A case of myxoid adrenocortical neoplasm: computed tomography and magnetic resonance imaging characteristics

Hiroki Fukuhara,[1] Vladimir Bilim,[1] Hiroya Ohtake,[2] Yoshie Yahagi,[3] Yoshihiko Tomita[1]

[1]Department of Urology, [2]Department of Pathology, [3]Department of Diagnostic Radiology, Yamagata University Faculty of Medicine, Yamagata, Japan

Abstract

Myxoid adrenocortical neoplasms are rare; to our knowledge, only 56 cases have been reported in the literature. Therefore, distinguishing benign from malignant cases is challenging. Although the histopathological features of myxoid adrenocortical neoplasia have been amply demonstrated, their imaging characteristics are yet to be reported. We describe here these characteristics for such a neoplasm. Our patient, a 70-year-old male, was found to have a 3-cm left adrenal incidentaloma through a non-enhanced computed tomography. Attenuation measurements were 22 Hounsfield units on precontrast imagery, and percentage enhancement washout was 92%. Magnetic resonance imaging showed no loss of signal intensity in T1-weighted out-of-phase images, but high signal intensity on T2-weighted and diffusion-weighted images. Left adrenalectomy was performed and the pathological diagnosis was confirmed as myxoid adrenocortical neoplasm. The imaging characteristics reported here will be beneficial to the differential diagnosis of myxoid adrenocortical neoplasms based upon image analysis and will help distinguish benign from malignant neoplasms.

Introduction

Myxoid adrenocortical neoplasms (MANs) are rare. Since Tang *et al*. first reported a case of myxoid adrenocortical carcinoma in 1979,[1] only 56 cases have been reported: 29 carcinomas, 24 adenomas, and 3 borderline tumors.[2-4] MANs are characterized by the presence of abundant extracellular Alcian blue-positive myxoid material, and cells are positive for melan-A, α-inhibin, synaptophysin, and vimentin. Although the histopathological characteristics of MAN have been thoroughly investigated, it is challenging to distinguish benign from malignant cases because of MAN's rarity and the lack of strict diagnostic criteria. However, although many reports have described the application of diagnostic imaging methods to adrenal neoplasms, no imaging findings for MAN have been reported. Therefore, this report may be helpful in the differential diagnosis of MAN.

Case Report

A 70-year-old man was found to have an adrenal mass on non-enhanced computed tomography (CT) scanning, performed as part of a detailed examination for liver dysfunction by the attending physician. He was referred to our hospital for further examination and treatment. Examination on admission revealed that the patient was moderately overweight (weight, 71.5 kg; height, 167.8 cm; BMI, 25.6) and hypertensive (133/75 mmHg); hypertension was treated with nifedipine. Laboratory findings were within normal ranges except for γ-guanosine triphosphate, which was 51 IU/L (normal range 10-47 IU/L). He also underwent endocrine evaluation, which showed no functional abnormalities. CT scanning demonstrated a solid, homogeneous mass (24×38×34 mm) with well-defined edges in the left adrenal gland. Attenuation measurements were 22 Hounsfield units (HU) on the precontrast image, 111 HU on the arterial phase image, and 29 HU on the delayed phase image (Figure 1). Magnetic resonance imaging (MRI) showed no loss of signal intensity in T1-weighted out-of-phase images but high signal intensity on T2-weighted and diffusion-weighted images (DWI) (Figure 2). A temporal enhancement effect was seen on dynamic MRI. Left open adrenalectomy was performed.

The mass was macroscopically visualized as a well-circumscribed, golden yellow tumor (Figure 3A), histologically characterized by an incomplete capsule and focally infiltrative margin. The tumor cells were arranged in gland-like structures and the background of the tumor was myxoid. In some areas, a trabecular pattern was also recognized. Tumor cells contained scant cytoplasm, although clear cells with relatively abundant cytoplasm were focally observed (Figure 3B, C). Hematoxylin and Eosin staining revealed that tumor cells were present outside the capsule and had infiltrated the fatty tissue without disruption of the reticulin network (Figure 3C, 3E). Mitotic figures were rare (<1/20 under high-power field). Tumor cells immunohistochemically stained positive for melan-A, α-inhibin, synaptophysin, and vimentin, and negative for p53; the MIB-1 index was 2%. The tumor fulfilled 2 of the Weiss criteria (paucity of clear cells, high nuclear grade only focally) (Figure 3D). Hough score and van Slooten index were 1.21 (diffuse growth pattern, pleomorphism) and 7.4 (regressive changes, structural changes, nucleoli), respectively.[4,5] Mitotane was not used as an adjuvant therapy. Neither recurrence nor metastasis was detected during the 10 months of follow-up. Long-term follow-up with imaging and adrenocortical hormonal measurement was implemented because two cases of recurrence have previously been reported.[6,7]

Discussion

Differentiation between malignant and benign of adrenocortical neoplasms is still challenging. Two cases of recurrence have previously been reported.[6,7] One of these relapsed five years after surgery. The patient's primary symptom was abdominal pain, and imaging demonstrated a large abdominal tumor.[7] The other case presented with increased levels of adrenocortical hormones preceding metastasis.[6] Several histopathological criteria have been proposed and developed to classify adrenocortical neoplasms.[4,5,8] Hough *et al*. indicated the mean histologic indices of benign

Correspondence: Hiroki Fukuhara, Department of Urology, Yamagata University Faculty of Medicine, 2-2-2 Iida Nishi, Yamagata, 990-9585, Japan.
Tel. +81.236.285.368 - Fax: +81.236.285.370.
E-mail: h-fukuhara@med.id.yamagata-u.ac.jp

Key words: adrenal gland attenuation, chemical shift imaging, histopathological analysis, myxoid adrenocortical neoplasms, percentage enhancement washout.

Contributions: HF, VB, YT acquired clinical data and performed patient follow-up; YY analyzed the neoplasm in detail using CT and MRI; HO performed and interpreted the histological examination.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 31 May 2013.
Revision received: 11 August 2013.
Accepted for publication: 11 August 2013.

Rare Tumors 2013; 5:e54
doi:10.4081/rt.2013.e54

tumors, indeterminate tumors, and malignant tumors were 0.17, 1.00, and 2.91, respectively.[4] Van Slooten *et al*. suggested that tumors with an index greater than 8 are associated with malignancy.[5] The Weiss scoring system is widely employed in diagnosing adrenocortical neoplasms and the presence of 3 or more criteria correlates with subsequent malignant behavior.[8] In this case, the tumor fulfilled 2 of the Weiss criteria. Paucity of clear cell is not an intrinsic phenomenon in MAN because 25 of 56 reported cases of MAN did not fulfill this criterion (24 adenoma, 1 borderline). It is hard to assess whether this tumor is benign or malignant because several criteria in these scoring systems are subjective and a lack of reproducibility, particularly in myxoid variants of adrenocortical tumors or *borderline* tumors with a Weiss score of 1 or 2.[2,9]

Therefore, other pathological parameters, such as frequency of mitosis, MIB-1, p53 immunoreactivity, and reticulin network, are used for accurate differential diagnosis of adrenocortical tumors.[9,10] MIB-1 has been reported to be present in at least 4% of cells in myxoid adrenocortical carcinoma, 3% or 4% in borderline tumors, and less than 3% in adenomas.[3,6,7] Nevertheless, because the presence of MIB-1 does not always reflect malignancy, it is difficult to judge whether the tumor in this case is benign or not using only this marker. Marco *et al.* proposed a *reticulin* diagnostic algorithm that focused on disruption of the reticulin framework. Disruption of the reticular network was observed in malignant cases, which also contained at least one of the three following additional parameters: necrosis, high mitotic rate, and the presence of vascular invasion.[10] Disruption of the reticulin network may possibly be useful for differential diagnosis, particularly in MAN. There are two reported borderline cases of MAN, both of which fulfilled Weiss score 1 (clear cell cytoplasm present in less than 25% of the tumor cells). One case had no evidence of recurrence or metastasis 9 months following surgical resection. In the other case, the presence of metastatic tumors in the small intestine 5 years after the surgery was confirmed.[7] Characteristics such as weight, myxoid area, gross pattern, and Ki-67 index, of both cases were similar; however, the reticulin framework was intact in the former case, as opposed to the latter case. Though capsular penetration is seen, in view of the intact reticulin framework, our case is likely to be a benign tumor.

Although the histopathological characteristics of MAN have been described in detail, the imaging features remain unreported. Approximately 70% of adenomas contain intracytoplasmic fat, whereas in nonadenomas the cytoplasm is relatively lipid poor, and thus, by evaluation of intracytoplasmic fat content, preoperative differential diagnosis can be performed by CT and MRI. Hounsfield unit values in fat-containing adenomas are lower than those in other soft-tissue structures, resulting in lower attenuation values on unenhanced CT than in nonadenomas. Furthermore, adenomas are well defined and often homogeneous in attenuation. Boland *et al.* showed that a threshold of 10 HU had 71% sensitivity and 98% specificity for characterizing adrenal masses, and specificity approached 100% when other features, such as adrenal size, shape, and alteration in lesion size, were considered.[11] Thus, dynamic contrast-enhanced CT should be performed to distinguish lipid-poor adenomas from malignancy.

Caoili *et al*. indicated that adenomas and

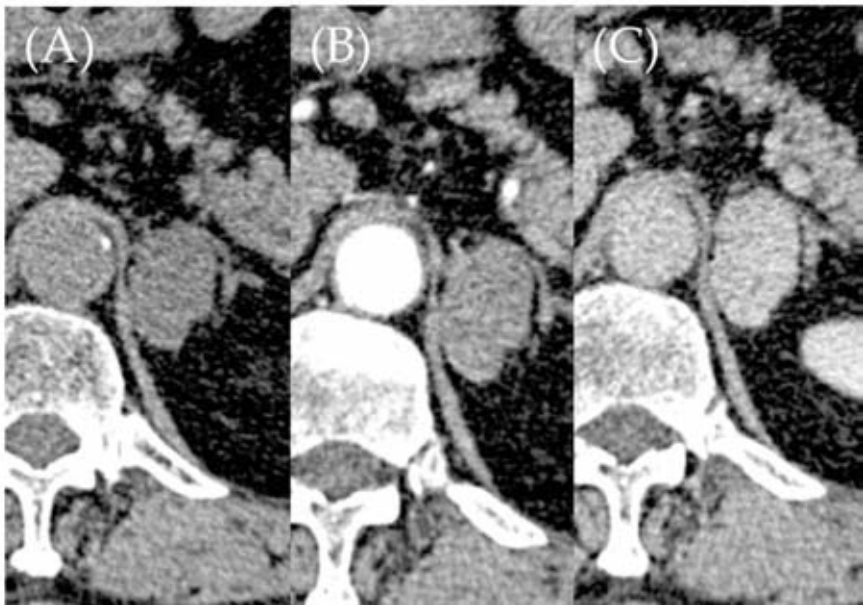

Figure 1. Computed tomography (CT) revealing a solid, well-defined edge and a homogeneous mass in the left adrenal gland. A) Unenhanced CT scan showing left adrenal mass (22 HU); B) enhanced CT scan showing left adrenal mass (111 HU); C) delayed enhanced CT scan showing left adrenal mass (29 HU). Enhancement washout = 82 HU (111-29 HU); enhancement = 89 HU (111-22 HU); percentage enhancement washout = 92% [(enhancement washout/enhancement) = (82/89) × 100].

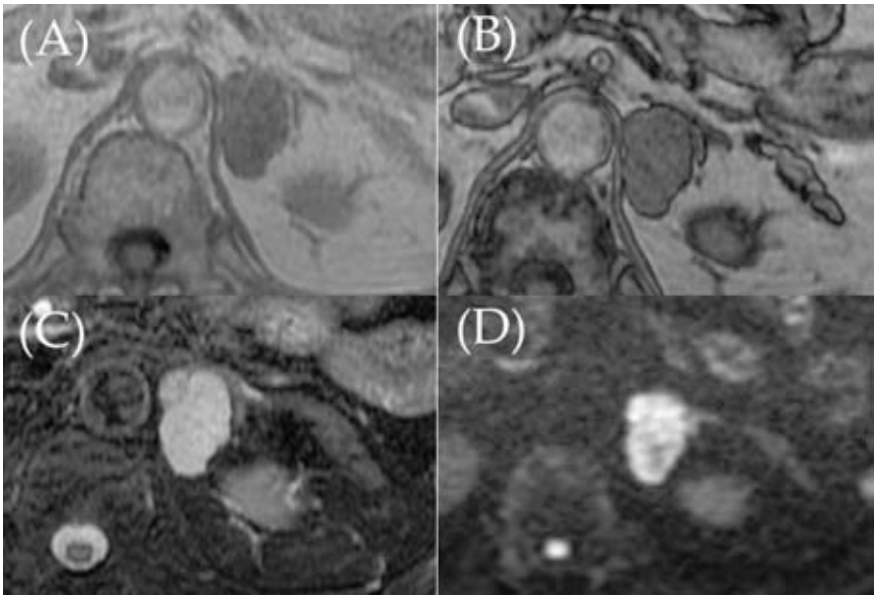

Figure 2. Magnetic resonance images showing an adrenocortical neoplasm exhibiting no loss of signal intensity on out-of-phase imagery. The neoplasm showed high signal intensity on T2-weighted and DWI images. A) Axial in-phase; B) out-of-phase; C) T2-weighted; D) DWI.

nonadenomas can be distinguished using a combination of unenhanced, contrast material-enhanced, and delayed enhanced CT. Percentage of enhancement washout is calculated as follows: enhancement washout/enhancement × 100, and the optimal threshold value of percentage enhancement washout for both lipid-poor and lipid-rich adenomas was reported to be 60%.[12] When CT findings are indistinct, MRI is the next imaging study of choice for characterizing adrenal lesions. Chemical shift MRI is the most sensitive technique for distinguishing adrenal adenomas from metastases, and this method also utilizes differentiation of intracytoplasmic fat content. Lipid-rich benign tumors appear darker on out-of-phase images than on in-phase images. In adrenal tumors containing no cytoplasmic fat, there is no significant signal loss on out-of-phase images, *i.e.*, adrenal signal intensity is the same on both in-phase and out-of-phase images. In this case study, the neoplasm showed well-defined edges and was homogeneous in attenuation on precontrast CT (attenuation measurement was 22 HU on the precontrast image and percentage of enhancement washout was 92%). These results suggest that this neoplasm exhibited the same pattern as typical lipid-poor adrenocortical adenoma. However, on MRI, this tumor did not show a loss of signal intensity in T1-weighted out-of-phase, indicating a different pattern to that of classic adrenocortical adenoma. In addition to the finding of loss of signal intensity, this tumor demonstrated high signal intensity on T2-weighted images and DWI, imaging features similar to those of pheochromocytoma. Although this tumor showed a paucity of clear cells and high nuclear grade, its characteristics were in accord with the pattern of lipid-poor adenoma with regard to imaging features. Our study will be helpful in distinguishing benign from malignant MANs.

Conclusions

Our study will be helpful in the differential diagnosis of adrenocortical neoplasms, where it is difficult to distinguish benign from malignant tumors solely based on imaging features. Myxoid adrenocortical tumor is very rare, and the only detailed report on the imaging features of MAN is the current one. It is therefore important to follow up this patient and to search for additional reports on the imaging features of MAN.

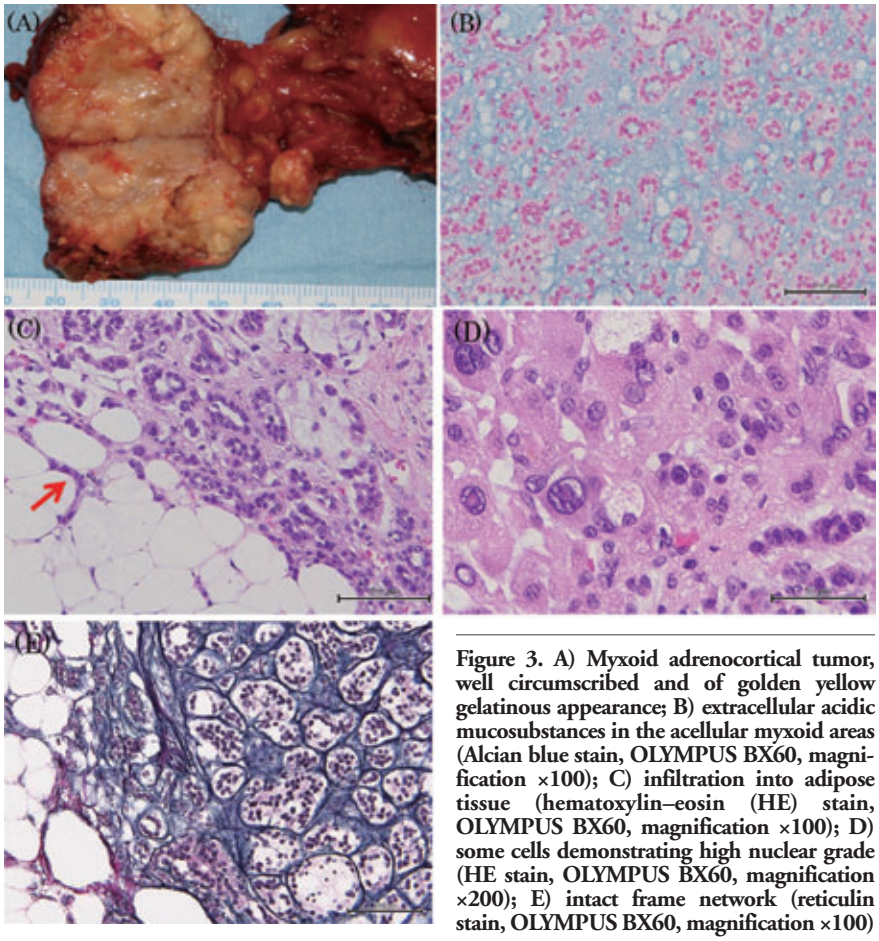

Figure 3. A) Myxoid adrenocortical tumor, well circumscribed and of golden yellow gelatinous appearance; B) extracellular acidic mucosubstances in the acellular myxoid areas (Alcian blue stain, OLYMPUS BX60, magnification ×100); C) infiltration into adipose tissue (hematoxylin–eosin (HE) stain, OLYMPUS BX60, magnification ×100); D) some cells demonstrating high nuclear grade (HE stain, OLYMPUS BX60, magnification ×200); E) intact frame network (reticulin stain, OLYMPUS BX60, magnification ×100)

References

1. Tang CK, Harriman BB, Toker C. Myxoid adrenal cortical carcinoma: a light and electron microscopic study. Arch Pathol Lab Med 1979;103:635-8.
2. de Krijger RR, Papathomas TG. Adrenocortical neoplasia: evolving concepts in tumorigenesis with an emphasis on adrenal cortical carcinoma variants. Virchows Arch 2012;460:9-18.
3. Zhang J, Sun J, Liang Z, Gao J, et al. Myxoid adrenocortical neoplasms: a study of the clinicopathologic features and EGFR gene status of ten Chinese cases. Am J Clin Pathol 2011;136:783-92.
4. Hough AJ, Hollifield JW, Page DL, et al. Prognostic factors in adrenal cortical tumors. A mathematical analysis of clinical and morphologic data. Am J Clin Pathol 1979;72:390-9.
5. van Slooten H, Schaberg A, Smeenk D, Moolenaar AJ. Morphologic characteristics of benign and malignant adrenocortical tumors. Cancer 1985;55:766-73.
6. Sheng JY, He HC, Zhu Y, et al. Myxoid adrenal cortical tumor: report of four cases. Chin Med J 2012;125:1672-4
7. Papotti M, Volante M, Duregon E, et al. Adrenocortical tumors with myxoid features: a distinct morphologic and phenotypical variant exhibiting malignant behavior. Am J Surg path 2010;34:973-83.
8. Weiss LM. Comparative histologic study of 43 metastasizing and nonmetastasizing adrenocortical tumors. Am J Surg Pathol 1984;8:163-9.
9. Papotti M, Libè R, Duregon E, et al. The Weiss score and beyond--histopathology for adrenocortical carcinoma. Horm cancer 2011;2:333-40.
10. Volante M, Bollito E, Sperone P, et al. Clinicopathological study of a series of 92 adrenocortical carcinomas: from a proposal of simplified diagnostic algorithm to prognostic stratification. Histopathology 2009;55:535-43.
11. Boland GW, Lee MJ, Gazelle GS, et al. Characterization of adrenal masses using unenhanced CT: an analysis of the CT literature. AJR Am J Roentgenol 1998; 171:201-4.
12. Caoili EM, Korobkin M, Francis IR, et al. Delayed enhanced CT of lipid poor adrenal adenomas. AJR Am J Roentgenol 2000; 175:1411-5.