CASE REPORTS

EXTROVERSION OF THE PRIMITIVE HIND GUT

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Developmental abnormalities should always be of interest for the illustration they may afford of the many still obscure stages in development, and for the challenge they may issue to accepted views on the different stages in organogenesis. The present case is of interest in connexion with mechanism of production of a complicated form of ectopia vesicae.

Clinical history. The third child of an otherwise normal family was born at full term and was referred to hospital. On examination when two days old a most unusual condition was revealed. The baby was small, and the skull, vertebral column and limbs appeared normal. The trunk was normal above the level of the middle of the abdomen. Below this level and situated in the middle line of the anterior abdominal wall was a yellow rounded tumour with blood vessels coursing beneath its surface and forming the base of attachment of the remains of the umbilical cord. This swelling was later represented by a horizontal granulating tissue scar. Below it, and separated by a few millimetres of pale skin, there projected a large, circular mass of red mucosa. Through the central aperture of this prolapsed portion of bowel, faecal material was passed at intervals. More posteriorly, but continuous with this mucosa was a much smaller opening directed upwards and backwards. Immediately behind the smaller opening the perineum was covered by skin and was without dimple or depression to mark the site of any proctodeal ingrowth.

Situated on either side of the larger bowel aperture, but apparently separated at least on the right side by a narrow bar of pale skin, were two areas of red, wrinkled epithelium. From a minute aperture on the left area urine trickled. Just below each of these was a little tubercle covered with pale, smooth epithelium and beneath each of these and forming the anterior part of the perineum was a rounded elevation covered with slightly wrinkled, but normal skin. The infant lived for twelve days taking three-hourly feeds.

Post-mortem examination. By promising to reveal the true sex of the child permission was obtained to carry out a limited autopsy. This was performed within two hours of death. The usual midline incision was carried laterally on each side from just above the middle of the abdomen. After removing the chest organs and liver, the whole peritoneal aspect of the posterior abdominal wall, the pelvic floor with portions of sacrum, coccyx and iliac bones and the lower part of the anterior abdominal wall was taken in one block for

dissection. There was a slight terminal peritonitis owing to spread of infection from the umbilicus. This area, extending as a transverse linear scar, was oedematous and unprotected by underlying muscle and tore readily.

FIG. 1.—Anterior aspect. The structures have been dissected from the posterior abdominal wall. The upper bowel and its orifice are seen and the glass rod marks the opening of the blind inferior tube. s.b. upper portion of bowel opening to exterior on central red area ; inf. mes. A. inferior mesenteric artery supplying the inferior blind tube ; t. testicle ; u.o. left ureteric orifice ; g.t. genital tubercle.

The bowel, normally situated within the abdomen and supplied by the superior mesenteric artery, opened at the large upper aperture in the middle of the anterior abdominal wall (fig. 1). The mucosa was directly continuous with squamous epithelium which intervened between it and the umbilical scar.

The longitudinal muscle was uniformly distributed around the wall. There was nothing resembling a caecum or appendix. Below its orifice was the aperture of the small posterior tube, which was directed backward; it terminated blindly opposite the upper part of the sacrum and showed no extension even as a fibrous cord. Its artery arose from the anterior aspect of the abdominal aorta just before its division into the iliac arteries, and dividing and forming an arcade, ran in the rather redundant peritoneal mesentery situated somewhat to the left of the tube (fig. 2). The peritoneal cavity extended from the right side round the tube which was only attached to the dorsal abdominal wall along the line of its artery. The superior mesenteric artery supplied the entire extroverted area and a branch ran backwards in the mesentery along the posterior tube to

FIG. 2.—Posterior aspect after dissecting away the posterior abdominal wall. The mesentery of the superior part of the bowel is largely cut away. A black thread is holding out the mesentery of the lower blind tube, the artery of which unites with the superior mesenteric artery in this mesentery. A white glass rod marks the orifice of the blind bowel tube. r. and l.u. right and left ureters; s.b. upper part of bowel; b. blindly ending posterior tube; m. thread holding out mesentery of inferior bowel tube.

form an anastomotic loop with the lower mesenteric artery. Histologically, the longitudinal muscle of the two parts of the bowel was continuous. The mucosa of the superior portion of the bowel near its termination showed mucous-secreting cells lining acini and a few well marked villi. The muscle of the lower tube was uniformly distributed around it and the mucosa did not differ significantly from that normal to the large bowel, but submucous lymphoid tissue was present. The superior and inferior portions of the bowel showed continuity of the mucous membrane only at the narrow line of their junction. The mucous membrane of the upper part of the bowel almost encircled the opening of the lower bowel with a wide arm-like extension on each side. A transitional type of epithelium covered the narrow area intervening between the two and the extreme posterior end of the central red area.

The internal iliac arteries each gave off a branch to the lateral red area of their own side and formed the umbilical arteries, both of which were almost obliterated and changed into fibrous cords. The umbilical vessels ran in the retro-peritoneal tissue of the abdominal wall and above the upper bowel opening to the area of scarring representing the attachment of the umbilical cord. From this same area the obliterated strand of the umbilical vein passed up to the liver.

The left ureter and kidney were macroscopically and microscopically normal. The left vas deferens passed round the ureter, dilated slightly, and opened through a minute aperture on the red epithelium just above the small tubercle. The urinary orifice was visible as a tiny slit at a slightly higher level, but rather below the middle of the same lateral red area (fig. 1). The area between the two was covered by a many-layered columnar pseudo-stratified or

FIG. 3.—The cortex of the right kidney. Some of the smaller cysts are seen and are surrounded by abundant, rather primitive connective tissue.

transitional epithelium differing from the single layer of columnar cells lining the patent sex duct. In the underlying connective tissue and running to open round the orifice of the sex duct where the numerous acini of the accessory sex glands, lined largely by mucus-secreting cells.

The right kidney was pale and reduced in size, and contained numerous small cysts, many of which lay just beneath the capsule. No separation into cortex or medulla was visible. Histologically, the numerous small cystic spaces, varying in size and often arranged in groups, were lined by high columnar or rarely somewhat flattened epithelium and were surrounded by considerable connective tissue of an embryonic type with large, rather vesicular nuclei (fig. 3). There were few properly formed tubules or glomeruli. The renal pelvis was only slightly dilated and was not trilobed. The ureter was enormously dilated and slightly convoluted and provided with a median mesentery; its lumen was equal to that of an infant's ileum. The lining cells were greatly flattened and almost indistinguishable, and the almost transparent wall was very largely composed of connective tissue. There was, however, an abundant nerve

plexus beneath the peritoneum. The nerve plexuses around the right and left renal arteries showed no significant microscopical difference. The right vas deferens was a solid fibrous cord until it came into relationship with the right ureter. Passing through the medial ureteric wall, which was thickened at this point, it acquired a minute lumen. After communicating with the cavity of the ureter it opened on the right lateral red area in a similar position to the left. A little before its orifice it was surrounded by developing prostatic acini. The ureter had no other opening, but the right lateral red area was similar in size to the left and both, especially the left, showed areas of transition to a squamous type of epithelium. Whilst in some such areas the deeper cells were arranged with their longer axis at right angles to the surface it was often impossible to be certain of any real morphological difference from squamous epithelium. In the underlying connective tissue there were numerous plain muscle cells. Thin walled, dilated blood channels, sometimes containing inflammatory cells were largely responsible for the reddish colour of these areas. Below these areas of extroverted bladder, the forwardly directed tubercles showed a central mass of erectile tissue and on their superior surface were partly covered by transitional epithelium. Histological examination of all the other abdominal, thoracic and neck viscera revealed no abnormality.

Discussion

An explanation must be found for several features of considerable interest. The intestinal tract, supplied by the superior mesenteric artery, opens on the anterior abdominal wall below the attachment of the body stalk and is separated from it by normal skin. The umbilical arteries are normally developed and pass into the stalk from each side above this opening. There is no real development of the bowel below this level, and no attempt to form any connexion with a proctodeal depression. Widely separated from each other by the bowel apertures are the right and left genito-urinary orifices. They open on surfaces covered in part by transitional and in part by squamous-like epithelium. The central red area, whilst largely covered by mucus-secreting epithelium, shows areas of transitional epithelium. Changes, interesting from the viewpoint of comparative morphology, are present in the kidney and excretory ducts of one side.

During the past half century or more a number of somewhat similar cases have been described. Few have been adequately studied histologically and confusion must often exist as to the identity of some structures. This has not prevented many speculations as to the manner of their production and of that of the simpler forms of ectopia vesicae. The value of many of the earlier explanations is reduced by incorrect views about the formation of the bladder. The useful earlier papers are adequately considered by Johnston (1914).

The work of Sternberg (1927) and especially of Florian (1930) on the earliest stages of the formation of the hind gut and on the cloacal membrane is of the greatest interest as providing an adequate explanation for the simpler degrees of ectopia vesicae. The formation of the infra-umbilical portion of the abdominal wall has also recently been studied by Wyburn (1937). It has been shown that in the human embryo the short body stalk is modified to form a part of the sub-umbilical body wall (fig. 4 and 5). This is achieved by a process of differential growth of the embryo whereby this stalk, originally situated at the caudal end of the embryo, comes to arise from the ventral aspect. A portion of the

primitive yolk sac is thus enclosed at the tail end of the embryo and forms the primitive hind gut. There is a very precocious growth of an allanto-enteric diverticulum from the primitive gut cavity into the tissue of the stalk (fig. 4). This represents the primordium of the allantois. Forming the ventral wall of the gut, and for a time extending along this diverticulum on to the stalk is the cloacal membrane. Here ectoderm and endoderm are in contact, but, except where the future excretory passages are to form, should become separated by mesodermal tissue. Keith (1932, 1933) appears to accept the cloacal membrane as the hindermost part of the primitive streak and would accept the membrane as closing the blastophore or primitive mouth and consider that its fission reproduces the mouth of the primitive gastrula or coelenterate ancestor. Wyburn (1937) advances arguments that the primitive streak does not extend so far in the direction of the stalk. The cloacal membrane represents the

FIG. 4.—A diagram of an early stage of development showing the position of the body stalk and the precocious development of the allanto-enteric diverticulum. a. amnion; p.s. primitive streak; y.s. yolk sac; cl.m. cloacal membrane; a-e.d. allanto-enteric diverticulum; b.s. umbilical or body stalk. The extra-embryonic mesoderm is stippled and the whole embryonal formation is suspended in its cavity.

primitive area of contact of ectoderm and endoderm not yet separated by definite mesoderm. Defective development of the mesoderm, especially that derived from the hinder end of the primitive streak, which is less productive in man than in any other form, may result in varying degrees of non-closure. Without the intervention of mesoderm the cloacal membrane will break down.

In the present case the sub-umbilical portion of the anterior abdominal wall is occupied in the mid-line by the openings of the bowel. Normally, apart from the attachment of the yolk sac just above the umbilical stalk, the bowel, except at both ends, is free from the anterior abdominal wall, and is attached only by its dorsal mesentery. It is thus free to develop at a rate disproportionate to the length of the embryo. This is the result of the development of the coelom, and is well described by Frazer (1931). An important stage is the drawing into the embryonic body of a part of the hinder end of the

yolk sac and its relatively excessive growth (fig. 5). This results partly from the relatively excessive growth of the dorsal (neural) aspect of the hinder end of the body producing a relative shortening of the ventral structures. The introduction of the extra-embryonic coelom, between the body stalk with its allanto-enteric diverticulum forming the infra-umbilical part of the anterior abdominal wall and the developing gut caudal to the yolk sac, leaves this latter free to develop and elongate. The term cloaca should be used for the common cavity into which opens the caudal end of the hind gut and the allantois, as the allanto-

FIG. 5.—The body stalk is now situated on the ventral aspect. The growth of the primitive hind gut behind the yolk sac is beginning and is associated with the formation of the extra-embryonic coelom which will intervene between the adult hind gut and the cloaca and its derivatives. Lettering as for fig. 4, and h.g. area of formation of hind gut ; cl. cloaca into which opens the allantois.

enteric diverticulum may now be called. The term hind gut is applied to the elongating bowel before its lower end enters this common cloaca.

The bowel might open anteriorly at the site of the yolk sac through a persistent vitelline duct. In the present case the umbilical arteries pass above the bowel opening and there is an area of skin intervening between the bowel opening and the body stalk situated above it. There is also no necessary connexion between such a condition and the extroversion of the genito-urinary orifices. The bowel might also communicate with the surface owing to deficiency of the anterior wall of the true cloaca similar to that in a simple extroversion. This would have to be associated with the failure of the cloaca to be divided into anterior genito-urinary and posterior rectal parts by the growth of a mesodermal septum. The upper orifice should then open out of bowel representing the large intestine ; some evidence of a caecum might be expected and it should

be supplied from both mesenteric arteries. The presence of the inferior tube would present insuperable difficulties of explanation as its proximal and not its distal end opens into the cloaca. There is no evidence to support the contention of von Geldern (1924) that this blind posterior tube represents a development and persistence of the post-anal gut.

If the gut caudal to the yolk sac fails to obtain its freedom from the anterior abdominal wall by the development of the extra-embryonic coelom it will be arrested in development. The anterior body wall, if its primitive cloacal membrane persisted, might then break down at any point below the body stalk leaving the bowel to open on to the surface. It is only with persistence of this condition that mechanical theories of overdilation of the cloaca need be considered. (Wood Jones, 1912 ; Russell, 1939). It should be unnecessary to emphasize that without such a primary abnormality, the cloacal membrane cannot rupture to open into any part of the bowel supplied from the superior mesenteric artery without also rupturing across the coelomic cavity. The normal cloacal membrane does not rupture before the second month, but no information is available as to when a more extensive membrane might rupture. In any case purely mechanical distension by urine and faeces (Russell, 1939) is highly improbable. A case described by von Berenberg-Gossler (1913) suggests that such an arrested development of the hind gut may arise without extroversion of the bladder. The ileum communicated by a passage with the bladder and behind this was the caecum, whilst a blind tube suspended from a dorsal mesentery represented the colon.

The condition may thus result from the abnormally early breaking down of the cloacal membrane before any attempted differentiation of the primitive hind gut into a hind gut freed of ventral attachment and a genito-urinary cloaca. No development could then close off a ventral urino-genital from a dorsal alimentary part. This is the view advanced by Johnston (1914). If the cases of Bryce (1895) and Emrys-Roberts (1906) can be taken as comparable, the presence in them of what appears to be a caecal dilation of the upper portion of the bowel suggests that, sometimes, there is some development of the hind gut between the yolk sac and the superior orifice. If no such division of the primitive hind gut occurs the upper bowel opening will correspond closely to the site of the yolk sac, but cannot be considered to be the opening of a vitelline duct as in Sequeira's paper (1896) and Keith's earlier one (1908). A difficulty is to correlate a failure of the extra-embryonic coelom and of the hind gut to develop with the defective formation of the mesoderm of the hinder end of the primitive streak, and its failure to close in the cloacal membrane.

The developmentally arrested portion of gut will retain its blood supply from both the superior and inferior mesenteric arteries. From the dorsal aspect of this primitive hind gut, which should have formed the gut caudal to the yolk sac, a diverticulum may grow into the dorsal mesentery. This will end blindly being without any normal controlling influences. In some cases it may show two small lateral processes considered by Wood Jones (1912) to represent paired appendices. Whether in the circumstances their occurrence is of such morphological significance is more doubtful. In the

present case, and in the cases of Bryce (1895), Doran (1881) and Johnston (1914) no appendix-like structures are present. The upper bowel opening must lie below the body stalk and may be separated by normal squamous epithelium from the umbilical cord. The umbilical vessels can only lie above the bowel orifice.

The lateral walls of the ventral part of the primitive hind gut, which should have become the true cloaca, and on which the Wolffian and related ducts must open, will be pushed to either side of the bowel aperture. If division of the primitive hind gut had proceeded normally the area between these orifices would have formed the dorsal wall of the true cloaca. In simple ectopia of the bladder this is the upper trilobed red area exposed. In the present case, if any attempt at division of the primitive hind gut had occurred, traces of this bladder epithelium might be expected between the mucous membrane of the bowel orifice and the abdominal wall below the stalk. Mucous membrane passed directly into squamous epithelium, but a metaplasia cannot be excluded. Von Geldern (1924) demonstrated intervening bladder epithelium at this site, and in a complicated case described by Russell (1939) a large area of bladder intervened between the umbilical stalk and the orifice of the bowel.

The appearance of the unilateral cystic kidney is not inconsistent with the view put forward by Kampmeier (1926). A metanephric blastema, composed of mesenchyma, forms a cap over a part of each of the branches of the upgrowth from the Wolffian duct. This normally becomes converted into a convoluted tubule and glomerulus, and establishes a junction with the related upgrowth which then forms the collecting tubule. That part of the upgrowth not in relation to the blastema continues to grow and by branching establishes further connexions with the formation of further blastemata. The first few generations should lose their connexion with the collecting system and should atrophy. They may persist as cysts and this may result in a reduction of the number of nephron units. The abundant connective tissue seen in the present instance around these primitive cysts forms a basis for the often enormous increase of interstitial connective tissue sometimes seen in congenital cystic disease of the kidney (Bell, 1935).

The enormously dilated right ureter opens only through the narrow sex duct, which is impervious at a higher level. There is thus a failure even of the first stage in separation of the ureter and Wolffian duct on the right side. This should consist in a dilation of the Wolffian duct and a 'taking up' of it into the cloaca so that the ureteric orifice may open directly into the future bladder. A further stage is dilation of the lower end of the ureter and its entering into the formation of the bladder wall so that the Wolffian duct is separated from the ureteric orifice. This stage has been attained on the left side. The condition of the right side has been described by Shattock (1895), Sequeira (1895-6) and Wood Jones (1912). It is similar to that normally found in the reptilia, especially in lizards. In the other cases described no cystic condition of the kidney, nor dilation of the ureter is noted. The dilation may be secondary to an almost, but not completely, obstructed urinary outlet. The right kidney is quite capable of secreting urine.

The apparent separation by normal skin of the epithelium of the genito-

urinary areas from that of the gut introduces difficulties. The appearance of the epithelium of the genito-urinary papillae is not inconsistent with a metaplasia. The macroscopic difference is largely determined by dilated blood sinuses. The embryonic line of junction may become invisible with subsequent growth.

The presence of two genital tubercles may be explained. Owing to the deficiency of the mesoderm at this site, the mid-line genital tubercle cannot be formed in front of that portion of the cloacal membrane destined to break down and form the normal excretory outlet of the cloaca. Owing to the wide separation of the parts the lateral genital folds of mesoderm cannot unite to close the deficiency in the membrane posteriorly. The first failure alone would produce epispadias. The case is quite distinct from those of posterior duplicity (Mainland, 1929).

Summary

A case is described of ectopia of the bladder associated with an opening into the bowel from the subumbilical part of the abdominal wall. The mechanism of development of the gut behind the vitelline duct is discussed, and apart from a small blind tube growing into the dorsal mesentery this part of the bowel is considered to be absent. The opening of the primitive hind gut is considered to result from the failure, over almost its entire extent, of the primitive line of junction of ectoderm and endoderm forming the cloacal membrane, to be invaded by mesoderm. This probably resulted from a deficient formation of mesoderm at the hind end of the primitive streak.

Atavistic developmental abnormalities of the right kidney are also present.

A detailed histological study of the exposed areas would suggest that the type of epithelium, other than mucus-secreting, provides no certain criterion for the separation of those parts of ectodermal origin from those of endodermal.

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