Composite Adenomatoid Tumor and Myelolipoma of Adrenal Gland
Report of 2 Cases

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Adenomatoid tumor and myelolipoma are benign, hormonally inactive tumors that are often incidental findings in the adrenal glands. Myelolipoma is more common than adenomatoid tumor in this location but both are rare, and as yet, the pathogenesis of both remains unclear. We report 2 cases of composite adenomatoid tumor and myelolipoma, incidentally found in the adrenal gland on investigation for other diseases. To our knowledge, composite adenomatoid tumor and myelolipoma of adrenal gland has not been previously reported.

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Clinical Histories and Radiology
Case 1.—A 47-year-old previously healthy man was referred for the investigation of incidental adrenal masses that were identified during a computerized tomography scan performed for diverticulitis. Magnetic resonance imaging was done and confirmed the presence of a 5.6 × 5.3 × 2.7-cm mass in the right adrenal gland that was interpreted as a predominantly lipid-poor adenoma with fat in the inferior aspect, and a 1.5-cm nodule in the left adrenal gland that was radiologically consistent with an adenoma. He was also found to have diffuse hepatosteatosis and a splenule (accessory spleen). Results of serum cortisol and 24-hour urine collection for cortisol and adrenaline metabolites were normal. A laparoscopic right adrenalectomy was performed. The postsurgical recovery was uneventful.

Case 2.—A 52-year-old obese man was investigated for persistent hypertension (150/100 mm Hg) of 3 months’ duration that was difficult to control with pharmacotherapy. The urinary vanillylmandelic acid, catecholamine, metanephrine, and cortisol levels were normal, however. Computerized tomography scan and magnetic resonance imaging of the abdomen showed a 2-cm mass in the right adrenal gland, and the patient underwent a laparoscopic right adrenalectomy. His postoperative course was uneventful.

Cross and Microscopic Findings
The right adrenal gland of the first patient weighed 64 g and contained a well-circumscribed mass that measured 7.0 × 5.8 × 3.8 cm. The tumor was solid with a variegated yellow and tan cut surface and focal yellow speckled areas.

The right adrenal gland of the second patient weighed 36 g and measured 7.5 × 4.5 × 2.0 cm. Within the gland there was a well-circumscribed heterogeneous cystic and solid mass with hemorrhagic areas (Figure 1); the nodule measured 5.5 × 1.5 × 1.2 cm. There was a rim of cortical tissue at the periphery.

Both adrenal tumors were composed of a mixture of elements with different appearances surrounded by compressed cortical tissue. The tumor consisted of adrenal cortical tissue and scattered aggregates of lymphocytes with occasional follicle formation (Figure 2). There were islands of adipose and hematopoietic tissues resembling mature bone marrow (Figure 3). Myeloid, erythroid, and lymphoid cells and megakaryocytes were present, but precursor myeloblasts were not seen. A prominent component was composed of anastomosing tubules and cystic spaces lined by flat or plump epithelioid cells with scant eosinophilic cytoplasm and round to oval fairly uniform nuclei without atypia or mitotic activity (Figure 4). These epithelioid lining cells of the AT showed strong immunoreactivity for D2-40 antibody and calretinin (Figures 5 and 6) and weak reactivity for cytokeratin 5/6 (not shown).

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Figure 1. Gross appearance. The gland contains a circumscribed tumor that has a yellow to tan rough surface with focal cystic spaces and hemorrhage. The cortical tissue is compressed at the periphery.

Figure 2. Composite adenomatoid tumor and myelolipoma of adrenal. Tumor showing admixture of mesothelium-lined tubules, adipose tissue, hematopoietic tissue, and normal adrenocortical tissue (hematoxylin-eosin, original magnification ×10).

Figure 3. Myelolipoma. Hematopoietic tissue with numerous megakaryocytes is present within fat. Myeloid precursor cells are absent (hematoxylin-eosin, original magnification ×40).

Figure 4. Adenomatoid tumor. Anastomosing tubules are lined by flat epithelioid cells with scant eosinophilic cytoplasm and fairly uniform nuclei without atypia or mitotic activity (hematoxylin-eosin, original magnification ×40).

Figure 5. Adenomatoid component. The lining epithelium stains with the D2-40 antibody (original magnification ×10).

Figure 6. Adenomatoid component. The lining epithelium exhibits immunoreactivity for calretinin (original magnification ×10).
Adrenal Adenomatoid Tumor and Myelolipoma

Adenomatoid tumor is common in the genital tracts of both male and female patients but is extremely rare in the adrenal gland. Among the 26 cases reported, the majority occurred in men. Myelolipoma is more common in the adrenal gland and is found in 0.08% to 0.2% of autopsy cases; it is extremely rare in extra-adrenal sites. The pathogenesis of AT and myelolipoma is speculative, and the reason why these tumors occur in the adrenal is unclear because they arise from tissues that are presumably foreign to that gland.

With the use of immunohistochemistry and electron microscopy, it was found that ATs are indeed mesothelial in nature, and it has been suggested that some of the early reported cases of lymphangioma of the adrenal gland were actually ATs. Because the adrenal gland is not lined by mesothelium, it has been proposed that AT in the adrenal gland is caused by mesothelial inclusions yielding a para-adenal or intra-adenal AT; this is consistent with the close embryologic relationship between adrenal gland and müllerian tract and explains both heterotopic adrenal cortical tissue in the periovarian regions and conceivably an AT in the adrenal gland.

Myelolipoma is more clearly understood than AT, perhaps because it is more common than AT, and therefore there are more existing cases to analyze and explain the disease. Bone marrow embolization, embryonic primitive mesenchymal cells, dysregulation of hematopoietic cell apoptosis, and adrenal cortical metaplasia in response to stimuli are proposed etiologies of adrenal myelolipoma; the last is currently the most accepted theory. Stimuli such as necrosis, infections, and stress have been known to induce myelolipoma. In fact, myelolipomatous change was induced in the adrenal glands of rat by injecting necrotic tumor and adrenocorticotrophic hormone. This theory provides a plausible explanation for the coexistence of other disease conditions in 63% of adrenal myelolipomas. Among the reported coexisting conditions with myelolipoma are hypertension, obesity, diabetes mellitus, nonfunctioning adrenal adenoma, Cushing syndrome, congenital adrenal hyperplasia, cardiovascular disease, nephrolithiasis, primary aldosteronism, Cushing disease, pheochromocytoma, hypernogadism, polycystic ovary disease, Carney complex, and acquired immunodeficiency syndrome. Recent studies have drawn attention to the possible clonality of myelolipoma, with the demonstration of a balanced translocation between 3q25 and 21p11 and nonrandom X inactivation in most tumors.

The significance of composite AT and myelolipoma in the adrenal gland is poorly understood at present. Understanding this phenomenon can perhaps clarify some of the issues that are currently controversial regarding the pathogenesis of AT and myelolipoma.

**CONCLUSION**

Adenomatoid tumor and myelolipoma are rare tumors of the adrenal gland with unclear pathogenesis. Increased awareness of the existence of a composite tumor can improve the recognition and diagnosis of this lesion that could perhaps lead to a better understanding of the pathogenesis of AT and myelolipoma.

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**References**