GLOMERULO-NEPHRITIS.

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FOR many years it has been known that the glomeruli are a special seat of lesion in certain cases of post scarlatinal nephritis; and Klebs separated the form in which this was the case from other forms of nephritis under the head of glomerulo-nephritis. He found here, accumulated between the capsule and the glomerulus, angular nuclei embedded in a finely granular mass, and the vessels of the glomeruli covered by nuclear masses.

Dr. Klein, in his well known account of the minute anatomy of scarlet fever, has shown that glomerular changes not only play a very important part in the tissue-alterations met with in the kidney in this disease, but occur at a very early stage. Like Klebs, he found an accumulation of nuclei between the glomerulus and the capsule, and an increase in the nuclei in the glomerulus itself; but, whilst Klebs attributed the cell-growth to proliferation of the connective tissue between the capillaries forming the glomerulus, Dr. Klein looked upon it as due to the proliferation of the epithelium lining the capsule and the glomerulus, and to a germination of the nuclei in the walls of the capillary vessels.

Very recently, it has been pointed out that glomerular changes very similar to, if not identical with, those observed in the scarlatinal kidney are met with in other forms of nephritis. Langhans, in the seventy-sixth volume of Virchow's *Archiv*, has described several cases of the kind; and Dr. Greenfield, under the head of subacute interstitial, describes a form of nephritis in which the clinical symptoms are those of acute desquamative nephritis, but to the naked eye the kidney resembles the large white, or the kidney of scarlatinal nephritis; whilst, on microscopic examination, interstitial change with affection of the glomeruli is found. He states, however, that the changes do not so distinctly commence in and around the Malpighian bodies, but more generally throughout the intertubular spaces. During the past eighteen months, three cases have come under my notice which, in most respects, correspond to those included by Dr. Greenfield under the head of interstitial nephritis, but in which, it seems to me, the glomerular change, as in post-scarlatinal nephritis, is the most prominent and essential feature of the lesion. I have ventured to allude to them as cases of glomerulo-nephritis, in order to indicate this prominence, though I know that objection may be taken to this term, for, in all three, interstitial and tubular changes, as well as glomerular, were present. I will briefly state the leading features of the cases, together with the pathological changes found after death.

CASE I.—J. E. L., a boy aged 17, was admitted into the Manchester Royal Infirmary on April 28th, 1879, suffering from albuminuria and excessive anasarca. No history could be obtained of previous syphilis, excess of alcohol, or infectious disorder. Fourteen weeks before admission, after a fall on the ice, an abscess formed in the left gluteal region, which discharged for some time after it was opened. Eight weeks before he came under my care, he noticed, for the first time in his life, a swelling of his feet, which soon spread to the legs, arms, and face. He lost ground very rapidly; the anasarca became very pronounced, the anaemia very marked, and he suffered from vomiting.

On admission, he was extremely white, and the tissues of his body were enormously distended with fluid. The area of superficial cardiac dulness was slightly enlarged, but there were no indications of considerable cardiac hypertrophy. He coughed frequently, and expectorated a little mucus. The scanty urine had a specific gravity of 1018; it contained much albumen and a little blood. In the deposit from it were found epithelial and granular casts. He died somewhat suddenly, apparently from lung-œdema, four days after admission. The average daily excretion of urine whilst he was in hospital was only twenty-six ounces.

At the necropsy, the heart was found slightly enlarged, the walls of the left ventricle being distinctly, but not greatly, thickened. The kidneys had the ordinary appearances of the large white kidney. The capsule stripped off easily; the cortex was thickened, and of a yellowish white colour.

On microscopic examination, it was found that the Malpighian bodies were the chief seat of tissue-change. Within the capsules of almost all of them a considerable cell-growth had taken place, which had assumed a more or less fibroid appearance; the capsule itself seemed thickened, and difficult to distinguish from the adjacent

structures. In some of the glomeruli, a thick fibroid and nucleated tissue was in close contact with the glomeruli, on which it appeared to press; the glomeruli themselves being squeezed to half or one-third their size. (Fig. 1.) In others, the growth between the capsule and

Fig. 1.

glomeruli seemed to consist of cells with elongated nuclei, arranged parallel to the capsular epithelium, with which it was continuous, and from which it appeared to spring; and all stages between this and the appearance represented in Fig. 1 were to be met with.

In very few places unattached cells or nuclei were seen, though in some of the least affected glomeruli, epithelial cell-proliferation seemed to have taken place.

The intervening tissue in some glomeruli cemented the capsules firmly to the glomeruli. In others spaces appeared between it and the capsule, or the glomeruli, or both, as represented in the drawing.

In all the new tissue dipped between the lobules of the glomeruli, appearing in some to cut the glomeruli into segments, hardly any healthy glomeruli were to be met with. In a few, the nuclei were unduly abundant; but in most they were less distinct than in the normal state, the glomeruli seeming to have undergone hyaline or fibroid change. Considerable interstitial change was present, especially round the Malpighian bodies outside the capsules; but it was also well seen between the convoluted tubes; some parenchymatous change was also present, and in some of the tubes casts could be seen. The vessels of the cortex exhibited but slight change. There might be a little increase of the muscle-nuclei, and thickening of the intima in some, but the change did not appear very considerable.

CASE II.—In my second case, the glomerular alterations were not so advanced, though the illness had run a longer course. F. F., a man aged 26, had enjoyed good health until five months before admission to the Manchester Infirmary. There was a history of alcoholic excess, none of syphilis or infectious disease. Five months before, he noticed that his legs and abdomen were slightly swelled; yet for two months he continued, as he thought, in fair health. Then, for the first time, he noticed his urine brown and scanty, and he felt ill.

When he came under my care, on May 27th, 1879, there was considerable general œdema and ascites. There was no increase of the superficial cardiac dulness, but he had an accentuated second sound at the aortic cartilage. He suffered slightly from bronchitis. The urine was scanty, amounting to from eight to fourteen ounces daily. It contained much albumen and a little blood. In the abundant deposit from it were found epithelial casts, free cells, and hyaline casts. The man continued under my care till June 15th, when he died from uræmia within six months of the first appearance of dropsy. He never once passed above thirty-two ounces in twenty-four hours, often much less. The specific gravity varied from 1012 to 1017. Towards the fatal termination, the amount of albumen in the urine became very large.

At the *post mortem* examination, the heart weighed thirteen ounces; both cavities were somewhat dilated, and the thickened walls seemed streaky, mottled, and easily torn. The kidneys were very large. Their outer surface was smooth and mottled; the capsule stripped easily. On section, the cortex was increased in thickness, yellowish-grey in colour, and contrasted strongly with the dark-coloured pyramids.

The microscopic examination showed that the glomeruli were largely involved in the lesion, much parenchymatous and some interstitial

change being also present. The glomerular affection differed somewhat from that observed in the first case. The cell-growth, with fibroid appearance, was much less distinct, adjacent to the capsule. The capsule itself was thickened, and several layers of spindle-shaped cells were found lining the capsule in many of the Malpighian bodies. Inside this were nuclei more or less free, round or oval; and further inwards, in many glomeruli, a second fibroid arrangement of the cells, most advanced near the glomerulus, sometimes in contact with it, but often slightly separated from it. (Fig. 3.) Many of the glomeruli were divided into segments, the fibroid tissue seeming to penetrate between the component lobes. Some of the glomeruli were little, if at all, affected; in others, the cell-growth had not assumed a fibroid change, and it seemed to me that all stages of its development from the glomerular and capsular epithelium could be traced. The glomeruli themselves were not nearly so much altered as in the first case, the nuclei being in some instances unduly abundant, in some normal; whilst in some, fibroid and hyaline changes had occurred. Parenchymatous, as well as glomerular, changes were very marked, and there were also some interstitial changes, especially around the capsule. Figs. 2, 3, and 4, represent different stages ob-

and capsule is more fibrous, but where it is separated from the capsule, nuclei, some free, some united in small masses, are seen.

Fig. 2.

Fig. 3.

served in the capsular contents. Like Fig. 1, they have been drawn for me by Dr. Bary, from sections shown the Pathological Museum.* In Fig. 2, an early condition is seen; epithelial increase appears to have taken place, both on the capsular and glomerular surfaces (*a* and *b*, Fig. 2), whilst at *c* there is a collection of nuclei, in fine granular material, to which the epithelium of capsule and glomerulus seem contributing. At *b'*, large nucleated cells, one having a double nucleus, are very noticeable.

In Fig. 3, a more advanced condition is seen. The growth at *b*, close to the glomerulus, and at *c*, adjacent to the capsule, is more fibrous in appearance than in the intermediate position.

In Fig. 4, a still later stage is shown; the growth between glomerulus

Fig. 4.

CASE III.—For the third case, I am indebted to my colleague, Dr. Dreschfeld, under whose care T. M., aged 24, was admitted into hospital on June 17th, 1879. He stated that he had suffered for a week from swelling of the legs, headache, and vomiting; before this, he said he had enjoyed good health, but some faint cicatrices on the penis showed that he probably had suffered from syphilis at one time. The urine was loaded with albumen, scanty, and had a specific gravity of 1015; it contained blood and epithelial casts. At first, he improved somewhat under active purgation, and the urine increased in amount, though it never became normal; but during the third week of residence in hospital, he became worse. The general oedema increased; the urine became less copious, was more albuminous, and of lower specific gravity. Diuretics, vapour-baths, etc., failed to give relief, and the man died on the 5th of September, three months after the first symptoms of kidney-disease showed themselves.

At the *post mortem* examination, the heart was found normal; the kidneys looked like the large white variety, but, under the microscope, glomerular changes were very manifest. Interstitial change, too, was well marked, but parenchymatous alterations, though present, were slight. The glomerular alterations were very similar to those observed in the last case, but less advanced, that is to say, there was less of that fibroid appearance which was well marked in the cell-accumulations between capsule and glomerulus in the first two cases, but the thickening of the intima and the proliferation of the muscle-cells in the arterial coat was better seen than in either of the other cases.

The three cases I have recorded presented very similar clinical symptoms. They ran a course of two to six months. In all, general oedema was a conspicuous symptom, and the urine, small in quantity and of low specific gravity, contained a large amount of albumen. In none of them was the heart considerably hypertrophied. Pathologically, too, they resembled one another in this, that the glomerular changes seemed to depend on cell-accumulation between the glomerulus and the capsule, which assumed, to a greater or less extent, a fibroid appearance, and eventually led to destruction of the function of the glomerulus.

The changes resemble those which are met with in scarlatinal nephritis. The origin of the cell-accumulation and fibroid appearance which is observed in scarlatinal nephritis and the cases I have recorded is difficult to determine. There are three views held on this point.

1. It arises from proliferation of the connective tissue contained in the glomerulus, as held by Klebs.

2. It is due to wandering leucocytes.

3. It is the effect of proliferation of the epithelium, which lines the capsule and also the glomerulus.

The latter view is the one which Dr. Klein advanced in explanation of the appearance presented by his scarlatinal cases, and it is the one,

* Cambridge Meeting of the Association.

too, to which the examination of my own cases and sections from the kidneys of those dying of scarlatinal nephritis leads me.

I believe that the fibroid appearance which I have mentioned is due to the flattened condition of the proliferated epithelial cells arising partly from natural mode of growth, partly from pressure, and that this change may take place both in the epithelial cells from the glomerular surface and in that of the capsular surface. I think, however, that the epithelial change is not the only source of cell-accumulation, but that wandering leucocytes take part in the process; for in some instances I see collections of round cells without corresponding changes in the adjacent epithelium. I doubt whether the cell-elements are derived from the interstitial tissue contained in the glomerulus: firstly, because the appearance of the cell-growth between the glomerulus and the capsule appears to me to betoken, as I have said, an epithelial origin; secondly, because it appears to me not yet proved that interstitial tissue exists in the glomerulus. It is true that Axel Key has asserted its presence; and recently Dr. Waller, in a paper on Scarlatinal Nephritis in the *Journal of Anatomy and Physiology*, has stated that the connective tissue can easily be shown by injecting the fresh kidney with gelatin tinged with carmine, and then staining with logwood. I have certainly failed to find proof of its existence in this way, and it has to be remembered that there are many sources of fallacy in the examination.

Langhans, in the paper to which I have referred, has lately given the result of his examinations of the constitution of glomeruli; and he is wholly unable to detect any connective tissue in the glomerulus, further than the division of the vas afferens. Runebergs, too, who has still more recently studied the structure of the glomerulus, is unable to find in it connective tissue.

There was a very marked distinction in the appearance of the glomeruli in the first case, and in the second and third cases. In the first, the changes seem largely connected with the capsular epithelium, though there were in many parts indications that the glomerular epithelium was also affected. In the second and third cases, whilst the capsule was thickened, and its epithelium considerably changed, the cell-accumulation seemed connected for the most part rather with the epithelium covering the glomeruli, than with that over the capsules.

Langhans has distinguished three kinds of structural alteration in the glomeruli: 1. Glomerular, where the proliferation of the glomerular epithelium takes place; 2. Capsular, where the capsular epithelium is the chief seat of proliferation; 3. Swelling of the capillary nuclei. Of the third form I have met with no examples, but I think the cases I have described bear a close relation to the two first divisions he has drawn, but that both changes are apt to occur together.

In the cases I have brought under notice, the glomeruli themselves have evidently undergone great changes apart from epithelial alterations. In some, the nuclei seem unduly numerous; in some, the glomeruli seem changed into fibrous tissue. The increase of the nuclei may be due to proliferation of the epithelium deeply seated within the glomerulus, or to increase in the capillary nuclei. The fibrous appearance may be due to simple obsolescence from pressure.

Dr. Klein has described a hyaline change as taking place early in the capillaries of the glomeruli in scarlatinal nephritis.

The cause of the special implication of the Malpighian corpuscle in glomerulo-nephritis can only be guessed at; but, if we look upon the capsular epithelium as being a continuation of the epithelium lining the tubules, as some hold it to be, then we may consider the glomerular nephritis as allied rather with parenchymatous than interstitial affections; but, like parenchymatous nephritis, it is usually accompanied by interstitial changes.

Dr. Klein seems to consider the glomerular affection as secondary to the blocking up of the afferent arteries, owing to changes in the arterial coat; but the arterial changes met with in many cases do not seem to me sufficiently great to lead to this result.

With regard to the effect of changes in the capsule and its epithelium, and in the glomerulus and its epithelium, it is evident that we may possibly have different results, if, as seems probable, these changes can occur separately, or one can greatly predominate over the other. Of course, in late stages, when the surfaces of the glomerules and capsules are united, the function of the glomerules is abolished; but, in an earlier stage, effects of capsular changes may possibly differ from those of glomerular epithelial changes, and eventually be recognised clinically.

There seems every probability that the albumen present in the urine in nephritis transudes through the glomeruli; and Lépine, in a recent article on the pathogenesis of albuminuria, in the *Revue Mensuelle*, sums up evidence giving fair ground for the belief that this transudation is probably connected with alteration in the epithelium lining the glomerulus, which he believes has much to do in health in preventing this transudation.

On the other hand, we might expect that capsular changes would only influence slightly the passage of albumen into the blood. Now we find, in cirrhosis of the kidney, where the capsules are commonly found greatly thickened, but extensive glomerular epithelial changes do not seem to be present, that the urine is copious, and the amount of albumen it contains small, until a late period of the disease is reached. It may be, of course, that a large number of glomeruli escape affection till a late stage, but the absence of any effect of capsular change on the amount of urine and albumen passed, seems to me the more probable explanation; whilst the fact that, in the cases where I have found a glomerular epithelium affected the albumen has been copious, leads me to think that this structural change may be at least one of the conditions, though by no means the only one which influences the amount of albumen present in the urine.

In Cases I and II, the amount of albumen was not due to undue vascular pressure, for the sphgmographic tracing registered no indication of increased tension. On the arterial condition in the third case, I have no record. In all these cases, the rapidity with which the patients succumbed seemed to be dependent on the glomerular affection. In Case I, where it was most extensive and advanced, life lasted the shortest time. The rapidity with which intrascapular growth can occur is very remarkable. Unless we are to suppose that it can exist without giving rise to symptoms—a most improbable supposition—it would appear that in Case I two months was sufficient for the advent of most extensive and advanced glomerular nephritis. In this case, too, the influence of glomerular changes on the production of dropsy was very plain. I never before met with such enormous anasarca.

The cases which I have brought forward seem to indicate that the glomerular changes may play a most important part in the production of the clinical phenomena in Bright's disease; and it is somewhat remarkable that, until a very recent period, these changes have not received that attention to which, it seems to me, they are entitled.

ON THE TREATMENT OF UTERINE FLEXIONS.

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I PROPOSE in this paper to bring forward a few practical observations on the subject of uterine flexions. On its general pathology, I do not wish to say anything beyond expressing my agreement with the proposition laid down by Dr. Graily Hewitt, that, in cases of acquired flexion, an unhealthy condition of the uterine tissue, an "undue softness", connected probably in a large proportion of cases with general malnutrition, is the condition antecedent to the bend; and I would add my belief, that the recognition of this factor is of primary importance in relation to the treatment. A healthy uterus may be displaced as a result of a change in the correlation of its supports; but a healthy uterus will not, I believe, bend upon itself as a result of any force which may be applied to it, unless its normal firmness and resiliency be diminished or lost. One other general remark I would make is this, that the importance of flexions depends very much upon the amount of obstruction in the utero-cervical canal produced by the bend. If there be no obstruction, I believe the bend, *per se*, to be in many cases, at all events, of small consequence; but, if there be obstruction, and in direct proportion to its amount, then a series of pathological results follows, including obstructive dysmenorrhœa, endometritis, uterine hyperplasia, ovarian irritation, and pelvic hyperæmia. Thus, I have been consulted in many cases of sterility, as to its probable cause; and, on making examination, I have found distinct flexion in the uterus, but no evidence of any other disease whatever; and no complaint of any interference with menstruation, no local pains, and no difficulty in locomotion. In some of these cases which I have had the opportunity of watching, the reposition of the uterus, and its maintenance in a correct position by a pessary, has not resulted in the issue wished; and so, probably, the malposition was not the cause of the sterility, as certainly as it was not of any other pathological conditions. I do not wish by these remarks to be supposed to undervalue the importance of flexions. On the contrary, I believe that, in the large majority of cases, they are conditions of extreme importance; but I believe that importance is in direct proportion to the obstruction produced, and that, in the few cases in which there is no obstruction, the direction in which the fundus uteri looks is of small consequence.

In the majority of text-books, the treatment of flexions is described, without any guidance as to its applicability in individual cases; and I believe this is why disappointment is frequently experienced by practi-