PICTORIAL REVIEW

Embryology of the adrenal glands and its relevance to diagnostic imaging

T.D. Barwicka,*, A. Malhotraa, J.A.W. Webb, M.O. Savageb, R.H. Reznek

Departments of aDiagnostic Radiology, and bPaediatric Endocrinology, St Bartholomew’s Hospital, London, UK

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An understanding of the embryology of the adrenal glands is necessary to appreciate the location of adrenal ectopic, or rest, tissue which can occur anywhere along the course of gonadal descent. This tissue usually has no clinical significance, but may become hyperplastic in patients with primary or secondary adrenal pathology. In congenital adrenal hyperplasia, hyperplastic rest tissue may present as a soft-tissue mass, particularly in the gonads and retroperitoneum, and may be mistaken for tumour. The adrenal in the neonate is proportionately much larger than in the adult; in renal ectopy or agenesis the ipsilateral adrenal is normally sited and may be mistaken for a kidney because of its size. This review article illustrates the embryology of the adrenal with particular emphasis on the relevance of embryology to pathology.

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Embryology of the adrenal glands

The adrenal gland has a dual embryological origin. The adrenal cortex arises from the coelomic mesoderm of the urogenital ridge, and the medulla arises from neural crest tissue (Figs. 1 and 2).1,2 During the 5th week of fetal development, mesothelial cells from the posterior abdominal wall, between the root of the bowel mesentery and developing mesonephros/gonad (urogenital ridge), proliferate and form the fetal or primitive cortex of the adrenal. In the 6th week, a second wave of mesothelial cells surrounds the primitive cortex and later forms the adult or definitive cortex.1,2 By 8 weeks, the cortical mass separates from the rest of the mesothelial tissue and is surrounded by connective tissue.3

The adrenal medulla arises from neural crest tissue in the adjacent sympathetic ganglion at the level of the coeliac plexus (Fig. 1).1,4 These neural crest cells, which stain yellow or brown with chrome salts, are called chromaffin cells and migrate towards the adrenal cortex at 7 weeks. They gradually invade the medial aspect of the cortical tissue along its central vein to gain a central position.

Complete encapsulation of the medulla does not occur until late fetal development. The adrenal cortex differentiates fully into the three zones by 3 years of age (Fig. 2).1,3 The zona glomerulosa and zona fasciculata are present at birth, but the zona reticularis develops later.

Anatomy

At birth the adrenals are 10 to 20 times larger than adult glands relative to body weight, and approximately one third the size of the neonatal kidney.1 The fetal and neonatal adrenal gland consist
predominately of cortex which has an active role in the synthesis of glucocorticoids, precursor steroids, sex steroids, oestrogens and progesterone in the third trimester and the first 3 months after birth. On US, the neonatal adrenal characteristically has a thin reflective core surrounded by a thick transonic zone (Fig. 3). The gland rapidly decreases in size as the fetal cortex regresses; the size of the adult adrenal is approximately 8% that of the kidney.

The right adrenal lies between the liver, inferior vena cava and right crus of the hemidiaphragm and superior to the upper pole of right kidney. The left adrenal lies between the left crus of the hemidiaphragm and the tail of the pancreas, and is superomedial to the upper pole of left kidney. On CT, the adrenal typically has an inverted "Y" or "v" shape on the left and a linear or inverted "v" on the right, depending on the level of section. The 95th percentile maximum width of the body of the normal adrenal is less than 1 cm, and that of each limb is less than 5 mm. The normal length should be less than 4 cm.

Figure 1  Fetus at 7 weeks. Transverse sections at level of the adrenals show developing gonads and adrenal cortex within urogenital ridge. Migration of neural crest cells from sympathetic ganglion forms adrenal medulla.

Figure 2  Fetal adrenal development. Diagram of fetal adrenal cortex and medulla, showing encapsulation of medulla and differentiation of adrenal cortex into three layers.
Developmental abnormalities of the adrenal

Developmental abnormalities of the adrenal gland can be divided into ectopic or accessory tissue and heterotopia.

Ectopic or accessory adrenal tissue, known as adrenal rest tissue, occurs when fragments of tissue break off during development. The adrenal rests may contain cortical tissue only or other cortical and medullary tissue, depending on whether the fragments break off before or after migration of neural medullary tissue into the cortex. Thus, accessory adrenal tissue close to the original position of the adrenal may contain medulla; but more distant accessory adrenal tissue, which usually migrates with the developing gonad, contains cortex only. Adrenal heterotopia may be complete or partial, depending on whether none or a portion of the adrenal remains in its normal position. Although rare, death from adrenal insufficiency following excision of heterotopic adrenal gland has been reported.

The adrenals and adrenal rest tissue in congenital adrenal hyperplasia

Congenital adrenal hyperplasia (CAH) describes a group of autosomal recessive disorders characterized by enzyme defects in the pathway of cortisol synthesis. Deficient cortisol production leads to increased ACTH production and hyperplasia of the adrenal cortex (Figs. 5 and 6). In patients with untreated CAH, there is typically bilateral diffuse enlargement of the adrenals with preservation of the normal configuration, but occasional nodular or mass-like transformation may occur. The enhancement pattern of the adrenal gland on CT in persons with CAH has not been documented. In our own limited experience, the bilateral adrenal masses enhance inhomogeneously, with foci of non-enhancement and foci of marked enhancement often simulating an adrenal tumour (Fig. 5). In CAH, sustained elevation of ACTH stimulates any adrenal rest tissue, which becomes hyperplastic and may be functionally active. The rest tissue may be a presenting feature or a sign of poor hormonal control, and can be found anywhere along the course of testicular descent.

Retroperitoneum

Rest tissue in the retroperitoneum, particularly at the level of the coeliac axis, is well documented. Adrenal rests within the testis occur in 7.5% to 15% of neonates and normally regress in early infancy. The rests are usually an incidental finding at surgery or autopsy, rarely greater than 3 to 5 mm in size and usually of no clinical significance. However, they may become important if there is excess adrenocorticotropic hormone stimulation resulting in hyperplastic change with excessive hormone production, or associated neoplastic change occurs. Ectopic adrenal tissue should be considered in the differential diagnosis of soft-tissue masses closely related to the urogenital system or to the course of gonadal descent.
manifest unless hyperplasia secondary to ACTH stimulus occurs. There are no specific features of the retroperitoneal mass that result from hyperplasia of this rest tissue, and it is indistinguishable from other types of retroperitoneal mass (Fig. 7).

**Testes**

Some patients with CAH develop testicular masses secondary to hypertrophy of testicular rest tissue. The testicular masses atrophy under the influence of high doses of glucocorticoids. In CAH, hyperplastic adrenal rest tissue within the testis has been described at US in 24% to 27% of cases, but recently it has been suggested that the prevalence of testicular rest tissue may be much higher, up to 94% at US and MRI.

Typically, ultrasonography shows bilateral,
multifocal, intratesticular masses of reduced reflectivity,\textsuperscript{22,24–26} which may be associated with acoustic shadowing (Fig. 8).\textsuperscript{27} The MR features of testicular adrenal rest tissue are similar to those of normal adrenal glands. Most of the masses are isointense to muscle on T1-weighted images, hypointense on T2-weighted images and enhance diffusely after contrast administration.\textsuperscript{25,26} Unfortunately, both US and MR features are indistinguishable from testicular tumours without an appropriate clinical history and endocrine profile.\textsuperscript{26}

Although the clinical features of CAH are usually present, occasionally the testicular lesion may be the only clinical finding at presentation.\textsuperscript{15,24} Therefore CAH must be excluded in any child presenting with bilateral testicular masses and precocious puberty.\textsuperscript{16} Recognition of hyperplastic adrenal rest tissue as a cause of intratesticular masses in patients with CAH means that unnecessary biopsy or even orchidectomy can be avoided.\textsuperscript{21,25} The presence of bilateral adrenal masses and reduction in size of the testicular masses with glucocorticoid treatment is diagnostic. In difficult cases, or if the mass is unresponsive to steroid treatment, percutaneous sampling of the gonadal veins for adrenal precursor steroids may be helpful.\textsuperscript{15,25,28}

**Figure 7**  Retroperitoneal adrenal rest tissue. Three-year-old boy with severe genital virilization, rapid growth and an abdominal mass. (a) Axial T2-weighted MR image shows bilateral smooth adrenal enlargement (arrows) consistent with hyperplasia. Signal intensity of adrenals is uniform and intermediate compared with liver. (b) Axial T1-weighted image shows retroperitoneal mass (arrowed) of intermediate signal intensity encasing aorta and origin of renal arteries. (c) After 18 months of hydrocortisone replacement treatment, T2-weighted axial MR image shows normal adrenals bilaterally and (d) complete resolution of retroperitoneal mass, suggesting adrenal rest tissue. The normal aorta (arrow) and right crus of diaphragm (curved arrow) are clearly seen.
The adrenals in renal agenesis/ectopia

The adrenals and kidneys have separate embryological origins. Like the adrenal cortex, the kidneys develop from mesenchymal tissue. However, they develop in the pelvis and ascend to the upper lumbar region, where they meet the adrenals at 8 weeks of fetal life (Fig. 4). In renal agenesis, the ipsilateral adrenal is usually present and normally sited, appears enlarged and flattened and has been described as discoid. This is thought to relate to the absence of pressure from the kidney which usually gives the adrenal the normal “y” or “v” configuration. In persons who do not have a normally sited kidney, the disc-shaped adrenal appears linear on CT (Fig. 9). In renal agenesis in the neonate, where the adrenal is relatively large (Fig. 3), care must be taken not to mistake it for kidney.

Conclusion

Hyperplasia of adrenal rest tissue is a rare but important manifestation of conditions with excessive adrenocorticotrophic hormone stimulation, such as CAH. Knowledge of the embryology of the adrenal glands is essential to appreciate the location of this rest tissue. In males with CAH, the radiological features of testicular rest tissue help in the differentiation from tumour, thereby avoiding unnecessary biopsy or even orchidectomy. In neonates with renal ectopia or agenesis, the normal relatively large adrenal should not be mistaken for kidney.

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References

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