Computed tomographic findings of radiation-induced acute adrenal injury with associated radiation nephropathy: a case report

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Abstract
Radiation nephropathy was first recognized in 1906. The kidney is a radiosensitive organ with a tolerance dose (5% complications in 5 years) of 20 Gray. The imaging findings of acute and chronic radiation induced renal injury are previously described. Radiation-induced adrenal injury, to our knowledge, has not been described in the literature. Unlike the kidneys and other upper abdominal organs, the adrenal glands are traditionally thought to be radio-resistant, protected from radiation-induced injury by proximity to adjacent organs and by the adrenal medulla which reportedly has increased radio-resistance. We present the computed tomographic imaging findings of a patient with acute radiation induced adrenal injury which resulted in adrenal insufficiency following radiotherapy of an adjacent thecal metastasis.

Keywords
Radiation, radiotherapy, kidneys, adrenal glands, nephropathy, computed tomography

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Introduction
Radiation-induced renal injury or radiation nephropathy is a well-known clinical entity with characteristic imaging findings. Radiation-induced adrenal injury is, to our knowledge, previously unreported in the clinical and imaging literature. We present a case of radiation-induced adrenal injury with associated radiation nephropathy.

Case report
A 42-year-old male patient with a diagnosis of rectal cancer status post neo-adjuvant 5-Fluorouracil – external beam radiotherapy (RT) and subsequent low anterior resection presented for routine follow-up imaging. Contrast-enhanced CT (CECT) of the chest, abdomen, and pelvis was performed March 2011, which demonstrated locally recurrent tumor with pulmonary and L2 thecal metastases. The adrenal glands and kidneys were normal at the first presentation (Fig. 1). The patient subsequently underwent systemic chemotherapy and external beam RT of the spine to treat the thecal metastasis. Follow-up CECT was performed November 2011. At time of repeat imaging, the kidneys demonstrated bilateral medial upper pole decreased density (delayed nephrogram) in keeping with acute radiation-induced renal injury or radiation nephropathy (Fig. 1). The adrenal glands also demonstrated diffuse, symmetric, low density, bilateral thickening without nodularity or mass. A thin rim of preserved cortical enhancement was distinctly preserved (Fig. 1.). The patient had no clinical or biochemical findings of adrenal dysfunction. The imaging findings were thought to be on the basis of acute radiation-induced adrenal injury. A third follow-up CECT was performed in March 2012 which showed imaging findings

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consistent with progression of both radiation nephropathy (Fig. 2) and radiation-induced adrenal injury (Figs. 2 and 3). At this time, preserved adrenal cortical enhancement was no longer apparent (Fig. 3). Loss of adrenal cortical enhancement was associated with biochemical findings of adrenal insufficiency, which had developed in the interim period. Intra-cerebral hemorrhage led to patient death. No autopsy was performed.

Discussion

Radiation nephropathy is commonly encountered in clinical practice (1) with the accepted threshold dose that will cause radiation nephropathy reported to be 28 Gy, fractionated in 5 weeks or less (2,3). Clinically, patients present with azotemia, hypertension, and anemia which can progress to renal failure (1). Radiation-induced renal damage is often referred to as radiation nephritis, which is a misnomer, as the histologic findings are not inflammatory but rather that of glomerulosclerosis or tubulointerstitial fibrosis (1). Imaging findings of radiation nephropathy have been previously described, ranging from normal (3) to geographic delayed or persistent nephrogram (2,3) in the acute phase. Chronic radiation nephropathy results in atrophy and contraction of the renal cortex with a smooth contour (3).

Radiation-induced adrenal injury has not been described in the literature (4) and the adrenal glands are reported to be relatively radio-resistant (5). Adrenal cortical hypertrophy/hyperplasia has been described after RT presumed to be related to a non-specific response of the adrenal glands to stress (5). In experimental animals and in humans, loss of adrenal cortical cells and atrophy can occur as a result of radiation exposure to the hypothalamic-hypophyseal axis and decreased ACTH secretion (6). Low dose irradiation of the adrenal glands in mice is known to cause adrenal cortical adenomas (5,7), however, there are no known oncogenic effects of radiation therapy in human adrenal glands (5).

Imaging findings from our case are consistent with a diagnosis of acute radiation-induced adrenal injury. Following external beam RT of the spine, our patient developed progressive bilateral, diffuse, symmetric low density thickening of the adrenal glands with inflammatory stranding in the adjacent retroperitoneum (Figs. 1–3) and associated radiation nephropathy. Differential considerations for the imaging findings in our patient are limited. Adrenal neoplasms, both
primary (adenoma, carcinoma, pheochromocytoma) and secondary (metastases, lymphoma) do not result in smooth, symmetric, low density thickening (8). Lymphoma may be diffuse and infiltrative (8) but is rarely primary in origin and there was no history of lymphoma in our patient. Diffuse adrenal processes could also be considered as potential causes. Bilateral adrenal hyperplasia can result in diffuse adrenal gland thickening. However, hyperplasia favors the limbs of the adrenal glands (over the body) in both hyperaldosteronism and hypercorticolism due to a predominance of adrenal cortical tissue (9), findings which were not present in our case. Furthermore, the thin enhancing adrenal cortex was preserved at time of second follow-up imaging (Figs. 2 and 3) and our patient had no clinical or biochemical findings of increased adrenal function at any time. Adrenal hemorrhage can also be diffuse, although typically resulting in mass-like asymmetric enlargement with only 20% of cases being bilateral (10). Acute hemorrhage is of increased density on CT and resolves over time (10), whereas our patient had low density thickening which progressed over time. Lastly, it has been reported that oncology patients can have smooth or nodular enlargement of the adrenal glands at CT (>6 mm) without a focal adrenal mass (8). This entity would also not account for the imaging findings in our patient who only developed adrenal gland enlargement after RT.

In conclusion, imaging findings of radiation-induced adrenal injury could be mistaken for other primary and secondary causes of adrenal thickening and should be considered as a cause of adrenal thickening in an oncology patient receiving radiotherapy in the upper abdomen, particularly when there is co-existing imaging findings of radiation nephropathy. Radiation-induced adrenal injury may be a clinically relevant finding, as in our patient, adrenal insufficiency ultimately occurred in the course of the disease.

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Fig. 2. Initial follow-up axial and coronal CECT (a) images performed after RT demonstrate radiation-induced renal (white asterisk) and presumed adrenal (white arrows) injury. Repeat axial and coronal CECT (b) images performed 2 months later depict worsening radiation nephropathy (black asterisk) and progression of radiation-induced adrenal injury (black arrows).

Fig. 3. Baseline (a), initial post RT follow-up (b), and final follow-up (c) axial CECT images demonstrate progressive findings of radiation induced adrenal injury. After initial RT (b) there is development of diffuse, symmetric, bilateral low density thickening of the adrenal glands without nodularity. Note preservation of thin enhancing adrenal cortex in (b) (white arrows) with retroperitoneal stranding (S). Final CECT follow-up (c) demonstrates progression of findings with loss of normal enhancing adrenal cortex (black arrows) associated with biochemical findings of adrenal cortical insufficiency.
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