Bilateral cavernous hemangiomas of the adrenal glands
Presentation and management of an unusual incidental finding

Ann. Ital. Chir., 2013 84: 693-697
pii: S0003469X13018964

Laura Lorenzon*, Vincenzo Ziparo*, Salvatore Caterino*, Andrea Vecchione**, Alessandra Camboni**, Marco Cavallini*

Faculty of Medicine and Psychology, University of Rome "La Sapienza", Rome, Italy
**Surgical and Medical Department of Clinical Sciences, Biomedical Technologies and Translational Medicine*
***Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology*

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BACKGROUND: *Cavernous hemangiomas are rare tumors, mainly localized in the liver and skin, but also reported in the cerebellum and eye fundus as a part of von Hippel Lindau Syndrome. Adrenal hemangiomas are less than 1% of all the adrenal neoplasms and usually are reported as benign, non-functioning tumors, originating from the adrenal cortex and surrounded by normal or hyperplastic adrenal tissue.*
CASE REPORT: *We report the case of patient with bilateral hemangiomas of the adrenal glands associated with a subclinical hypercortisolism, incidentally detected during the pre-operative staging evaluation of a right colon cancer.*
DISCUSSION: To *the best of our knowledge, this is the third bilateral adrenal hemangioma ever reported case, the first one treated with surgical resection (right adrenalectomy and surgical resection of the left adrenal mass, sparing the left adrenal gland below). Pathogenesis, presentation and management of this rare neoplasm are here reviewed and discussed.*

KEY WORDS: Adrenal glands, Cavernous hemangiomas, Liver, Skin

Introduction

Cavernous hemangiomas are rare tumors, mainly localized in the liver and skin, but also reported in the cerebellum and eye grounds as a part of von Hippel Lindau Syndrome [1].
To the best of our knowledge, there are less than 80 cases of adrenal cavernous hemangiomas reported in literature, just 2 bilateral cases, the last one reported in 1933 [2,3].
Adrenal hemangiomas have been reported as <1% of all the adrenal neoplasms and the vast majority have been described as benign, non-functioning tumors, originating from the adrenal cortex and surrounded by normal or hyperplastic adrenal tissue [4,5].
We report the case of patient with bilateral hemangiomas of the adrenal glands associated with a subclinical hypercortisolism, incidentally detected during the pre-operative staging evaluation of a right colon cancer.

Pervenuto in Redazione Febbraio 2012. Accettato per la pubblicazione Aprile 2012
Correspondence to: Laura Lorenzon, Surgical and Medical Department of Clinical Sciences, Biomedical Technologies and Translational Medicine, Faculty of Medicine and Psychology University of Rome "La Sapienza", "St. Andrea" Hospital, Via di Grottarossa 1035-39, 00189 Rome, Italy (email: laura.lorenzon@uniroma1.it)

Case Report

A 77-year-old man was admitted to our Department complaining rectorrhagia, abdominal pain and weight loss. His past medical history was consistent with hypertension, benign prostatic hyperplasia and emphysema. Physical examination revealed a palpable abdominal mass localized in the right lower abdominal quadrant.
Chest and abdominal CT scan documented a neoplasm in the cecum and a solid and well capsulated mass of 10 cm in the left adrenal gland with irregular enhancement after intravenous contrast; another 3 cm solid mass was documented in the upper side of right adrenal gland (Fig. 1a); no other anomalies were documented in the abdomen or chest.
Colonscopy documented a neoplasm in the cecum and the histological examination of the biopsy disclosed a mucinous adenocarcinoma; laboratory tests including hormonal evaluation documented a sub-clinical hypercortisolism (lack of suppression of cortisol values at midnight with undetectable ACTH values).
The patient underwent right hemicolectomy, right adrenalectomy and surgical resection of the left adrenal mass (Fig. 1b), sparing the left adrenal gland below.
The histological examination of the colon was consistent with an adenocarcinoma of the colon staged pT3 pN0, G3 Stage II, Dukes B; macroscopic examination of the adrenals revealed two masses, respectively of 4 and 10.2 cm in size, solid and capsulated with hemorrhagic areas and necrosis, with the histological pattern of cavernous hemangiomas, surrounded by adrenal nodular hyperplasia. Microscopic evaluation disclosed multiple large blood vessels filled with erythrocytes and blood clots. A fibrotic capsule divided enlarged vascular vessels from surrounding adrenal tissue; several hemosiderophages were found in the stroma. Flattened endothelial cells were lining in the vascular spaces (Fig. 2).
Further 5-FU based adjuvant therapy was recommended after the oncological consultation, with a 25% age-related reduction of standard dose. Follow up has been carried out with a total body CT scan at the end of chemotherapy (six months after the surgical treatment) and was negative for recurrences.

Discussion

Adrenal hemangiomas have been reported as <1% of all the adrenal neoplasms as benign, usually non-functioning tumors, originating from the adrenal cortex [4-5]; the size has been reported ranging between 2.5 and 25 cm [6-7], and patients' age ranging between 25 and 79 years, with a higher prevalence in women [1]. In 1906 Terrier and later Ellis in 1952, classified adrenal cysts in: parasitic cysts, retention or congenital glandular cysts, cystic adenomas, endothelial cysts and pseudocysts. Endothelial cysts were subdivided into angiomas and the far more common lymphangiomas [8-9]. Hemangiomas are classified as cavernous, capillary, sclerosing or hemangiopericitoma [1,10]. Most adrenal hemangiomas are cavernous, as Factor VIII immuno-peroxidase stain demonstrates an endothelial cell lining in the cavernous space [1].
We reported the third case of bilateral adrenal hemangioma, the first one treated with surgical resection. We consider treating the patient with right adrenalectomy and surgical removal of the left adrenal mass in order

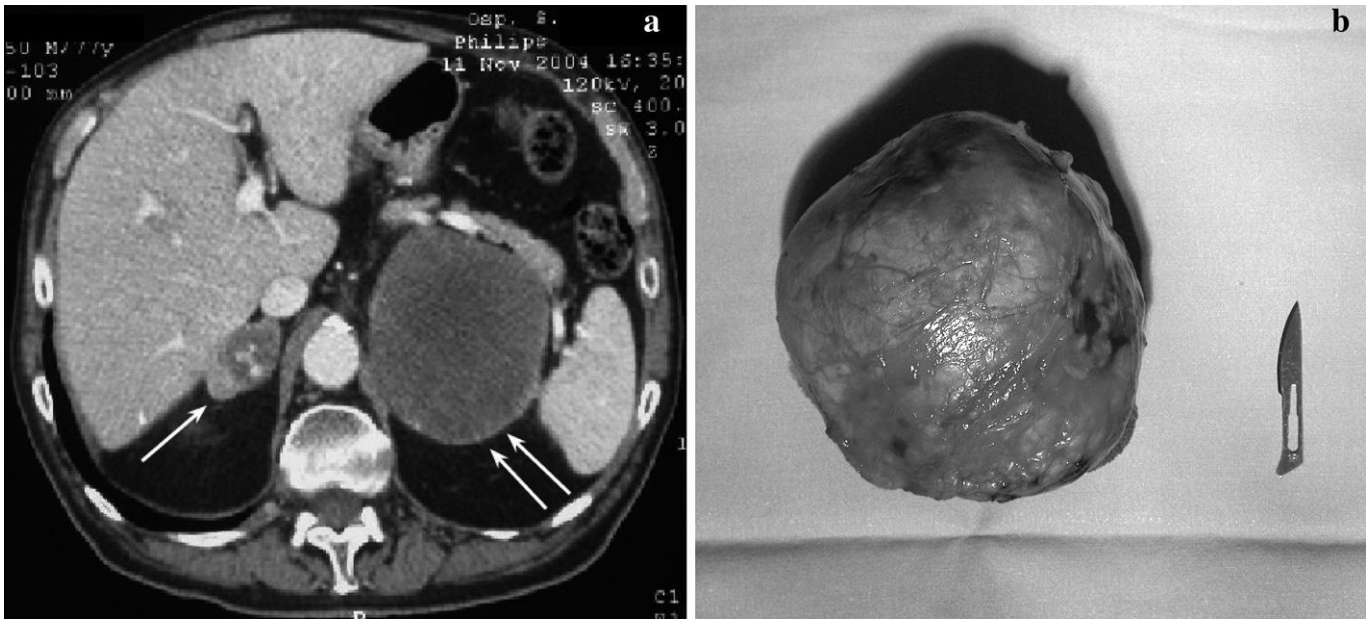

Fig. 1: A) Bilateral cavernous hemangiomas of the adrenal glands. The CT abdominal scan shows the two adrenal neoplasms (arrows); B) Left adrenal mass, surgical specimen.

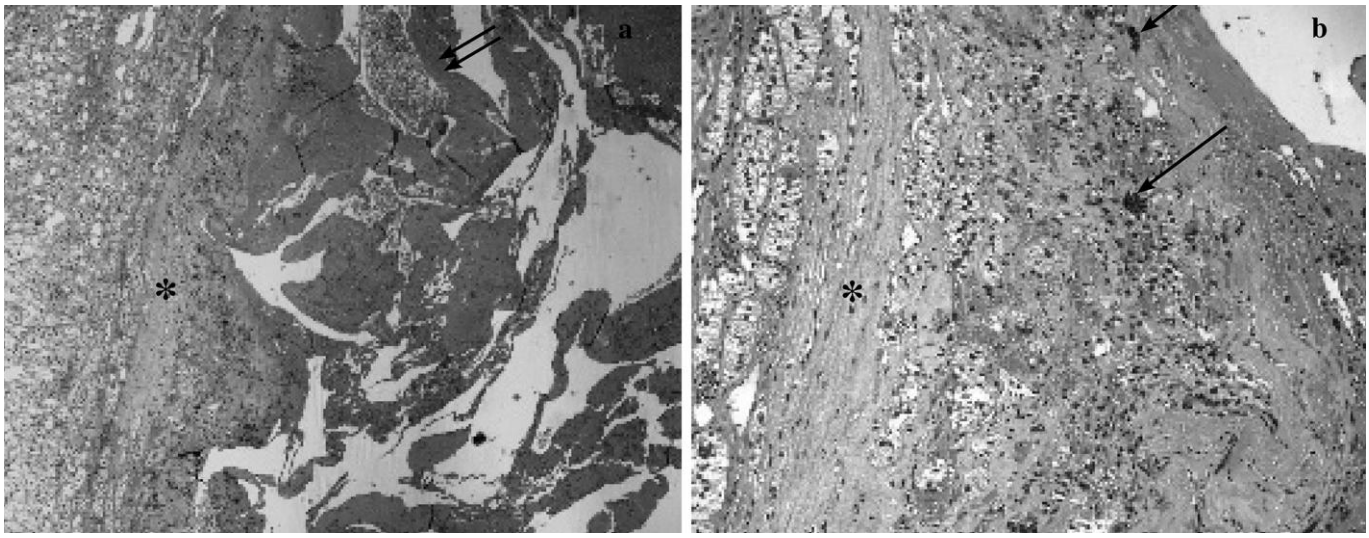

Fig. 2: Histological findings. A) The lesion is composed of large-size vessels separated from the adrenal tissue by a fibrotic capsule (asterisk). Flattened endothelial cells lining vascular spaces (two arrows). B) Some hemosiderophages in the stroma (arrows) (H&E stain, magnification a: 2.5x; b: 10x).

to stage the patient and define histology, suspecting adrenal metastases.

The surrounding adrenal tissue showed adrenal hyperplasia, however, the pathogenesis of these tumors is still unclear. It could be hypothesized that a sub-clinical hormonal dysfunction (hypercortisolism) could have caused an alteration in the blood supply and a consequent bilateral adrenal hyperplasia leading to an hemangioma development, otherwise an alteration in the blood supply due to the presence of hemangiomas could have provoked the adrenal hyperplasia.

According to Willis, hemangiomas are congenital malformations originating from mesenchymal cells [11]. Some authors claim traumatic and hemorrhagic phenomena inside cystic lesion, others claim hormonal dysfunction which leads alteration in the normal blood supply. Johnson postulated that the associated adrenal hyperplasia could be related to an increased hemangiomatous blood supply [12-13]. Pignatelli described a case of non-functioning adrenal cavernous hemangioma in a setting of congenital adrenal hyperplasia due to 21-hydroxylase deficiency: according with the author, the occurrence of hemangioma could be a consequence of the cortisol deficit or a consequence of the patient's arterial hypertension [4].

Cavernous adrenal hemangiomas are usually non-functioning; some patients may have non-specific symptoms due to the mechanical/space–occupying effect of the tumor or acute bleeding into the cystic tumor [14]. There are just three cases in literature of adrenal hemangiomas associated with hormonal dysfunction: the first one simulating pheochromocytoma [15], another one associated with mineralocorticoid excess [16], the last one with aldosterone and catecholamine hyper-secretion [17].

Diagnostic evaluation is usually carried out with ultrasound, CT scan and MRI. The sonographic findings are usually non-specific, including: well circumscribed mass with heterogeneous echogenicity in the suprarenal region, or irregular anechoic areas with hyperechoic septa [6].

A consistent radiographic finding on plain radiography or CT scan is the presence of phleboliths (smooth, calcified bodies with lucent centres, irregular or star shaped) which could be found in 27-64% of the cases, but could also be observed in other adrenal diseases as carcinomas or tubercular lesions, so are considered suggestive but not pathognomonic of hemangiomas [18].

CT scan shows an hypoattenuating mass with necrotic areas, with enhancement of peripheral vascular lakes after intravenous contrast [19]. MRI has the best diagnostic potential showing peripheral enhancement of the tumor; the dynamic study and the delayed phase images show spotty peripheral enhancement, which correlated with the dilated vascular spaces.

Hyperintensity on T1-weighted images is believed to represent focal hemorrhages in the tumor. T2-weighted images can show hyperintensity due to central necrosis and hemorrhage, or hypointensity do to central fibrosis [20].

US biopsy is not clinically helpful and may cause bleeding in a high vascular lesion [21].

Management of adrenal hemangioma is surgical: resection is indicated for histological definition, for ruling out possible malignancies (since an association with hemangioendotheliomas has been reported in the past) [5] and for preventing bleeding, or spontaneous rupture [6,18].

Johnson described the first surgical resection for an adrenal hemangioma in 1955 [13], and since then, the vast majority of adrenal hemangiomas reported were treated with open surgery. Nowadays laparoscopic and retroperineoscopic removal of adrenal tumors are proposed as standard procedure, and minimally invasive removals of

adrenal hemangiomas (up to 12 cm) has been reported [22-23].

Management of adrenal masses incidentally detected is still a clinical and surgical clue: morphological appearance and past medical history should be consider, hormonal setting should be evaluated in order to differentiate functioning and non-functioning tumors, and size should be consider to stratified any risk of malignancies or bleeding. According with the NIH Consensus Conference Statement of 2002 adrenalectomy is indicated for incidentaloma that: a) are functioning, b) are larger than 6 cm, and c) have images characteristics suspicious for malingnacies. However, for lesions between 4 and 6 cm, and after exclusion of the reported criteria, the optimal strategy remain controversial (observation *vs* minimally invasive adrenalectomy) [24]. Beside this, according with a panel of experts appointed by the Italian Association of Clinical Endocrinologist, surgery is recommended for adrenal masses causing hormonal excess, otherwise suspicious for malignancy, but the threshold size indicative for a malignant disease is unknown; moreover there are insufficient evidences for or against surgery in subclinical Cushing's syndrome [25].

Indeed the proposed algorithm for characterize adrenal incidentalomas suggests to perform an hormonal and biochemical evaluation, evaluate the clinical and past medical history (for known malignancies) compare the incidental finding with a previous imaging evidence (if available), evaluate the attenuation values of the mass (since homogeneous mass with low attenuation value < 10 HU are usually benign), and evaluate the CT washout, otherwise MRI, PET and biopsy could be considered if the lesion remains difficult to determinate [26].

Beside this, the risk of bleeding related to size for an adrenal hemangioma is not generally consider in international literature, and further studies are advocated in order to help clinicians and surgeons in defining a common approach to these tumors.

Conclusions

Presentation of this rare case report and literature review has been herein discussed. Moreover, we would like to encourage further studies aimed to define the pathogenesis of these tumors and the pathological link with the adrenal hyperplasia, which is commonly observed in the surrounding adrenal tissue.

Riassunto

INTRODUZIONE: Gli emangiomi cavernosi sono neoformazioni rare, principalmente localizzate a livello del fegato e della cute, ovvero riportate a livello oculare o del cervelletto in quanto parte della sindrome di von Hippel Lindau. Gli emangiomi surrenalici rappresentano meno dell'1% delle neoformazioni surrenaliche e generalmente sono riportati come neoformazioni benigne, non funzionanti, che originano dalla corteccia surrenalica e circondate da tessuto surrenalico normale o iperplastico.

CASO CLINICO: Gli autori riportano il caso di un paziente con un emangioma bilaterale delle ghiandole surrenaliche associato a un ipercortisolismo sub-clinico, incidentalmente diagnosticato durante la stadiazione pre-operatoria di un tumore del colon destro.

DISCUSSIONE: Il caso riportato rappresenta il terzo caso di emangioma surrenalico biletarale riportato in letteratura, e il primo caso ad essere trattato con resezione chirurgica (surrenalectomia destra e resezione della massa surrenalica di sinistra con conservazione della surrenale sottostante). La patogenesi, le modalità di presentazione e il management di queste rare neoformazioni sono state affrontate e discusse.

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