Received:
28 April 2015

Revised:
23 June 2015

Accepted:
1 July 2015

doi: 10.1259/bjr.20150352

Cite this article as:

Kok HK, Sherlock M, Healy NA, Doody O, Govender P, Torreggiani WC. Imaging features of poorly controlled congenital adrenal hyperplasia in adults. *Br J Radiol* 2015; **88**: 20150352.

PICTORIAL REVIEW

Imaging features of poorly controlled congenital adrenal hyperplasia in adults

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ABSTRACT

Congenital adrenal hyperplasia (CAH) is a genetic autosomal recessive condition most frequently as a result of a mutation in the 21-hydroxylase enzyme gene. Patients with poorly controlled CAH can manifest characteristic imaging findings as a result of adrenocorticotrophic hormone stimulation or the effects of cortisol precursor excess on various target organs. We present a spectrum of imaging findings encountered in adult patients with poorly treated CAH, with an emphasis on radiological features and their clinical relevance.

INTRODUCTION

Congenital adrenal hyperplasia (CAH) is an autosomal recessive condition resulting most commonly from the deficiency of the 21-hydroxylase enzyme, which is essential for the physiological formation of cortisol and aldosterone via the adrenal steroid biosynthesis pathway.^{1,2} The lack of cortisol synthesis promotes increased pituitary adrenocorticotrophic hormone (ACTH) release, which stimulates the adrenal glands to produce excess cortisol precursors such as 17-hydroxyprogesterone and androgens. The classic form of CAH is associated with virilization from androgen excess and results in ambiguous genitalia in newborn girls as well as varying degrees of salt wasting from associated mineralocorticoid deficiency. A recent cohort study from the UK suggests that a majority of adult individuals with CAH are not adequately managed and can present to health services for a variety of issues.³ We present a spectrum of imaging findings encountered in patients with poorly treated CAH, with an emphasis on radiological features and their clinical relevance.

ADRENAL GLANDS

Hyperplasia and nodular enlargement of the adrenal glands is seen in long-standing and poorly controlled CAH.² Adrenal tumours are also well recognized, with myelolipomas being the most commonly seen tumour, and other tumours such as adenomas and pheochromocytomas reported less frequently.⁴ Myelolipomas are benign tumours which consist of mature adipocytes and haematopoietic cells from the

myeloid, erythroid and megakaryocytic cell lines, resulting in characteristic imaging features owing to the dominant presence of macroscopic and microscopic fat.⁵ Myelolipomas appear as hyperechoic masses on ultrasound (Figure 1) and as fat-containing adrenal masses on CT (Figure 2). The fat component within each individual lesion is variable and small areas of calcification can be seen. With increasing size, lesions are at risk of haemorrhage, rupture or necrosis and can exert mass effect on adjacent abdominal viscera. Lesions complicated by haemorrhage are readily demonstrated on CT or MRI but can be mistaken for other adrenal masses such as adenomas or adrenal cortical carcinoma if >5–6 cm. The signal characteristics of myelolipomas on MRI depend on the relative proportions of fat, myeloid and haemorrhage, if present. Lesions show T_1 weighted signal hyperintensity due to the presence of macroscopic fat, variable T_2 weighted signal depending on the presence of marrow-like elements or internal blood products, signal loss on fat-suppression sequences and signal loss within mixed components on opposed-phase sequences (Figure 3).⁵ Myelolipomas can reach very large sizes but rarely undergo malignant transformation and generally do not require surgical intervention in the absence of complications or suspicious imaging features.

GONADS

Male patients with poorly controlled CAH develop testicular adrenal rest tumours (TART) which arise from aberrant

Figure 1. Abdominal ultrasound in a female patient with poorly controlled congenital adrenal hyperplasia secondary to 21-hydroxylase deficiency demonstrates hyperechoic suprarenal masses bilaterally compatible with bilateral adrenal myelolipomas.

adrenal cells which descend with the testes during embryological development. These aberrant adrenal cells can be found in all male testes; however, in CAH, stimulation by ACTH promotes cellular hyperplasia leading to the formation of TART—so called because of their resemblance to adrenal tissue histologically.⁶ Despite the name, TART do not represent true neoplasms as the cells do not undergo uncontrolled increased proliferation, and surgery is generally not indicated as lesions can regress with optimization of hydrocortisone replacement.^{1,7} There is a reported prevalence of 24% in patients with CAH, and ultrasound is the preferred modality for the diagnosis and follow-up of TART as it is superior to physical examination alone in detecting smaller lesions.^{2,8} TART do not have malignant potential; however, large lesions can cause compression of the rete testis and seminiferous tubules, ultimately resulting in testicular atrophy and infertility. Milder forms of CAH, known as non-classical CAH, may present primarily with TART in adolescence or adulthood, and this should be considered in the differential of a testicular mass in younger patients. Typical sonographic appearances of TART in both forms of CAH are that of a predominantly hypoechoic mass adjacent to the mediastinum testis (Figure 4). Lesions are usually bilateral and taken together with the characteristic location may help distinguish TART from malignancy. Larger lesions may show more heterogeneous internal echotexture with hyperechoic areas (Figure 4d).⁹ Most lesions are well circumscribed but sonographic assessment of margins can be

difficult with larger lesions. MRI is superior to ultrasound in defining the margins of larger lesions, particularly if surgery is contemplated; however, MRI features alone are non-specific.⁹ In females, ovarian adrenal rest tumours have been described but are very rare; therefore, routine ovarian imaging in patients with CAH is not indicated in the absence of ovarian dysfunction.¹⁰

Central nervous system

CAH is not typically associated with central nervous system manifestations. However, there have been increasing case reports of meningiomas seen in association with poorly controlled CAH, postulated to be due to the high levels of sex steroids in these patients.^{11,12} The imaging features are similar to sporadic meningiomas and are that of an avidly enhancing extra-axial mass following contrast administration with characteristic osseous hyperostosis (Figure 5).

Musculoskeletal system

The skeletal imaging features in CAH are mainly related to accelerated bone age in pre-pubertal patients with resultant short stature in adult life.² Treatment-related complications from excess glucocorticoid therapy can result in osteoporosis, Cushing's syndrome and the metabolic syndrome which consist of a combination of central obesity, hypertension, dyslipidaemia and insulin resistance, resulting in increased risk for diabetes and cardiovascular diseases. Patients on high-dose glucocorticoid therapy should be monitored for the

Figure 2. (a) Coronal and (b) axial contrast-enhanced CT of the adrenals in the same patient with poorly controlled congenital adrenal hyperplasia show bilateral adrenal hyperplasia [white arrows in (a)] with heterogeneous fat-containing masses consistent with myelolipomas. These lesions demonstrate areas of macroscopic fat [white arrow in (b)], mixed density myeloid components [asterisk in (b)] and a focal area of calcification [black arrow in (a)].

Figure 3. (a) Axial T_1 weighted in-phase sequence in congenital adrenal hyperplasia shows hyperplasia of both adrenal glands (asterisks). An exophytic mass arising from the left adrenal gland shows areas of hyperintense (white arrow) and isointense signal (arrowhead) consistent with fat and mixed myeloid-fat components. (b) Axial T_1 weighted out-of-phase sequence demonstrates signal loss in both areas (white arrow and arrowhead) with an India ink artefact at the interface of both components. (c) Axial T_1 weighted fat-saturated sequence confirms the presence of macroscopic fat (white arrow) with less marked fat suppression within the myeloid component (arrowhead). (d) Axial contrast-enhanced CT of a myelolipoma in a separate patient shows both fat (black arrow) and myeloid components. (e) Corresponding axial T_1 weighted in-phase sequence shows signal hyperintensity in the fat component (black arrow) and isointensity in the myeloid component. (f) Axial T_1 weighted out-of-phase sequence shows hyperintense signal in the macroscopic fat component (black arrow) signal loss within the myeloid component consistent with admixed microscopic fat and an India ink artefact at the interface of both components (arrowhead). (g) Axial T_2 weighted fat-saturated sequence shows the suppression of signal within the macroscopic fat component (white arrow). The myeloid component shows relative signal hyperintensity due to internal water content.

development of osteopenia and osteoporosis with dual-energy X-ray absorptiometry and a baseline scan in adolescence is recommended.

CONCLUSION

CAH is a complex condition with characteristic imaging features involving different organ systems. As the prognosis from

Figure 4. (a) Longitudinal ultrasound image shows a well-circumscribed and hypoechoic intratesticular lesion in a male patient with congenital adrenal hyperplasia (CAH) consistent with testicular adrenal rest tumour (TART). (b) Internal vascularity is demonstrated on colour Doppler assessment of this lesion, which is adjacent to the mediastinum testis, a relatively characteristic feature of TART (white arrow). (c) Axial image shows the relationship of the TART to the mediastinum testis (white arrow). (d) Larger hypoechoic and ill-defined intratesticular mass with a focus of central macroscopic calcification in a different patient with TART secondary to CAH.

Figure 5. (a) Axial contrast-enhanced CT and (b) corresponding bone windows in a 45-year-old female patient with poorly controlled congenital adrenal hyperplasia show an enhancing extra-axial mass arising from the right sphenoid wing (black arrow) with associated hyperostosis of the middle cranial fossa and sphenoid bone (white arrowhead). (c) Contrast-enhanced T_1 weighted axial MRI confirms the CT findings and demonstrates an enhancing dural tail (white arrow), typical for meningioma.

childhood CAH continues to improve, more patients will invariably undergo imaging studies in adulthood, and both radiologists and

physicians should be familiar with the indications and significance of imaging findings in this patient population.

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