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CASE REPORT AND REVIEW

Disappearing adrenal masses

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Abstract Adrenal incidentalomas are a common finding due to the increasing use and improved technology of imaging studies. The majority of these enlargements are non-functional and irreversible. Publications on reversible adrenal enlargement are sparse. Our patient, a 66-year-old man, was admitted to the hospital due to abdominal discomfort. He was treated for rectal carcinoma 3 years before, and was now free of disease. Computed tomography (CT) scan showed no abnormalities other than the incidental finding of bilateral adrenal enlargement. Metastasis was suspected. The CEA-level, however, was within normal range and there was no evidence of hormonal overproduction. After 1 month the patient was reviewed. Physical examination and laboratory testing were normal. Surprisingly, the CT-scan showed a decreased size of both adrenals and after 3 months even showed completely normalized adrenals. Reversible adrenal enlargements are rare. Commonly described causes of adrenal enlargement are haematomas, cystic lesions and infections of the adrenal glands. The patient in this case did not show any clinical, laboratory or radiological signs of any of these diagnoses. The current existing differential diagnosis for bilateral adrenal enlargement is not sufficient to explain the findings in our patient.

Keywords Adrenal incidentaloma · Adrenal enlargement · Bilateral · Reversible

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Introduction

Due to the increasing use and improved technology of imaging studies, the prevalence of adrenal incidentalomas is increasing and many clinical questions arise.

Approximately 4% of all patients undergoing CT examination have an incidentaloma of the adrenal [1]. The high prevalence of this pathology induces a lot of clinical questions. Most adrenal masses are non-functional, irreversible adenomas without further health consequences. Publications on reversible adrenal enlargement are sparse. We describe a patient with unexplained reversible adrenal masses.

Case report

A 66-year-old man was admitted to the hospital due to abdominal discomfort and constipation. He was treated for rectal carcinoma (Dukes C) 3 years before with radiotherapy and amputation after which he was free of disease. A clinical diagnosis of ileus was made due to motility disorder and scar formation because of the previous treatment or tumour recurrence. He was treated initially with distal laxatives and iv fluids. With this regimen the ileus resolved and the abdominal symptoms disappeared in several days

During hospitalization he developed erysipelas of the right foot with fever and chills for which he was treated with flucloxacillin. In this period he also developed atrial fibrillation with mild circulatory consequences for which he was treated with iv fluids and lanoxin.

He converted to sinus rhythm after 1 day. There was no evidence of myocardial damage on ECG and laboratory examination.

An abdominal CT-scan was made during hospital stay because of the ileus and the differential diagnosis with tumour recurrence. This CT-scan (Fig. 1a) showed no abnormalities other than the incidental finding of a bilateral enlargement of the adrenals. The right adrenal was measured 2.5 cm; and the left was 3.7 cm. They were oval-shaped without calcifications or necrosis. Attenuation was measured 70 s after contrast-enhancement and showed values of 60HU (left) and 65HU (right).

Because of his medical history metastases were suspected. The CEA-level, however, was within normal range (<0.2 μg/l (<4.3 μg/l)). Chest radiograph showed no lymphadenopathy or other abnormalities. No extensive endocrinological investigations were performed at this time. Only random cortisol (300 nmol/l) was determined. Because of clinical improvement the patient was sent home.

One month later the patient was seen in an outpatient setting for further evaluation of the adrenal masses. At that point he had no complaints of abdominal discomfort, fever, joint pain, dyspnoea, cough, constipation, hypotension, arrhythmias or other symptoms of hormonal overproduction or systemic disease. Physical examination showed no abnormalities. No rash, arthritis, conjunctivitis or bruises were observed. Basic laboratory testing were normal [CRP < 3 mg/l (< 6 mg/l), Haemoglobin 7.8 mmol/l (8.5–11.0 mmol/l), MCV 86 fl. (80–100 fl), leucocyte count 6.6 × 10^9/l (4.0–10.0 × 10^9/l), platelet count 283 × 10^9/l (150–400 × 10^9/l), glucose 6.5 mmol/l (<7.8 mmol/l), creatinine 60 μmol/l (60–110 μmol/l), urea 5.7 mmol/l (2.5–6.5 mmol/l), LDH 160 U/l (<250 U/l), ASAT 19 U/l (<35 U/l), ALAT 22U/l (<45U/l)]. A follow-up non-enhanced CT-scan showed a decreased size of both adrenals (Fig. 1b). The right adrenal had completely normalized in 1 month, in size, shape and attenuation. The left adrenal mass shrunk from 3.7 to 1.4 cm and showed an attenuation value varying between −10HU and +30HU. Further biochemical testing at that point showed other than a high ACTH (19.6 mmol/l), decreased DHEA-S (1,1 mmol/l) and slightly elevated normetanephrines in urine with no abnormalities [serum: potassium 4.2 mmol/l (3.5–4.5 mmol/l), sodium 139 mmol/l (135–145 mmol/l), cortisol circadian rhythm; 8.00 a.m 356 nmol/l (150–700 nmol/l),16.00 p.m 262 nmol/l (<60% 8.00 a.m), ACTH 19.6 pmol/l (2.2–13.2 pmol/l), DHEA-S 1.1 μmol/l (2.2–15.2 μmol/l); 24 μmol/l h urine sample: cortisol value 188 nmol/l (40–340 nmol/24 h), metanephrines (2 times; 812 nmol/l, 728 nmol/l) (<1500 nmol/24 h) normetanephrines (4980 nmol/24 h, 5120 nmol/24 h) (<3000 nmol/24 h)]. To exclude auto-immune disease as cause of adrenal enlargement, additional auto-immune serology was

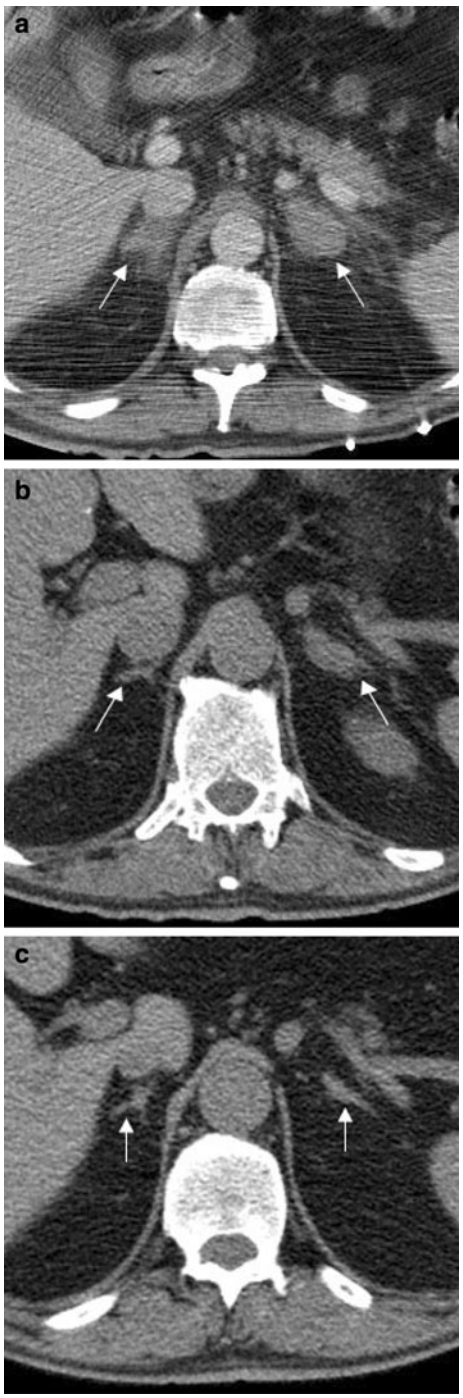

Fig. 1 Three consecutive CT scans at the level of the adrenal glands (*white arrows*). **a** The initial contrast-enhanced CT scan, demonstrates bilateral adrenal enlargement. There is retroperitoneal fatstranding adjacent to the adrenal glands. **b** A follow-up non-enhanced CT at a 1-month interval, demonstrated residual enlargement of the left adrenal gland with minimal retroperitoneal fatstranding. The right adrenal gland size was normalised. **c** At 3-month follow-up from the initial CT, the non-enhanced CT showed normal sized adrenal glands. There is no residual retroperitoneal fatstranding, or signs of adrenal calcification or cystic changes

Table 1 Laboratory findings at time of adrenal enlargement

	Laboratory findings	
	Value patient	Normal limits
Serum		
CRP	<3 mg/l	<6 mg/l
Haemoglobin	7.8 mmol/l	(8.5–11.0 mmol/l)
MCV	86 fl	(80–100 fl)
Leukocyte count	6.6 × 10^9/l	(4.0–10.0 × 10^9/l)
Platelet count	283 × 10^9/l/l	(150–400 × 10^9/l)
Glucose	6.5 mmol/l	<7.8 mmol/l
Potassium	4.2 mmol/l	(3.5–4.5 mmol/l)
Sodium	139 mmol/l	(135–145 mmol/l)
Creatinine	60 μmol/l	(60–110 μmol/l)
Urea	5.7 mmol/l	(2.5–6.5 mmol/l)
LDH	160 U/l	<250 U/l
ASAT	19 U/l	<35 U/l
ALAT	22 U/l	<45 U/l
ACTH	19.6 mmol/l	(2.2–13.2 pmol/l)
DHEA-S	1.1 mmol/l	(2.2–15.2 nmol/l)
Circadian rhythm 8.00 a.m	356 nmol/l	(150–700 nmol/l)
Circadian rhythm 16.00 p.m	262 nmol/l	(<60% 8.00 a.m)
ANA	Weakly positive	
ENA	Negative	
ANCA	Negative	
dsDNA	Negative	
24-h urine		
Cortisol value	188 nmol/l	(40–340 nmol/24 h)
Metanephrines	812 nmol/l, 728 nmol/l	(<1500 nmol/24 h)
Normetanephrine	4980 nmol/l, 5120 nm/l	(<3000 nmol/24 h)

performed. No abnormal results were found (ANA, weakly positive; ENA, negative; ANCA, negative and dsDNA, negative) (Table 1).

Because of the spontaneous regression of the masses and the unclear biochemical test results, it was decided to perform a follow-up CT-scan after 3 months (Fig. 1c). This scan showed complete normalization of both adrenals (shape, size and structure) without calcifications.

Discussion

We describe a 66-year-old man with bilateral incidentalomas of the adrenals without signs or symptoms of hormone overproduction. His medical history showed rectal carcinoma, but the CT findings and the evolution do not suggest the enlargement was due to metastatic disease. What can be the cause?

Adrenal incidentaloma

An adrenal 'incidentaloma' is an adrenal mass, generally 1 cm or more in diameter, which is discovered coincidently during a radiological examination performed for indications other than an evaluation of adrenal disease [1].They are found in 4–5% of the radiological investigations [2, 3]. 10–15% of these adrenal incidentalomas are bilateral [4, 5]. At least 38 different diagnoses of adrenal incidentalomas have been reported [1], with most incidentalomas being non-functional benign adenomas [6].

Bilateral adrenal enlargement

Bilateral adrenal masses can be contributed to metastatic disease, congenital adrenal hyperplasia, lymphoma, infection, haemorrhage, ACTH-dependent Cushing's syndrome, pheochromocytoma, amyloidosis and infiltrative disease of the adrenal glands [1, 7]. In patients with a known history of extra-adrenal cancer up to 52% of the incidental adrenal masses are found to be metastases [8]. Tumours that commonly metastasize to the adrenals include carcinomas of the lung, kidney, colon, etc. Metastases of the adrenals are frequently bilateral [9]. If metastatic disease is suspected fine-needle aspiration biopsy is the next step in diagnosis [8, 9]. The reversible nature of the adrenal masses excludes the possibility of metastatic disease in this case. The possibility of auto-immune diseases was excluded because of negative auto-immune serology and the absence of symptoms indicating autoimmune diseases. Other causes have to be considered.

Adrenal mass size reduction

Reduction in size of the adrenal mass has been reported in approximately 4% of all incidentalomas [10–15]. The most commonly described causes of these adrenal enlargements are haematomas, cystic lesions and infections of the adrenal glands.

Although non-traumatic haemorrhage of the adrenal glands is a very common cause it is rarely seen. Stress, haemorrhagic diathesis or coagulopathy and idiopathic disease can cause such adrenal haemorrhages [16]. Stressful events like surgery, sepsis, hypotension or cardiovascular disease make the adrenals more susceptible to haemorrhage [17]. CT-examination of adrenals with haemorrhages show adrenal enlargement that may be asymmetric in case of bilateral haemorrhage. The glands become rounded or oval-shaped and have high attenuation (50-90HU) without contrast enhancement in the acute setting. Several weeks after the acute adrenal haemorrhage the masses show gradual decrease in size and attenuation. In addition, the adrenals may have a cystic appearance. Several months after the

acute event CT-scan of the adrenals shows progressive atrophy with the variable appearance of calcifications.

The CT findings in our case report do not match these typical findings as the adrenals completely normalised without the appearances of calcification. Furthermore, with large bilateral haematomas adrenal insufficiency would have been expected to arise. Haemorrhage of the adrenals seems unlikely, however, it cannot be excluded since no CT examination without contrast was made at time of first CT evaluation.

Infection of the adrenal glands is very rare. The adrenal gland can be infected by different pathogens including fungi, viruses, parasites and bacteria. Immunocompromised individuals are at greatest risk for either primary adrenal infection or disseminated microbial disease involving the adrenal gland. Nevertheless, several case reports have described individuals with objective normal immune function and adrenal infection. Diagnosis of adrenal infection is rare due to the non-specific nature of symptoms and laboratory manifestations. The true overt Addiosonian symptoms will only arise when 80–90% of the gland has been destroyed.

During recent active infection the adrenals are enlarged on imaging techniques, whereas inactive or remote infection show small, atrophied or calcified glands. In Waterhouse–Friderichsen syndrome, bacterial sepsis appears to induce bilateral adrenal haemorrhage. Etiological agents associated with this syndrome are *N. meningitidis*, A streptococcus, pneumococci, *Haemophilus influenzae* and others [17]. The patient in our case was immunocompetent, showed no signs of adrenal insufficiency or sepsis. The imaging findings do not show the characteristics of a bilateral infection. A diagnosis of adrenal infection seems unlikely.

Cystic lesions of the adrenals are an uncommon finding. They are often unilateral and more frequently seen in woman [18]. CT has been found useful to differentiate between a cystic lesion and an adenoma. Characteristics of cystic lesions are non-enhancement and calcifications [19]. As these characteristics are not seen in CT examination of our patient, cystic lesions are highly unlikely the cause.

Chronic stress exposure has been shown to induce adrenal hyperplasia and hypertrophy in a study conducted upon rats [20]. No such cases are described in humans, neither is there any literature about acute stress as a cause for adrenal growth in adults.

Conclusion

In the above-described case, we presented a 66-year-old man, with a history of Dukes C rectal carcinoma and an incidentally found, reversible, bilateral adrenal mass, during a period of stress, with a serious infection of the right foot, fever, abdominal discomfort, hypotension and arrhythmia, with chest pain. There was no hormonal overproduction found and the masses completely normalized within 3 months. There was no clinical suspicion or laboratory test results suggesting adrenal insufficiency. There was no sign of systemic infection and imaging characteristics were not specific for cystic lesions, infection and adrenal haemorrhage.

For that reason the current existing differential diagnosis for bilateral adrenal enlargement was not sufficient to explain the findings in this case.

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