted, and is supported by clinical and experimental evidence showing that lipid and myeloid cells can originate from the adrenal reticulum in response to certain stimuli 7.

Association of adrenal myelolipomas with obesity, arteriosclerosis and hypertension is frequently reported 21,22. Generally myelolipomas cause no adrenal dysfunction but may be associated with Cushing's syndrome, 21-hydroxylase deficiency, hermaphrodism, Addison's disease and hyperaldosteronism 9,21,22,23. Myelolipomas are not extramedullary hema-topoiesis, and generally not associated with hematologic disorder 2,7. But the development of extra-adrenal myelolipomas in patients with severe anemic complications has occasionally been reported 24. Some authors even suggested that prolonged erythropoietic stimulation might play the etiologic role in some patients, and with regression of hemolysis after splenectomy, the hematopoietic component then degenerated into a fatty component 24. Large adrenal myelolipomas have also been reported in patients with chronic hemolysis, including hereditary spherocytosis 24, sickle cell anemia and thalassemia 20. Such an association may suggest that tumor growth is also under the extrinsic stimulation of erythropoietin.

In this case, development of adrenal myelolipoma may be incidentally associated with thalassemia, but it is also possible that hematopoietic stimulus by chronic anemia of thalassemia might induce compensatory hematopoiesis in the adrenal gland. This assumption supports the choristoma theory, by introduction of differentiated hematopoietic tissue during embryogenesis, as the etiology of adrenal myelolipoma 24,25. We emphasis that in patients with incidental finding of myelolipoma, red cell disorders should be carefully excluded 20,24.

![Fig.1](image1.png) **A&B. Abdominal CT:** voluminous heterogeneous retroperitoneal masses of the bilateral adrenal gland, Right: 9x8x7 cm and Left: 12x10x8 cm, with a mixture of fat and marrow densities.

![Fig.2](image2.png) **A&B. Abdominal MRI:** huge heterogeneous masses on the upper poles of both kidney.

![Fig.3](image3.png) **Sella MRI showed atrophic adenohypophysis**

![Fig.4](image4.png) **A&B. Histological section of the tumor represents a myelolipoma characterized**
by large amount of hematopoietic cells of the myeloid, erythroid and megakaryocytic series and some mature adipose cells (H&E stain, reduced from X100 & X400).

References
15. El-Mekresh MM, Abdel-Gawwad M, El-Diasty T, El-Baz M, Ghoneim MA. Clinical, radiological and histological features of adrenal myelolipoma: review and

雙側腎上腺骨髓脂肪瘤合併地中海型貧血：
一病例報告暨文獻回顧

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摘 要

骨髓脂肪瘤是一種罕見的，含有成熟脂肪組織及骨髓成分的良性腫瘤，大部份位於腎上腺，但亦有位於腎上腺以外的部位。腎上腺骨髓脂肪瘤除非大到一定的程
腎上腺骨髓脂肪瘤的生成原因目前還不是很清楚，各種不同的學說曾被討論過。在此，我們提出一例雙側巨大腎上腺骨髓脂肪瘤合併地中海型貧血的病例報告。在這樣的病例中，慢性貧血所致血球生成之刺激，是否可能與腎上腺骨髓脂肪瘤的產生有關，值得我們進一步探討。對於意外發現的腎上腺骨髓脂肪瘤，應注意有無潛在的紅血球疾病導致骨髓外造血之可能性。