## Rhabdomyoma of the Urinary Bladder.

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## Vesicae urinariae tumor e telâ musculari transverse striatâ constructus (Rhabdomyoma).

SUMMARIUM.

E dysuriâ atque urinae retentione aegrotabat puer, haematuriâ semel modo observatâ: ex uraemiâ mortuus est.

Vesicâ post mortem incisâ tumores polyposi e membranâ mucosâ orti intus apparuerunt.

Hos e telâ musculari transverse striatâ constare scrutatio probat microscopica.

Inveniuntur fibrae musculares e cellulis ingentibus multinucleatis gradatim evolutae, cellularum nucleis in cytoplasmatis margine dispositis.

Neoplasmata nullas malignitatis notas in structurâ penitiori monstrant; nec invaditur tunica visceris muscularis.

Telae muscularis striatae evolutionem in hoc situ quomodo licet intelligere?

In plerisque certe heteroplasia heterotopiam significat, i.e., cellularum dislocationem abnormem de structuris quibusdam in telas adjacentes.

In vesicae urinariae exemplo cellulae embryonales, ut opinor, sphincteris vesicae externi in telam vesicae submucosam vagatae sunt.

Hujus musculi ad normam includuntur fibrae quaedam in glandulae prostatae substantiâ apud vesicae cervicem.

Illam thesem sustinent hae considerationes: (1) Tumores ad vesicae partem inferiorem limitantur; (2) Ingeniti probabiliter insuper erant.

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TUMOURS of striped muscle fibre are, wherever they may occur, of extreme rarity, and the growth of such a new formation in so unexpected a position as the urinary bladder will fully justify the record of the following specimen.

The bladder, which is that of a child aged 2 years, was presented to the Museum of the Royal College of Surgeons by Mr. C. S. Wallace, who

has kindly allowed me to record it. For about its lower two-thirds the interior is raised and deeply lobulated by the growth of a series of closely-applied sessile tumours, smoothly covered with mucous membrane. A portion of the new formation projects into and occupies the vesical orifice of the urethra, but the mucosa of the prostatic portion itself is free of disease. The right ureter is considerably dilated, its aperture being completely surrounded by the growth; the wall of the left ureter is thickened, although the canal is not obviously enlarged. The muscular wall of the bladder is somewhat hypertrophied. The prostate is normally developed.

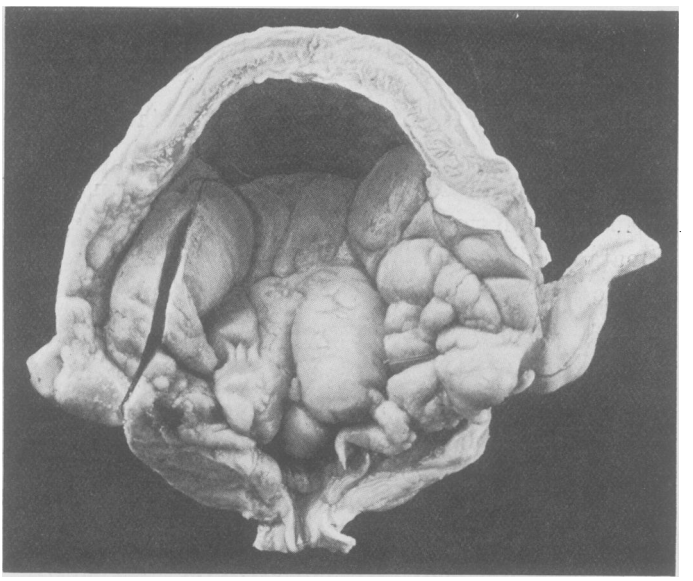

FIG. 1.

Pueri (annorum duorum) vesica urinaria, pariete posteriori diviso. Monstrantur tumores in cavum projecti qui e telâ musculari transverse striatâ praecipue constant. Magnitudinis naturalis.

The specimen referred to in the text, the bladder being laid open, and viewed, from behind. For its lower two-thirds the interior is raised and deeply lobulated by the growth of a series of closely applied sessile tumours, which consist chiefly of striated muscle. (Museum of the Royal College of Surgeons. Natural size.)

The child (A. B.) was admitted into the Children's Hospital, Shadwell, under the care of Mr. C. S. Wallace, on November 22, 1906, with a history of four months' pain on micturition; on one occasion, three

months before admission, the passage of blood had been noticed. There was no family history of importance.

When admitted the patient was well nourished. There was no pain on palpating the abdomen, and nothing was detected by it; rectal examination was equally negative. On the day following admission an attack of retention occurred; the urine was drawn off and the bladder sounded, but nothing was discovered to explain the retention. This was the only occasion on which retention took place. Micturition gave, apparently, no pain. The urine was neutral; specific gravity, 1015; it contained a thick cloud of albumin and a fair number of pus cells, but no blood or casts.

A fortnight later diarrhœa and vomiting set in; these resisted all treatment, and rapid wasting ensued. Unconsciousness supervened and all the symptoms of uræmia, death occurring in a state of coma, but without convulsions. The amount of urine passed daily was from 15 to 25 fluid oz. No hæmaturia was observed.

## Histology.

The tissue as studied in vertical sections of one of the chief of the tumours consists throughout of a close felt work of extremely delicate and wavy fibrils, well provided with normal connective-tissue cells. The fibrillæ are not disposed in bundles, but form, by their interlacing, a uniform felt, the whole structure being that typical of a soft fibroma. The cells are as devoid of any arrangement as the fibre, and, as they are subject to no compression, show large oval, as distinguished from fusiform, nuclei. The free surface of the growth is raised in low, simple elevations, without being papillary. At the free or vesical surface there is a comparatively narrow zone in which the cells are more thickly clustered, and amongst them have wandered a certain number of polymorphonuclear leucocytes, the appearances being indicative of an inflammatory process involving the surface of the growth, a result attributable to the cystitis present during life. Well-developed arterioles are distributed in the new tissue. There is nowhere any suggestion of a sarcomatous transformation being in progress, the more cellular tissue being limited, as already stated, to the free surface immediately beneath the epithelium.

None of the proper muscular wall of the bladder appears in the section, and as no mucosa remains differentiated from the new growth, the latter, it may be concluded, has arisen in the mucous and submucous

coats. So far the growth would be a soft fibroma. It may be added that there is no neurofibromatosis.

But here arises the real matter of histological interest: the fibrous tissue is throughout, but in different degrees, pervaded by striated muscle fibres in all stages of development. In some spots these form a slender, wide-meshed net, in others they are sparse; and fields may be selected where there are none. They are least abundant in the deepest part of the growth, and they are most densely aggregated in the region of the free surface, where they are disposed in closely intersecting fasciculi. The striated fibre varies somewhat in the details of its structure.

As studied with one-sixth objective, the closely intersecting bundles last referred to consist of long, narrow fibres of no greater breadth than the cells of unstriped muscle. The cross-striation, however, is quite unequivocal, for whilst the longitudinal may be hardly or not recognizable, the other is sharp, parallel, and extends regularly across the whole breadth of the fibre. The great majority of the fibres present it. But besides such there is elsewhere striated fibre in the ordinary stages of development, and in positions where the latter can be clearly followed by reason of the fibres being isolated in the midst of the delicate connective tissue. These appear as multinuclear masses of protoplasm of diverse form according to the direction of the section, the nuclei lying at the periphery and being very irregularly distributed with regard to the length of the developing fibre; in some areas the sarcoblasts occur in groups, in others singly. The middle or widest portion of such developing fibres is of considerable thickness.

Where divided transversely the cytoplasm appears finely granular, and in such views the nuclei are invariably disposed peripherally in it, sometimes on one side in a horseshoe form. When viewed longitudinally these multinuclear elements are irregularly fusiform, and the cytoplasm is, in a certain number, doubly striated—i.e., both longitudinally and transversely.

By the elongation of such structures and the separation of their nuclei, there result the long, doubly striated fibres which are present in other parts, and many of which present a series of nuclei parted longitudinally by considerable intervals. These fibres may be of striking length, and it is noteworthy that the nuclei of such are not centrally but peripherally disposed; nor have the latter the length of those of unstriped cells. This peripheral disposition of their nuclei alone would serve to differentiate such fibres from the unstriped kind, although in

actual breadth they may not exceed that of well-developed plain cells. In one cross-striated fibre the sarcolemma was brought into view by the rupture and retraction of the included substance.

Such slender fibres at times run in twos and threes in a wavy course, but remain discrete, with narrow and not always regular interspaces. None of the fully developed striated fibres attain the breadth of those of common voluntary muscle.


FIG. 2.

Structurae e sectione microscopicâ tumorum unius selectae. Monstrantur fibrae quaedam musculares, transverse striatae, in gradibus diversis ad normam evolutae.

From a microscopic section of one of the tumours, showing a selection of developing and developed striated muscle fibres. The smallest element is a cross-section of a multinucleated sarcoblast with peripherally disposed nuclei. The supporting basis of fine connective tissue is not shown. (One-sixth objective.)

In the deeper part of the growth a few isolated bundles of unstriped muscle cells occur in the fibrous tissue, but these seem to be distinct in nature from the rest of the muscular tissue, and may be regarded, I think, as stray elements of the muscularis mucosæ, or deeper muscle, which have become entangled in the new formation.

It is well known that the cells of unstriped muscle may present a longitudinal striation and indistinct traces of a (spurious) transverse one; and it is necessary, in order to anticipate criticism, to state that a study of the microscopic sections under $\frac{1}{12}$ oil immersion fully confirms the foregoing account, and makes it clear that there is a large amount of striated fibre present in the growth. The transverse darker markings appear as broad equidistant bands of perfect regularity, and in some the intervening lighter zone is crossed by a finely punctated line (Dobie's line). The broader darker zones in some cases are resolvable into bundles of sarcous elements. Many of the long multinucleated fibres, however, whilst they exhibit good longitudinal fibrillation, show no transverse striation; and this is true even of some of the broad multinucleated fusiform elements. Even in the course of the same developing, elongated, and sometimes varicose fibre, the cross marking may be well pronounced in certain places, whilst the longitudinal is alone discernible in others. And lastly, even the most slender fibres, such as those which are gathered in intersecting groups, show in cross-section a difference from unstriped cells in that when a nucleus happens to be divided it is not centrally located, but lies at the periphery of the cytoplasm, which is, moreover, particularly granular from the presence of the fibrils included within it.

Let me next refer to a second specimen (No. 3,693) which is also in the Museum of the Royal College of Surgeons, and which is even a purer example of rhabdomyoma than the foregoing. Here, too, the growth takes the form of multiple polypi, and comes from a child who was likewise aged about 2 years. The lower part of the viscus is thickly beset with polypoid growths, the smaller of which arise from the neck and project into the prostatic portion of the urethra; most of these are cleft into secondary processes, or subdivided, without being, however, papillary. Higher up the growths are of considerably larger size but fewer in number, and are attached by broader bases, and merge into sessile thickenings of the mucosa. The upper half is quite free. At the apex of the bladder, on the external aspect of the muscular coat and covered by the peritoneum, there is a sessile nodule about as large

as a haricot, in which there is an irregular central cavity; the inner surface of the organ is here free of new growth. The muscular wall of the bladder is hypertrophied. The ureters are dilated. The child was aged 1½ years when first under observation; for more than a month previous to this, micturition had been frequent and painful, and was attended with great straining. No calculus was detected by the sound. A perineal cystotomy was eventually carried out, and portions of the growths were cut away with scissors as they appeared in the wound, into which they were forced by the straining efforts of the patient. Death occurred forty-eight hours later. The specimen is engraved in a "Treatise on Calculus," by Mr. J. G. Crosse.

The histological study of these polypi, in sections made vertically to and including the free surface, shows that they consist almost entirely of well-developed, though slender, transversely striated muscle fibre. In the deeper part of the growth the fibres lie in a basis of soft fibrous tissue with few pertaining cells; but at and for some way below the free surface they constitute the whole of the structure, the intervening finely fibrillar connective tissue being quite insignificant in amount and provided with but few proper cells. All the fibres show the cross-striation. There are no spindle or other cells suggestive of a sarcomatous formation. Many of the muscle fibres show a very pronounced longitudinal fibrillation in addition to the cross-marking. The component fibrils are particularly clear in the transverse sections of the fibres. In addition to this there occur amidst the fibres short, broader, fusiform masses of protoplasm enclosing groups of nuclei, and representing developing striated fibre; in these the stages of striation are traceable just as in human fœtal muscle. Generally speaking, the muscle fibres are not thicker than unstriped cells, though a certain number exceed such.

Mr. J. H. Targett[1] has referred to this specimen, but the presence of multinucleated developing muscle fibre has escaped his notice, although he remarks that in some of the "long spindle cells" a transverse striation can be recognized, but that the microscopical features are not so distinct as could be wished. This reserve I cannot explain, unless it is to be attributed to the use of a faulty objective and the omission to study the sections with an oil-immersion.

The small nodule at the apex of the bladder, mentioned in the description, is at first suggestive of a metastatic growth; yet microscopically it shows no striated fibre, and nothing at all resembling the

[1] *Trans. Path. Soc. Lond.*, 1896, xlvii, p. 291.

tumours within the bladder. The cavity in its centre is surrounded with fibrous and fibromuscular tissue, and is lined with a cellular exudate. It lies in the situation of the urachus, with which structure it is probably related; and I should be inclined to disconnect it altogether from the other growths in the sense of its being a metastasis. So abundant is the striated muscle, and so small the fibrous tissue in the intravesical growths in this case, that the new formations must be classed without qualification as rhabdomyomata.

There is a third specimen in the Museum of the Royal College of Surgeons which, as interpreted in the light of the two foregoing, must be placed in the same category. The preparation (No. 3,692), which is one of Hunter's, is a lateral section of the bladder and urethra of a young girl. Numerous lobulated polypi arise from the mucous membrane and nearly fill the cavity. The largest has a base nearly 2 in. in diameter; the others have narrow pedicles; two of them have grown from the neck of the bladder into the urethra, and have protruded beyond its external orifice, their ends being ulcerated and flocculent. In places the growth is low and sessile, as around the orifice of the right ureter. The muscular wall is uninvaded and readily separable from the diseased. The upper half of the viscus is unaffected. The preparation is figured in Baillie's "Illustrations," fasciculus vii, pl. 4, fig. 2. A study of microscopic sections, under $\frac{1}{12}$ immersion, discloses a considerable number of multinuclear giant-cells, with granular cytoplasm, the nuclei in all cases being peripherally disposed. In some, when viewed in the longer axis, the cell body shows a well-marked longitudinal fibrillation. The chief bulk of the tissue consists of long, slender, intersecting fibres in not very well-defined bundles, the intervening tissue being very scanty and of a delicate, open, fibrillar kind. The giant-cells first referred to lie amongst the fibres, sometimes congregated in clusters. The fibres in question, though not in general broader than unstriped cells, differ from such in the fact that they are provided with more than a single nucleus. Oftentimes a series of nuclei, in longitudinal apposition, lie along the fibre; in these fibres, moreover, there is a well-marked longitudinal fibrillation. Some of the fibres presenting these characters are wider than the rest, and some are swollen out in parts of their length, there being a cluster of nuclei in the swollen parts. Notwithstanding these characters, which show that the fibres belong to the cross-striated kind, the transverse striation is present in but few; where it is to be seen, however, it is quite distinct, the component

fibrillæ, which are traceable individually, being regularly subdivided into darker and lighter segments.

The presence of multinucleated cells in this specimen was noticed by Mr. Targett (loc. cit.), but he did not attempt to give any interpretation to them.

And, to close the list, there is a fourth specimen in the Museum of St. Thomas's Hospital (No. 2,163). This is the bladder of a young male child. Over its lower half the mucous membrane is raised in low, smoothly rounded ridges, from which gradations may be traced to the prominent polypi which are clustered about the neck of the bladder. Some of these hang from long, narrow stalks, and appear to have been forced into the urethra beyond, which is much dilated. The mucous membrane of the prostatic portion of the urethra is beset with similar but more minute outgrowths. The microscopic sections of one of these polypi show that it consists of delicate connective tissue, which is traversed by numbers of long, narrow fibres, furnished with eccentric or peripheral nuclei. Some of the fibres are of striking length, and a considerable number exhibit a typical transverse striation; the nuclei are disposed at intervals in the course of the fibre. The fibres produce a wide-meshed net and run in intersecting groups composed of a few elements only, and these not closely compacted but loosely accompanying one another. Those that present no transverse striation are of the same kind in that they are of marked length and furnished with multiple nuclei. Fusiform, multinuclear sarcoblasts occur abundantly with the larger fibres, conformably with which they are disposed; some of these show an exquisite cross-striation. The tissue in which the fibres lie is that of a soft fibroma, and is composed of a loose felt work of very delicate, wavy fibrillæ, furnished with a moderate number of connective-tissue cells. Histological marks of malignancy are entirely absent.

### Remarks.

Such an anomalous specimen naturally raises the question, Where can the striated fibre in a submucous vesical tumour come from? Speaking generally, it is simpler to explain the presence of heteroplastic structures as due to a process of dislocation having taken place during development, from some adjacent organ or part in which such structures normally occur, than to regard them as produced *ab initio* at the site in which they are found. Of dislocation and the shifting of parts during

normal development embryology teems with examples. But as for new growths, it is usual, e.g., to view the striated muscle fibre found in rhabdomyosarcomata of the kidney in infants, as having been originally derived from the embryonic muscle-plates with which the metanephros is so closely related; or, if the tumour does not involve but only lies against the kidney, to regard the tissue as having been misplaced into the precursor of the permanent kidney, the Wolffian body. The correctness of such a view is strongly supported, if it is not proved, by the straying of adrenal tissue (apart from tumour formation) witnessed in the kidney, or in the liver, the broad ligament, and elsewhere. Analogous displacements are well-recognized phenomena in the development of the spinal cord, where the grey matter may be "heterotopic," or abnormally disposed in the white; and the same term might be usefully extended to other examples of the same phenomenon. Heteroplasia in tumours is in most cases heterotopia.

In connexion with the bladder, then, it may be remembered that striated fibre is to be found normally in the fœtus, the child, and also in the adult, around, and to some considerable depth in, the substance of the anterior or superior portion of the prostate, the structure in question constituting the sphincter vesicæ externus of Henle. As Henle's figures show,[1] the fibres completely encircle the apex of the prostate, but in the cross-sections carried further back they appear only on the anterior or upper aspect. From the front of the gland they pass obliquely upwards and backwards round the neck of the bladder in the groove between the viscus and vesicula seminalis, constituting a superficial or external, though not strongly marked, sphincter. The absence of the striated fibre from the lower or posterior aspect of the prostate in transverse sections carried through the more proximal part of the gland, is due to the obliquity of the muscle. Some excellent recent figures showing the external vesical sphincter of Henle, as it appears in transverse sections of the prostate, are given by Mr. C. S. Wallace in his work on "Prostatic Enlargement."[2] Some of the fibres (as shown also in Henle's figures) lie well within the prostatic substance.

The explanation which I venture to put forward in the case of rhabdomyomata of the bladder is that the growth of muscle fibre has arisen from vagrant sarcoblasts which have abnormally extended or

[1] "Handbuch der systematischen Anatomie," Braunschweig, 1866, ii, p. 380; and "Grundriss der Anatomie," Braunschweig, 1888, Tafel cl.

[2] *Oxford Medical Publications*, 1907, figs. 5, 8, 9, 14, 17.

have been displaced, beyond their usual deeper limits, into the sub-epithelial tissue of the bladder. Such a misplacement or ingress might occur the more readily during the earlier stages of development in the male since the growth of the prostatic glandular tissue from the urethra would either not as yet have taken place or would offer but little obstacle as a barrier to it.

There are two considerations which may be advanced in favour of this hypothesis. One of these is that in three of the four cases the tumours were met with in infants, and were probably congenital. The child in Mr. Wallace's case was only two years old, and there was a history of four months' pain on micturition. In Crosse's case the patient was aged $1\frac{1}{2}$ years when first under observation, and for more than a month micturition had been painful and frequent. And the bladder in St. Thomas's Hospital Museum is that of quite a young child. In all of these the tumours were almost certainly present at the time of birth, but had not then attained sufficient size to produce noticeable symptoms. Hunter's case was that of a young girl, but the size and number of the growths shows that the disease must have been many years in progress, for the neoplasm is not malignant. And, secondly, it is significant that in all four cases the disease is limited to the lower portion of the bladder; the upper half of the viscus is, in every one, quite free of growth. That this is equally so in Hunter's case a recent examination of the specimen shows: although the whole of the vesical cavity is filled, no tumours are attached to, or arise from, any part of the upper half of the organ.