

AN ACUTE CASE OF HODGKIN'S DISEASE.

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THE case of Hodgkin's disease which I bring before the Academy this evening is remarkable for its rapid clinical course as well as for the widespread distribution of the enlarged glands and adenoid growths.

CASE.—The patient, a labourer, fifty years of age, was admitted to the Whitworth Hospital last December, complaining of difficulty in moving his left arm, owing to a swelling in the corresponding axilla. About two months previously he had noticed an enlargement in the left side of his neck. This gradually increased in size, but caused him no inconvenience. About a month ago he was conscious of a swelling in his left axilla, and soon afterwards in his left groin. He had always been a healthy man, and he gave no history of syphilis or intemperance. On admission he was somewhat emaciated; he did not look anæmic; his skin was dry and scurfy, and his temperature normal; his heart and lungs showed no signs of disease; the superficial glands all over his body were enlarged, the enlargement being most marked in his left axilla and groin and in the left side of his neck. Dulness beneath the sternum, and extending thence laterally, pointed to the presence of enlarged glands in his thorax; the spleen and liver were palpable. Examination of the blood disclosed nothing abnormal except a slight increase of the white cells—

Hæmoglobin - 100 per cent.

Red cells - 5,000,000 per cubic mm.

White cells - 11,200 " " "

Lymphocytes constituted 40 per cent. of the white cells.

Stained cover-glass preparations of his blood showed an absence of micro-organisms, and cultural experiments gave an equally negative result. His urine was normal. His appetite was good, and he did not feel sick. After a week his appetite began to fail, and

he became irritable; then day after day he became more and more prostrate and drowsy, whilst he was delirious at times. A few days before his death his temperature ran up to 100° and 101°. His death occurred about eleven weeks from the onset of the disease.

At the necropsy there was universal enlargement of the superficial lymphatic glands, as well as of the mediastinal, retro-peritoneal, and mesenteric glands. Adenoid nodules were found in both kidneys, in the small intestine, spleen, and liver. The spleen weighed 19 ozs., and the liver was also enlarged, and growing in from its capsule were many large masses of adenoid material. Below the liver a large mass of glands surrounded the aorta and involved the supra-renal bodies.

The nature of Hodgkin's disease is obscure. Clinically it can be distinguished from lymphatic leucocythæmia only by the examination of the blood; and it is interesting to note that reliable observers have recorded cases of the disease which were transformed into leucocythæmia. Indeed, Cohnheim called Hodgkin's disease an *aleukæmic vorstadium* of leucocythæmia. Much evidence can be adduced in support of the view that Hodgkin's disease is of an infective nature—micro-organisms have been demonstrated by numerous observers. One case at least of direct infection has been recorded by Obratzow; its resemblance to other infective processes, and its clinical features—enlarged glands, fever, hæmorrhages, anæmia, and its fatal termination—may be taken as evidence in the same direction.

In the case of my patient no micro-organisms could be detected in his blood or in the new growths.

In conclusion, I am indebted to my friend, Dr. McWeeney, for the following very complete investigation into the pathology and bacteriology of the case:—

“The clinical aspect of this remarkable case has been dealt with by Dr. Coleman. Through his kindness I had an opportunity of examining the specimens in an excellent state of preservation.

"I.—BACTERIOLOGICAL EXAMINATION.

"Pieces from the centre of one of the largest of the lymphoid nodules (which had been laid open with a hot knife) were torn out with sterile forceps, and smeared over the surface of a considerable number of tubes of ordinary agar, glycerine agar, ordinary serum (ox), Löffler's serum, and glycerine serum; other pieces were added to sterile broth. All the tubes were incubated at 37° C., and carefully watched from day to day. No development took place on any of them. Microscopic examination of the tissues after careful fixation, sectioning, and staining, failed to reveal any undoubted organisms. Granules that held the violet stain somewhat obstinately by Gram's method were, it is true, seen; but I do not think that they were organisms, but, rather, some product of cellular breakdown. They will be described later on.

"About three grammes of the material were pulped in a mortar with a few cc. of sterile broth, and injected into the peritoneal cavity of a rabbit. No morbid symptom followed; there was no loss of weight, and when, a month later, the animal was killed the cellular material had disappeared.

"II.—MORBID HISTOLOGY.

"A. *Methods*.—The pieces cut from the margins of the neoplastic nodules were fixed with formaline (10 per cent.), passed through graded alcohols, and imbedded in celloidin, with the object of obtaining as large sections as possible. Staining was done with Ehrlich's hæmatoxylin, followed by a mixture of acid fuchsin and picric acid (Van Gieson's method). For the demonstration of organisms the Weigert-Gram method, in combination with carbol-glycerine-fuchsin (Czaplewski's modification), was employed.

"B. *Results*.—1. *Liver*.—Nowhere was the organ quite normal. The intra-lobular capillaries were everywhere dilated, and the intervening liver-cells often atrophic, sometimes absent over entire low-power fields, so as to give the idea of an angiomatous change. The portal canals contained an excess of connective tissue, with here and there—far away from the nodule—groups of cells unmistakably identical with those composing the new growth. Towards the margin of the nodule these cells became somewhat more numerous. At the margin of the nodule all the hepatic structure, portal connective tissue as well as liver cells, seemed to melt away before the advancing swarm of neoplastic cells. Some way into

the nodule strands of compressed and atrophic liver cells could still be traced and recognised by the bile pigment they still contained; but further from the margin they, too, ceased, and only the neoplasm remained. I failed to observe any evidence of compression of the liver cells by a development of lymphoid cells within the portal canals. The hepatic tissue was destroyed, and its place occupied by an advancing swarm of new cells, exactly as in the case of a malignant new growth.

"2. *Kidney*.—Here the appearances were very like those just described. There was a certain amount of interstitial nephritis, with some thickening of the coats of the smaller arteries and occasional patches of infiltration with 'lymphoid' cells, which were quiet unlike the neoplastic cells soon to be described. Towards the margin of the nodules there began to appear, between the tubules, individual cells and groups of cells similar to those of which the nodules were composed. These new elements rapidly increased in number so as to separate the renal structures and convert them into islands, as it were, in the sea of the advancing neoplasm. Towards the centre of the nodule they gradually disappeared as though they had undergone solution. Before their disappearance they came to contain groups of granules, similar in size and appearance to those seen in renal or hepatic epithelium, that is in a state of fatty degeneration. These granules did not, however, consist of fat, but of some other substance, for they held the Gram. Here and there also in the epithelium larger granules, not unlike groups of minute yeast-cells, were seen in the dying protoplasm. These took the Gram imperfectly.

"*The medium size and small arteries of both liver and kidney, and the glomeruli and basement membrane of the tubules of the latter organ, were the seat of pronounced amyloid change and gave the typical colour reactions.*

"3. *Lymphatics*.—The enlarged lymphatic glands presented an appearance precisely similar to that of the neoplasms in liver and kidneys now to be described. They were sprinkled all over with mitoses, and presented numerous hyaline patches; but their structure was, in my opinion at least, clearly distinguishable from normal adenoid tissue.

"4. *The Neoplastic Nodules* consisted of small, polymorphous cells, with nuclei measuring from 4μ to 7μ across. Some of these took the stain deeply, so as to be almost black. Others of the nuclei were 'vesicular,' and contained numerous nucleoli. Others,

again—and this feature I am inclined to regard as very important—showed a distinct tendency to become elongated, sometimes assuming a spindle shape, sometimes thickened at the poles and linear in the middle, like those of connective tissue cells when developing under unfavourable circumstances—*e.g.*, in the periphery of a tuberculous focus. Many of the nuclei were undergoing division; but the chromosomes were, for the most part, ‘clumped,’ and few really typical nuclear figures were obtainable (Gram’s method).

“Various stages of karyolysis were observed, and a few enormous budding nuclei, similar to those figured by Fabre-Domergue in his well-known work, ‘*Les Cancers Épithéliaux*’ (Paris: Carre, 1898), were also noticed.

“The protoplasm was usually small in amount, hugging the nucleus pretty closely, and, in the case of the lymphoid elements, hardly visible around it. The great budding nuclei above mentioned were imbedded within relatively large masses of protoplasm; true giant-cells were absent. A few of the neoplastic cells contained eosinophil granules. The absence of *mast-cells* was particularly noticeable.

“Of stroma there was hardly a trace. The new cells seemed, so far as could be made out, to lie in immediate contact with each other, and the very few vessels that could be distinguished were supported by a very little connective tissue.

“*Mode of Invasion.*—In the *liver* this appeared to be by the increase in size of spherical nodules of the new growth exactly as in cancer. Whether these nodules owned an embolic origin, or started from the groups of similar cells already noted as occurring in the portal canals far from any nodule, I am unable to say.

“In the *kidney* the neoplasm entered the organ at the hilus and accompanied the branches of the renal artery—the adventitia of which was, in fact, in direct contact with the masses of new cells.

“*Lymphatics.*—Here it would be impossible to speak of any mode of *invasion*. The universal distribution of the mitoses and the unbroken chain of transitional forms between normal lymphoid and neoplastic cells seem to point unmistakably to the lymphatic glands as the seat of origin of the new formation. It would seem as though it had originated independently in the several adenoid structures, as if in response to some common stimulus.

“In the parenchymatous viscera (liver and kidneys) its histological and distributional characters seem to me identical with those of small round-cell sarcoma.

"A discussion of the voluminous literature of the subject would take me far beyond the limits of this communication, which is intended merely as a careful description of a case observed under favourable circumstances."

DR. E. J. MCWEENEY asked Dr. Coleman if there was any history of suppuration, syphilis, or tuberculosis to account for the lardaceous disease? In the absence of these, the lardaceous change must be considered part and parcel of the morbid appearances. One of the cardinal symptoms of Hodgkin's disease was absent in this case—viz., *oligocythæmia rubra*.

BRIGADE SURGEON-LIEUT.-COL. BURKE said when at Gibraltar and Malta he had seen many specimens of amyloid degeneration, and the liver specimens now exhibited were very like those he had seen due to syphilitic disease.

DR. COLEMAN, in reply, said that there was no history of syphilis or long-continued suppuration. He said that anæmia is not necessarily a part of Hodgkin's disease, and only becomes marked as the case progresses. Anæmia has been noted as absent in undoubtedly true cases of the disease, especially in the early stages. The synonyms of this disease were numberless. The current issue of The New Sydenham Society's Atlas of Pathology^a contains four plates, copied from drawings made by Sir Robert Carswell, illustrating a case of Hodgkin's malady. The specimens which are exhibited to-night bear a remarkable resemblance to those figured in the plates in question.

^a Fasciculus XII.

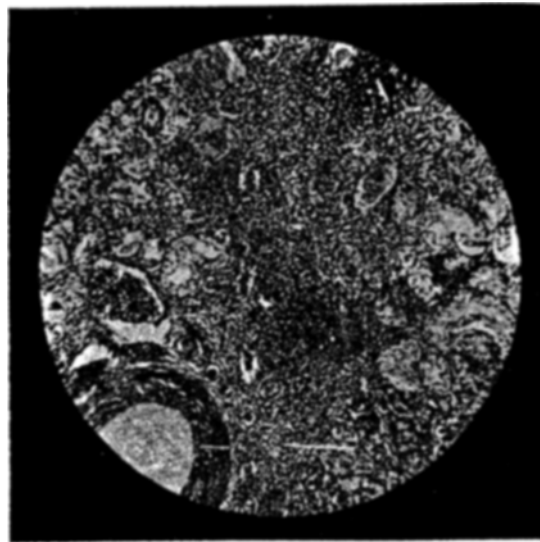


FIG. 1 ($\times 80$).—Patchy infiltration of kidney with ordinary "lymphoid cells."

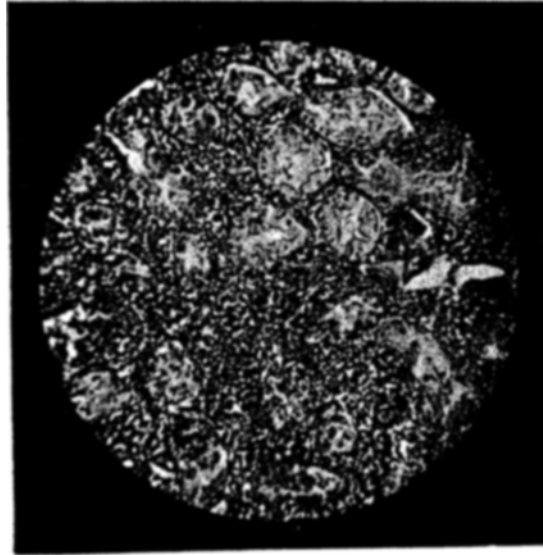


FIG. 2 ($\times 250$).—Mode of infiltration of kidney with neoplastic cells.

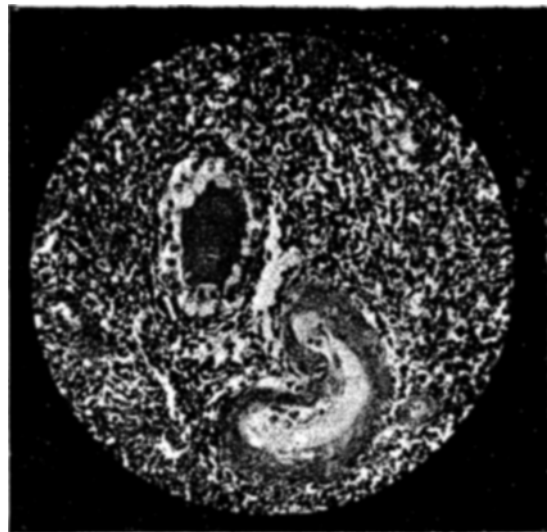


FIG. 3 ($\times 350$).—Further stage of infiltration of kidney with neoplastic cells.

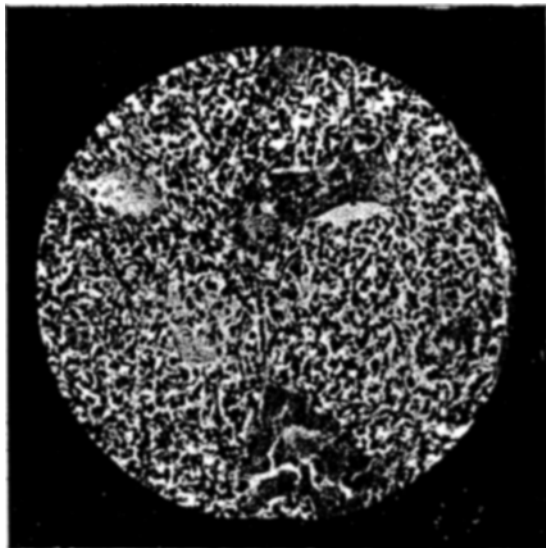


FIG. 4 ($\times 350$).—Isolation and destruction of renal elements by the neoplastic cells.