32. Neoplasm in an Indian Rhinoceros (Sarcoma of Heart and Lungs).

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[Received March 31, 1927; Read May 10, 1927.]

(Plates I., II.*)

The case here recorded is that of an Indian Rhinoceros (*Rhinoceros unicornis*) from Nepal. It was brought to the Gardens as quite a young animal on April 7th, 1922, and had always been in excellent health until the beginning of April 1926, when it was noticed to be losing its appetite. There were no other symptoms, and when seen on the evening of April 27th, though it refused food, it was not considered to be any worse than during the preceding days. The following morning, however, at 6 A.M., it was observed to be in much distress and died quite suddenly a few minutes later.

The post-mortem examination was started about three hours afterwards, and the findings were as follows:—

There was bleeding at the nose, thought to be due to injury sustained in falling at the moment of death; a slight anal prolapse was present, but no other external signs worthy of note.

On opening the body, the striking feature was the size and the general appearance of the heart. The pericardial cavity contained about 3 litres of slightly blood-tinged yellowish fluid; the membrane was not inflamed, nor thickened as a whole, but on its visceral surface were several nodules of new growth, more closely aggregated towards the base of the heart.

The anterior surface of the heart itself presented an enormous number of small nodular deposits, covering practically the entire surface (Pl. I.); some of them showed small hæmorrhages. They appeared to be most thickly aggregated over the right auricle, but were very numerous all over. The posterior surface of the heart also showed many deposits, but considerably less than were visible on the anterior aspect, covering in all about one-third of the surface and aggregated more towards the upper part, the base, of the heart.

On cutting open the heart, it was seen that the growths were not merely superficial. The wall of the right auricle was crowded with tumour-masses, and infiltration had extended

* For explanation of the Plates, see p. 510.

through to the surface. All the chambers showed that the thickness of the myocardium had been involved. Some of the masses in the left ventricular wall were as large as a golf-ball, and one even larger (Pl. II.). They give the impression from their position and relations of having arisen from without and extended inwards, rather than by embolism from within. Possibly, from the greater aggregation in the right auricle, this had been the first part of the heart to be attacked, and thence the growth had spread to involve the pericardium with resultant rapid, local or contiguous extension.

Some of the deposits in the wall of the right ventricle were more distinct on the internal surface and did not reach through to the outer. It is possible, perhaps probable, that these had arisen from fragments being carried from the right auricle to the ventricle and there developing.

The thymus was represented by remnants of tissue only, and the thyroid was normal.

The right lung contained a large deposit of growth near its root, the mass of the tumour being the size of a Tangerine orange. There were also several very minute, whitish deposits scattered irregularly through the lungs. The same remark applies to the left lung, while in the lower lobe, about the middle, there was a single mass as large as a cherry. The bronchial glands were not enlarged.

The minute deposits proved on microscopical examination to be each a small nodule of growth, as if there had been a number of emboli from the mass in the left auricle whipped off into the pulmonary circulation.

Thus would be accounted for the fact that embolic tumours were not found in any of the other viscera, liver, spleen, kidneys, etc.; in other words, the systemic circulation had not been invaded.

The only other condition of which mention should be made was that the intestine was somewhat acutely inflamed, the mucosa showed a few petechial hæmorrhages, while some areas were more uniformly red and blood-stained. In the peritoneum the fluid was in excess, though not measurable, and there were small masses of gelatinous coagula.

The liver was mottled and, on section, was seen to be "foamy," the tissue spongy and soft and the spleen, though not enlarged, was also softer than normal and frothed a little on section. The mesenteric glands were swollen and congested. Welch's bacillus—*B. aerogenes capsulatus*—was grown by anærobic culture from the liver, spleen, and heart-blood.

There was no swelling or softening of the bones noted at the autopsy, and subsequent maceration for the purpose of preparing a skeleton showed a splendid condition of all the bones, no abnormal localised swellings.

Histological examination.

Section of the *Heart* when viewed by a low power, such as a hand-lens, showed several small foci which appear as if separate and, in a way, encapsulated. Under higher magnification, however, it is seen that there is no true capsule, though the periphery is more fibrous than the interior and the surrounding tissue is compressed; at the same time this is fairly heavily invaded by small round cells. In more minute detail, the *stroma* varies in amount in different foci and in different parts of the same focus. In some situations there are many small round cells and little stroma, but over the greater part there is relatively abundant stroma, some of it of hyaline aspect, but made up of very fine fibrils, interspersed with elongated cells which have relatively large oval, or, more often, spindle-shaped nuclei.

The characters of the *cells* are those of a mixed large and small round-celled sarcoma, among which the latter greatly preponderate. A considerable number of the larger show mitotic figures.

In each of the foci of growth there are numerous *giant-cells*. Here and there may be seen one showing slight vacuolation, and others show a sort of tear or cleavage due probably to shrinkage in the preparation of the tissue. The giant-cells vary considerably in size, but in almost every case the edge is smooth and regular, nothing of the nature of the processes found in osteoclasts being seen. The nuclei are present in large numbers, some containing a hundred or more; they are situated centrally or dispersed through the cell, not peripherally, nor are they of a uniform size in a cell and several show mitotic figures.

Nowhere in any of the sections is there anything suggestive of bone-formation; within the tumour-nodules themselves no hæmorrhages have been seen, though extravasations are found at the periphery in certain parts.

Occasionally one can make out degenerated heart-muscle cells in the interior of the tumour nodules, especially at the periphery.

As regards the deposits in the *Lungs* the capsule-appearance is rather more marked and the fibrous stroma more prominent, especially at the periphery, where it is more dense, though infiltrated by round cells several of which show mitosis. The disposition of the stroma is very similar to that already described in the case of the tumours in the heart; that is, it exhibits considerable variation in amount, some areas showing very little and consisting almost entirely of small round cells with faint, fibrillar intercellular stroma, others with an alveolar arrangement, a little denser fibrous stroma arranged as a mesh, containing small round cells between which are the faintly-staining fibrils; giant-cells are numerous, rarely is any seen with vacuolation, the nuclei are many and resemble in all respects

those in the heart. At the periphery of the tumour-nodules the pulmonary tissue appears compressed and the alveolar walls thickened, and there is a fibrosis invaded by numerous small round cells. Here, as in the heart, no extravasations are seen within the deposits themselves, but in parts, particularly at the periphery of the nodules, the pulmonary tissue may show extensive foci of hæmorrhage, the alveoli being filled with corpuscles and shed cells; there is no broncho-pneumonia in the compressed parts of the lung.

Discussion.

The problem offered by this interesting case is the solving of the question as to the source of these tumours. There can be no doubt, from their enormous number in both heart and lungs, that in the case of each organ the deposits are secondary. The fact that extra-cardiac tumours were found only in the lungs is evidence that dissemination in the latter came by way of the pulmonary artery. This is borne out by the further fact that, though the tumours are widely distributed over the surface of the heart, the chamber most heavily involved is the right auricle which, as already stated, is crowded with growth and its wall infiltrated throughout. Fragments have, in all probability, been carried from the auricle to the ventricle and thence distributed as emboli throughout the lungs, which have become studded with minute sarcomatous deposits and others of greater size, as would result from repeated embolism.

Again, the wall of the auricle consisting as it does, of a mass of agglomerated deposits, has transmitted the cells to the overlying pericardium, and when once this was reached the spread would naturally be a rapid one by contiguity over the whole surface over the heart and its serous covering.

Primary malignant tumours of the heart, non-malignant also for that matter, are very rare, and in this instance may be excluded by their very number. If it be suggested that there was some primary growth in the heart which had extended to involve the pericardium and produce such generalized infection of the whole organ, we can only say that, if possible, such is highly improbable, because while all this local mischief was developing we should expect to find signs of embolic distribution of tumours in the parts supplied by the systemic circulation.

Regarding the condition of the heart, then, as secondary, we are confronted with the problem of the site of the primary growth. In most cases of cardiac neoplasm, when these are present in any number, the primary growth is probably the mediastinum, the pericardium becoming invaded, and the growth spreading thence to the myocardium. Sarcoma of the thymus may so extend. In the present case, however, there was no

growth seen in the mediastinum and the thymus was specially observed, as there was no knowledge of the age of the animal, except that it was believed to be a young one. The gland, however, had almost disappeared, being represented only by remnants of tissue.

Giant-cell sarcomata, as sources whence the heart becomes involved, have been reported in the mammary and thyroid glands (Hektoen and Riesmann), but these sites were examined and found free from disease.

We may, therefore, set aside any adjacent organ as the site of the primary growth.

The commonest source of origin of secondary tumours of the heart is unquestionably bone, and in the case of this Rhinoceros the histological picture with its preponderance of giant-cells in all the sections made tends to support this argument.

It is, of course, well known that too much importance in this respect must not be paid to the existence of giant-cells in a tumour. They are not uncommon in both spindle- and round-celled sarcomata, especially in the larger-celled examples. All the sections made from tissue taken from various parts of the heart and lungs in this case, however, show that, except for the numerous giant-cells, the majority of cells are of the small round type. Wherever these giant-cells are found in large numbers the question as to their significance is always a matter for debate. There are four possibilities to be considered, namely:—(1) Are they merely "foreign body" giant-cells? (2) Are we dealing with a myeloid sarcoma, secondary to or arising primarily from bone-reticulum? or (3) with a myeloma, arising from bone-marrow or, lastly, (4) with a "giant-cell sarcoma"?

The first can be disposed of in a few words; such cells are generally found in necrosing or degenerating areas, and are probably of endothelial or leucocytic origin. They do not attain the size of those present in sections of the tissues in this case, and in the great majority of them the nuclei are polar, or peripherally disposed. This was very exceptionally seen here; as mentioned already, the nuclei were either central or distributed generally throughout the cytoplasm.

A considerable degree of confusion exists as to the differences between myeloid sarcoma, myeloma, and giant-celled sarcoma of bone, which Professor Kettle has done much to elucidate. We need not go into the differences in detail here; suffice it to say that the first arise in the interior of bones (except epulis) and, in particular, certain parts of certain bones—adjacent ends of tibia and femur, upper end of humerus and lower end of radius. They expand and absorb bone rather than infiltrate it, are very vascular, and may pulsate, are often discoloured from hæmorrhage, and are, in a way, locally

malignant, but seldom if ever become disseminated. The giant-cells are of the osteoclastic type, having regular nuclei which do not show signs of abnormal activity. Such were not the characteristics, already given, of the giant-cells of the tumours in the Rhinoceros. Further, the giant-cells differ from those designated foreign-body giant-cells in that the nuclei are not arranged peripherally, there is no central degeneration; in fact, they are the analogues of the myeloplaxes normally found in bone-marrow. In such tumours there is a tendency to the formation of bone-spicules, and the cells generally are of the fibroblastic type, though often somewhat irregular in shape.

The second, myeloma, is by some authors regarded as synonymous with the last, and others who do not definitely state this as a fact are, judging from their descriptions, of the same opinion. According to Kettle, several of these tumours may develop simultaneously, or there may be a single growth at first, rapidly succeeded by others, but always in the bony skeleton, vertebræ, ribs, limb-bones, etc. The constituent cells are myeloblasts, or possibly plasma-cells, but the large cells of the osteoblast type, cells typical and characteristic of the myeloid sarcoma, do not occur.

Lastly, there remains the so-called Giant-cell Sarcoma. Some authorities dispute the existence of such a tumour as a distinct entity, regarding the giant-cells as either foreign-body cells or as modifications of the tumour-cells proper resulting from lack of cell-division and irregular mitosis, and common to neoplasms of various kinds, endothelioma, carcinoma, etc. Others, on the contrary, maintain that, though large multinucleated cell-masses occur at times in many sarcomata constituted by a mixture of cells, spindle- and round-celled, large or small, there is also a group in which these giant-cells are so constant and numerous as to form a characteristic feature and these are placed apart as Giant-cell Sarcomata. In the former, the mixed-cell sarcomata with giant-cells, the intercellular fibrillated stroma is usually scanty and any vessels present are of rudimentary form. It is true that such have been found in the majority of cases to arise primarily in connection with osseous tissue, and should, therefore, be classed with the osteosarcomata, but in others there is no apparent tendency to the formation of bone or cartilage. Among the latter there are met with sarcomata whose predominant constituent cells (apart from the giant-cells) are of the round-cell type, whose stroma is small in amount, finely fibrillated, but which may in some situations be disposed in definite fibrous trabeculæ enclosing the round cells, and, in fact, constituting a form of alveolar sarcoma or, yet again, showing in parts a more uniform, almost homogeneous material believed to be a secretion from the cells. Such tumours differ from the myeloid sarcomata, previously mentioned, in two important

particulars—namely, that the giant-cells vary considerably in the size of their nuclei and in their exhibiting abnormal mitoses, and that careful search will often reveal, as it were, transitional forms between the smaller cells of the tumour and these large multinucleated giant-cells.

To sum up the somewhat confused question of sarcomata of bone: It would appear that the majority of less malignant are of the spindle- or mixed-cell type containing giant-cells in varying number, some of the latter showing the general conformation of myeloplaxes. If arising from the periosteum tumour-formation in its strict sense is early in evidence; if from the interior—central sarcoma—they grow and slowly erode the framework of the bone, gradually replacing the bony tissue by the tumour-mass till spontaneous fracture results or attention is called to the bony swelling with pulsation and, perhaps, the characteristic "egg-shell" crackling.

Others contain a greater admixture of round-cells as the predominant cell of the groundwork, and so take on, as it were, a more truly sarcomatous character, namely that of small round-celled sarcomata which, whatever their situation, are generally regarded as the most malignant of these tumours. They probably give rise in their earliest stages to a certain degree of bone-erosion, but insufficient to cause any swelling recognizable externally; in fact, their malignancy is shown by early dissemination before there has been time for the local tumour to develop.

There is, it is true, a considerable degree of hypothesis in applying this reasoning to the case which forms the subject of this paper. Examination at autopsy revealed no primary tumour to which the secondary deposits in heart and lungs could be traced, and even after maceration for the setting up of the skeleton none of the bones showed the least deformity. Nevertheless, seeing that the commonest origin of secondary tumours of the heart is bone, that the neoplasm in this case contained numerous giant-cells, that the groundwork was of small round-cells, the most satisfactory, or perhaps we should say the least unsatisfactory, explanation would appear to be that there was some small round-celled endosteal sarcoma which became disseminated before any recognizable tumour had developed sufficiently to declare itself locally. This could only be proved by sections being made of all the bones of this animal, a matter now beyond our reach.

I wish to express my indebtedness to Mr. F. Martin Duncan and to Mr. F. W. Bond, the former for the photographs of the microscopic specimens, the latter for the macroscopic.

EXPLANATION OF THE PLATES.

PLATE I.

Fig. 1. The anterior surface of the Heart showing vast numbers of nodules of growth.

Fig. 2. Sections through the Left Ventricle of the heart showing one large and several smaller sarcomatous deposits.

PLATE II.

Fig. 3. Section of small nodule of growth in the heart showing the giant-cells, both central and peripheral, with infiltration at the border by small round-cells also, where invasion is progressing.

Fig. 4. Section of nodule in Lung. Note the large number of giant-cells in the main mass and the fibrosis at the periphery which gives the idea of encapsulation to the naked eye. This tissue is, however, fairly densely invaded by small round-cells and also by giant-cells. To the left are seen the pulmonary alveoli into the meshes of which round-cells are penetrating. There is no evidence of bronchopneumonia.

FIG. 1

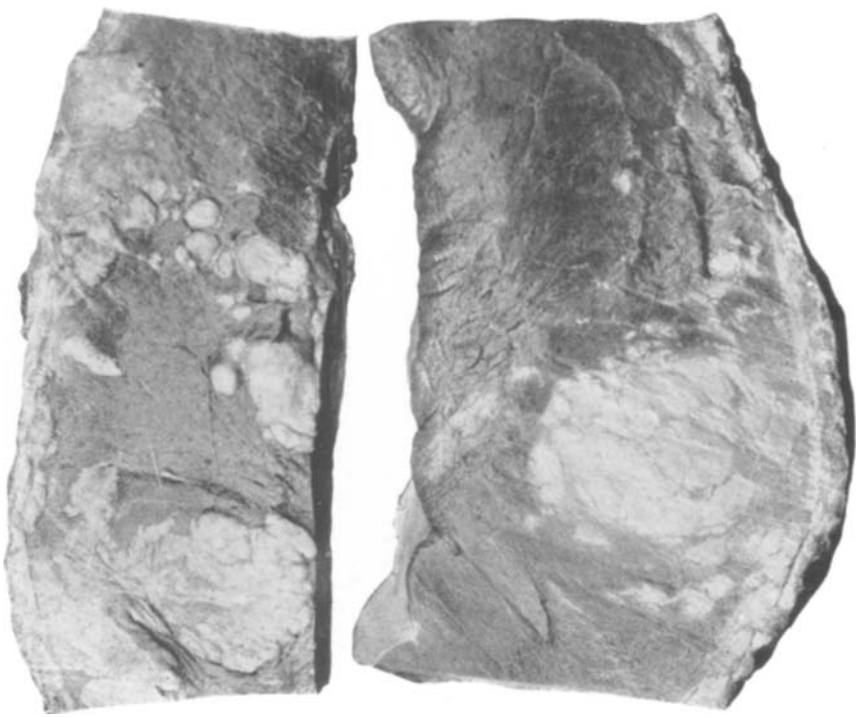

FIG. 2

NEOPLASM IN AN INDIAN RHINOCEROS

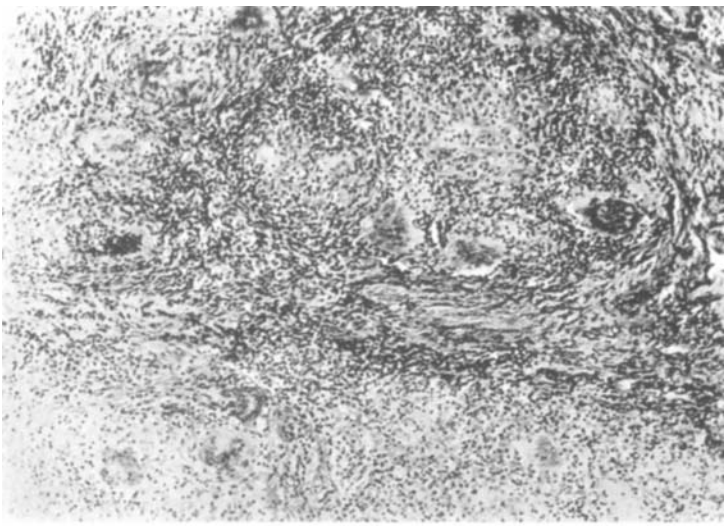

FIG. 3

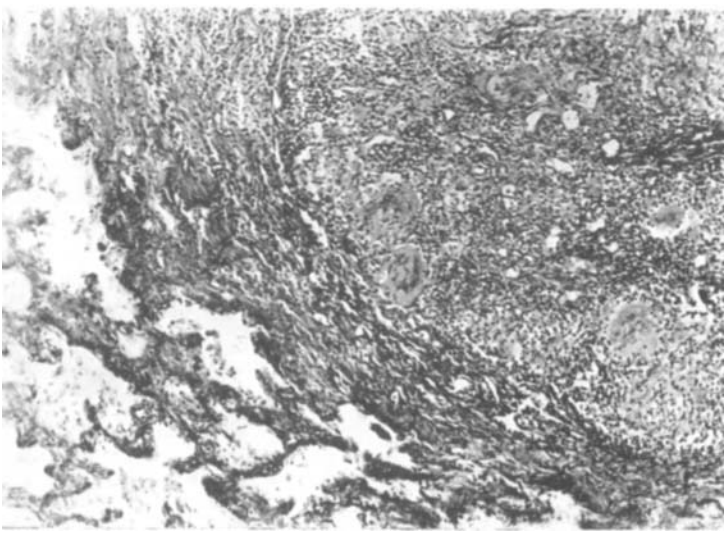

FIG. 4

NEOPLASM IN AN INDIAN RHINOCEROS.