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ROUND-CELLED SARCOMA OF THE ANTERIOR MEDIASTINUM; EXTENSIVE METASTASES, INCLUDING THE BRAIN, BOTH CHOROID COATS, OCULO-MOTOR AND OPTIC NERVES, AND EXTERNAL OCULAR MUSCLES.

BY ARTHUR V. MEIGS, M.D.,

G. E. DE SCHWEINITZ, M.D.1

[Read February 7, 1894.]

An Italian laborer, aged twenty-one years, was admitted to the Pennsylvania Hospital October 1, 1888. The history was as follows: He was well and strong until June, when he had ague of the tertian type. For forty days before admission he was unable to work, owing to pain in the head and shortness of breath, which for ten days amounted to orthopnœa; his breathing was wheezing. The urine was scanty and passed infrequently. On swallowing he had a burning sensation behind the sternum, and the act provoked coughing, but he did not vomit. He had no appetite and was wakeful at night. There was diplopia for at least ten days before coming to the hospital.

On admission the patient was a fine, strongly developed man. The face was dusky-red and congested, the neck broad and very thick-looking, and its veins and those in the upper part of the chest were full and turgid.

The eyeballs were markedly staring, and there was slight external strabismus of the right eye. The tongue, when protruded, was not deflected to either side.

The arms and hands were cyanotic, but there was no cyanosis of the feet or legs. The dyspnœa was very urgent, and he was entirely unable to lie down.

¹ The case was reported briefly by Dr. T. S. Westcott to the Philadelphia Pathological Society, October 25, 1888, and the report published in the University Medical Magazine, 1889, vol. i.

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There was, perhaps, some slight difference in the volume of the two radial pulses at the wrists. The heart-sounds were clear and no murmur was audible. There was dulness on percussion at the lower portions of the lungs posteriorly, and whistling, dry râles were to be heard over the lungs everywhere. There was a roaring sound as if from obstruction of the trachea or bronchi; this was more marked upon the right than upon the left side. He expectorated a good deal of watery, blood-stained fluid.

Death occurred in great agony from suffocation about twenty-four hours after his admission to the hospital.

The post-mortem examination revealed the presence of a large fleshy mass lying behind the sternum. This was wedge-shaped, with the base above, and was perhaps three inches wide by five vertically. It lay behind the sternum and over the pericardium, and completely surrounded the blood-vessels and the trachea, except a little of its posterior wall. The trachea was much compressed and pushed or dragged out of the median line.

The innominate artery divided within the mass, and its two branches were narrowed. The carotid, a short distance from its origin, showed destructive erosion so great that the wall was very thin. The left innominate vein was included within the tumor, and it and the carotid and subclavian veins which formed it were all markedly narrowed.

The heart appeared to be of about the normal size, and its valves, cavities, and openings looked natural. Upon its surface the vessels appeared tortuous and thick, and stood out in an unusual way. On cutting across such vessels they appeared to be surrounded with neoplastic material. At the apex there were several spots which were dark-red, resembing ecchymoses. At the base of the heart there was neoplastic material deposited upon the great vessels and on the auricles, and at one place this extended across to the parietal layer of the pericardium, which was ragged-looking.

The pleural sacs both contained bloody serum, the right being tightly distended, and the right lung compressed and carnified. Both lungs showed here and there upon their surfaces spots of neoplastic deposit, and upon the pleural surface of the diaphragm, upon the right side, there were a number of quite large nodules.

The liver was large, weighed four pounds fourteen ounces, and was very full of blood. On section it presented the nutmeg appearance.

The spleen was about five times the natural size and very firm in texture.

The mesenteric glands were greatly enlarged and were sarcomatous. The kidneys presented numerous nodules upon their surfaces, and on section areas of sarcoma were seen scattered through the parenchyma.

The brain itself presented no gross evidence of disease. The oculo-motor nerves were both enlarged, the right one being fully twice as large as the left and presenting a pear-shaped swelling just within the cranial cavity, before its entrance into the sphenoidal fissure.

Sections were prepared, for microscopical examination, of the primary growth which lay in the mediastinum. Of this, sections from three positions were cut, one taken from the body of the mass, and two including the right carotid artery—one of the eroded portion of the vessel, and the other of a portion in which the walls were still whole. Of the heart, sections were cut from two positions, one near the apex, and the other of the septum, on the anterior surface, including an artery in the pericardium. Two sections of the lung were prepared from different positions. Sections were cut of mesenteric glands, of the diaphragm, including a sessile growth upon its pleural surface, of the liver, spleen, and two from different parts of the kidney.

Of the nervous system, sections were prepared of the cerebellum, of both oculo-motor, and of both optic nerves, just within the cranial cavity and before their entrance into the sphenoidal fissures and optic foramina; of the posterior portions of both eyes showing the nerve entrances, and of the optic nerves and surrounding muscles and nerves behind the eyeballs.

The total number, therefore, of different portions of tissue subjected to microscopical examination was twenty-two, and all of them exhibited, to a greater or less extent, sarcomatous infiltration. The infiltrating material was of the commonly described round-celled variety, and in sections stained with carmine the cells seized the pigment with avidity, producing an intensely red color. This seems to be a marked peculiarity of the cells of sarcoma, the color generally being more intense even than that of carcinomatous growths.

The primary growth in the mediastinum, which very probably originated in some remnant of the thymus gland, presented the usual appearances of round-celled sarcoma. The only specially noticeable feature of the growth was the erosion of the carotid artery. The only portion of the walls of the vessel remaining upon the side where the erosion had occurred was the external fibrous coat; the muscular layer and intima had disappeared entirely.

The sections of the heart showed the neoplastic material to lie more abundantly in the adipose tissue upon the surface than, anywhere else. It followed the lines of the connective tissue, the rings constituting the boundaries of the fat cells being infiltrated. In places where the amount of deposit was still moderate the centres of the fat cells retained their usual appearance of being empty, but where it was great the cells had pressed inward until the spaces were filled up, and the appearance was one of a solid mass of neoplastic round cells. At the point of junction of the overlying fat with the muscular substance of the heart, the great abundance of the neoplastic material ceased abruptly, as though it had found the invasion of the muscular territory more difficult. The sarcoma cells, however, were plainly to be seen amongst the muscular fibres, especially along the connective-tissue lines, but they were few and sparse as compared with the

vast numbers of them in the fat layer. The invasion by the sarcomatous cells had penetrated very deeply into the muscular tissue, following the lines of the connective tissue and lying between the fibres.

In the lung the sarcomatous infiltration had followed the connective-tissue lines, the pulmonary trabeculæ being enormously thickened and presenting themselves as masses of round cells. The walls of the air cells were also infiltrated in places, and where the growth had fully taken possession of an area, the cells had multiplied so that the air spaces were filled, causing the lung to be quite solid. The nodules upon the pleural surface of the diaphragm were composed of masses of round cells, presenting no unusual features.

In the liver were many areas of varying size infiltrated with round cells, which had stained intensely red. None of these were large, nor had the macroscopical examination revealed the presence of any nodules sufficiently large to be seen with the naked eye. It seems fair, however, in view of the fact that sarcomatous infiltration had occurred so extensively into so many tissues and organs, to assert that these small infiltrations into the liver were but an early stage of the same malignant disease which had progressed so much further in other places.

The spleen and mesenteric glands were sarcomatous, as was easily seen from their gross appearance, but as their natural histological appearances so closely resemble those of a round-celled sarcoma, the only specially noticeable characteristic of them was the intense red staining of their cells.

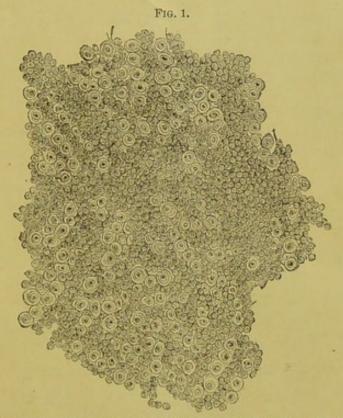
The kidneys presented numerous nodules, both upon the surface and more deeply seated within their substance. These, when examined microscopically, were seen to be sarcomatous, the neoplastic cells lying between the bloodvessels and renal tubules in the connective tissue, except where the deposit had become extensive, in which case the renal tissue was overwhelmed, and the appearance was simply that of a mass of the characteristic round cells. In one place there was found a layer, somewhat less than a thirty-second of an inch in depth, of sarcomatous deposit upon the surface of the kidney. The neoplasm included the capsule, and the separation of the diseased from the healthy renal tissue beneath it was very sharply marked. Hemorrhage into this neoplastic material directly beneath the capsule had occurred.

The appearances of the sections of the cerebellum were not easy to interpret. The portions of pia mater included were infiltrated, especially around the bloodvessels, with cells precisely similar in appearance to those which in other places were beyond doubt sarcomatous. In view of this fact it seems fair to assert that the disease had invaded the pia mater, and this is the more just and reasonable, as a precisely parallel condition existed in connection with the eyes, as may be seen from the following description:

Left oculo-motor nerve. The individual nerve fibres are of normal appearance, axis cylinder and medullary substance presenting their natural charac-

teristics. Here the normal constitution ceases, and the nerve bundles, and in many places the individual fibres, are separated by collections of round sarcoma cells, which have closely followed the connective-tissue septa and the bloodvessels supported by them. In other words, instead of the ordinary membranous investment of the fasciculi, this has been changed into one composed of the cellular elements of the sarcoma.

In the right oculo motor nerve precisely the same process is repeated, only the infiltration of the perineurium and endoneurium is so extensive that the appearance is that of a section of ordinary round-celled sarcoma, through



Section of right oculo-motor nerve showing extensive sarcoma-infiltration.

which are interspersed here and there single, normally constituted nerve fibres. (Fig. 1.)

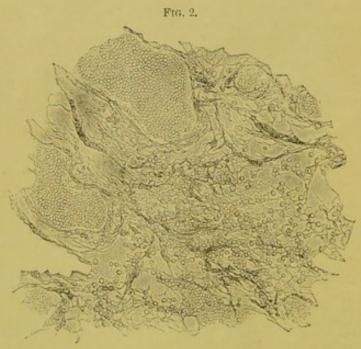
Portion of the posterior half of the right eyeball and 9 mm. of the optic nerve in longitudinal section. Beginning from the extra-ocular end of the optic nerve and passing to the lamina cribrosa, there is no marked change in the nerve bundles and no increase in the nuclei. The trabeculæ of connective tissue are more developed than in the normal nerve, but are not infiltrated with sarcoma cells. Toward the extra ocular end of the nerve are several capillary vessels, around which are clustered numerous round cells. The lumen of the central arteries contains a few blood cells, and in addition small collections of larger, deeply stained lymphoid cells—a condition which re-

peats itself more decidedly in several adjoining vessels or branches. The outer sheath is thickened, but not infiltrated; the inner sheath is unchanged. The intervaginal space contains numerous darkly stained round cells gathered in the meshes of loose fibres. The nerve entrance is free from changes, evidences of neuritis being entirely absent.

The retina is badly broken and misplaced, rendering an accurate study of its elements difficult, which, save for some proliferation of the internal nuclear layer and distinct thickening of the fibre layer, are free from pathological changes. The pigmented epithelium appears only in fragments clinging to the choroid coat.

The choroid to the left of the nerve entrance, so far as the lamina vitrea and chorio-capillaris are concerned, presents no abnormalities. The blood-vessels of the stroma are well filled with corpuscles and some darkly stained cells. Here and there the leucocytes of this region are gathered together in small collections. The pigment cells, very dark, appear in characteristic variety of shapes.

To the right of the optic nerve the choroid is detached from the sclera, is thicker than on the opposite side, and, in addition to the appearances just



Section or left choroid, showing large bloodvessels, pigmented cells, and secondary sarcoma-deposit.

described, presents in several spots in close relationship with vessels in the stroma considerable collections of round, darkly stained cells, which, in general character and grouping, undoubtedly belong to the sarcomatous infiltration. The sclera is free from abnormal appearances, but in the branches of the ciliary nerves passing through it there are small round cells suggestive of those which have infiltrated the oculo-motor to such a great extent.

Posterior half of the left eyeball and 8 mm. of the optic nerve in longitudinal section. So far as the optic nerve, optic-nerve entrance, retina, onehalf (left) of choroid and sclera are concerned, the description just given applies so nearly that it need not be repeated. The right half of the choroid remains in situ for 3 mm. from the optic-nerve entrance. Then it becomes detached from the sclera and is greatly thickened. The branching, pigmented cells are massed together on the outer part, and also surround the well-filled vessels of the stroma, between which are gathered areas of round sarcoma cells, interspersed with pigment granules and dark, spindle-shaped cells. The chorio-capillaris can be traced unbroken throughout the section, but is indistinct directly over the thickest part of the affected choroidal tissue. The sarcoma cells are dispersed through the layer of choroidal stroma containing large bloodvessels, but are especially massed in several localized areas. Some of the larger veins contain darkly stained cells analogous in their appearance to those which lie outside of the vessel walls. (Fig. 2.) This area of infiltration begins 3 mm. from the nerve entrance, and is 1 mm. in diameter at its thickest portion.

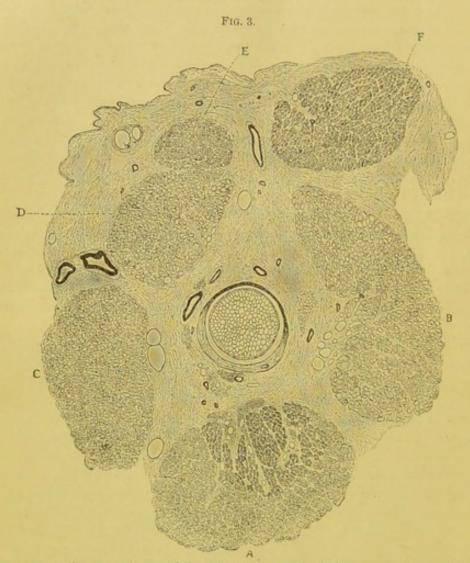
Transverse section of the contents of the left orbit about 14 mm. anterior to the foramen opticum.\(^1\) The relation of the parts (muscles, vessels, nerves, etc.) one to the other is undisturbed.

Muscles. The external, internal, superior rectus, and levator palpebræ superioris are normal in appearance; the inferior oblique is not included in the section. The inferior rectus contains a patch, constituting about one-third of the section, situated in the upper part, which presents an exquisite picture of infiltration with round sarcoma cells. The connective tissue investments of the individual fibres and of the fasciculi are literally replaced with the cells of the new growth; while the sheath of areolar tissue covering the entire muscle in the affected area is crowded with the elements of the neoplasm, which extend into the surrounding fibro-fatty tissue of the orbit. For the most part the diseased area is sharply separated from the portions of the muscle which remain unaffected, although in places small trains of cells proceed a short distance into neighboring areas along the internal perimysium.

The section of the superior oblique is more freely supplied with darkly stained nuclei and corpuscles than those of the other muscles, and in one or two spots, in the neighborhood of small bloodvessels, are collections of larger lymphoid cells, probably representing small foci of sarcomatous infiltration. (Figs. 3 and 4.)

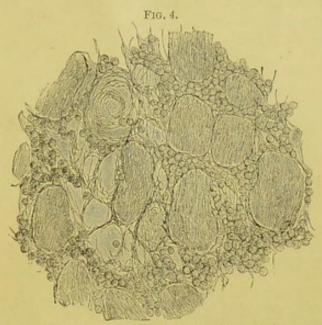
¹ This section corresponds almost exactly with Table VI. of Lange's Topographische Anatomie des menschlichen Orbital-Inhalts, and has been studied with the aid of this diagram.

Optic nerve. The nerve itself is normal, but in the intervaginal space, clinging closely to the inner sheath, are many small round cells, while in the fibro-fatty tissue, between the nerve sheaths and the inferior rectus muscles, are numerous collections of sarcoma cells, particularly immediately in relation with the cross sections of the ciliary arteries.



Transverse section of contents of left orbit 14 mm. anterior to foramen opticum, showing, A, patch of sarcoma in inferior rectus; B, C, D, E, external, internal, and superior rectus, and levator, unaffected; F, superior oblique; sarcoma cells lie between optic nerve and inferior rectus.

Other nerves. The ciliary nerves, naso-ciliary nerve, branches of the oculomotor, supra-orbital, and a branch of the trochlear have been identified. In none of them are the appearances repeated which have been described with the main stem of the oculo-motor. Of the nerves just named the supraorbital is more richly supplied with corpuscles and nuclei than the others, but there are no sarcoma cells between the nerve fibrils. The branches of the nerves supplying the inferior rectus, contained within the body of the muscle, although themselves not infiltrated, are liberally surrounded with sarcoma cells, which infiltrate their external connective-tissue investments.



Section of inferior rectus showing sarcoma cells between muscle-fibres.

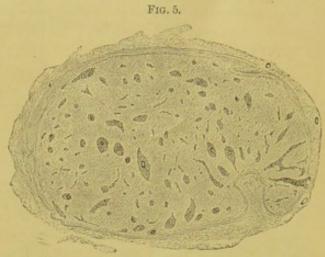
Bloodvessels. The following bloodvessels are evident in the section: the supra-orbital, ophthalmic, and ciliary arteries and branches of the ophthalmic veins. The coats of these vessels are free from infiltration, except in the case of the ciliary branches lying between the optic nerve and the patch of infiltration in the inferior rectus, and even in these the sarcoma cells lie rather in the loose fibro-fatty tissue adjacent to the vessels than in coats of the artery itself, although in some instances small foci may be seen in the adventitious tunic. In the small vessels supplying the inferior rectus muscle this character of infiltration (i. e., within the adventitious coat) is more conspicuous.

Transverse section of a portion of the contents of the right orbit. As the contents were fragmentary, the relation of the various constituents to each other, and consequently their identification, is imperfect.

Muscles. The following muscles appear to be included: superior rectus, levator palpebræ superioris, a fragment of the superior oblique, and the internal (or inferior) rectus. These structures have escaped the sarcomatous infiltration, with the exception of the last-named muscle, which contains two patches of diseased tissue exactly similar to the one described in the inferior rectus of the left orbit. The branches of the oculo-motor nerve supplying this muscle are not only surrounded by sarcoma cells, but the individual fibres have been separated by the elements of the new growth precisely as the same process has occurred in the main stems of both third nerves.

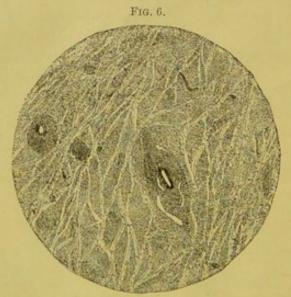
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The optic nerve is normal in appearance, but in the intervaginal space the collections of round cells are more evident than in the corresponding situation on the opposite side.



Transverse section of optic nerve just within skull, showing general plan of the sarcoma-infiltration.

The bloodvessels, except the small branches which supply the muscle in the area of infiltration, are free from sarcomatous deposits.



Portion of Fig. 5 more highly magnified, showing arrangement of sarcoma cells surrounding the bloodvessels.

Cross-sections of the optic nerves just within the skull. The dural sheaths are not visible in the section; the inner (pial) sheath is densely infiltrated with sarcoma cells, which, passing inward from this situation along the trabeculæ, infiltrate those in and within the margins of the nerves. In

general, the nervous tissue appears normal, and there is no undue development of nuclei. Each capillary and arteriole, however, is surrounded with a considerable area of neoplastic cells, which completely replace the adventitious coat and peri-vascular sheaths of the larger vessels, and entirely fill the spaces surrounding the smaller ones. Within the lumen of many of the vessels are cells exactly the counterpart of those which surround them. (Figs. 5 and 6.)

The case seems worthy of being described and recorded, as sarcoma of the mediastinum is by no means common, and as the metastatic growths were more fully examined and studied with the microscope than can or has been done in most of the cases recorded in the journals, but especially on account of the condition of the eyes and their appendages. As has already been said in connection with the description of the macroscopic conditions, at the post-mortem examination nothing abnormal was seen except the difference in size of the two oculomotor nerves. It would probably have escaped notice that the left, the smaller of the two nerves, was much larger than usual, had it not been for the fact that the right was still larger. The difference in size having been observed, of course further investigation was made to discover the cause.

Since seeing this case, now four years ago, one of us (Dr. Meigs) has seen another, which was in many respects parallel:

A man, aged forty-three years, who had always been healthy, was for a month annoyed by slight cough; but it was so slight that it had not prevented his starting on a long pleasure journey. Two weeks later he found he had shortness of breath, which soon became so severe that he was advised to come home. When seen he was dull of intellect and his mind disposed to wander; he had dyspnæa, and the face was much congested and swollen There was marked nystagmus, and the eyeballs seemed prominent. In the supra-clavicular fossa upon the right side was a tumor. This was not very hard and seemed to be pressing upward from the chest cavity, so that it almost entirely filled the fossa. It did not pulsate. Examination of the heart brought to light no evidence of disease, as the sounds were soft and clear, but the action was rather feeble. There were whistling and cooing râles to be heard over the lungs, but no signs of consolidation. The appearance of the lower extremities was in marked contrast to that of the head. The patient was a large, stout man, and the swollen head and bulging eyes hardly looked as if they could be a part of the same individual as the legs,

which were emaciated and shrunken. The history was that the tumor had existed only two weeks. This, taken in consideration with the fact that there had been severe dyspnæa for the same length of time, indicated strongly the presence of a rapidly growing intra-thoracic mass. Such a growth could only be a sarcoma, and the opinion was therefore expressed that the disease was mediastinal sarcoma.

It seemed almost certain, too, in the light of the other case that has been described, that the staring of the eyeballs and nystagmus must be due to an invasion of some part of the ocular apparatus by metastatic sarcoma. Within three or four days a tumor showed itself in the other supra-clavicular space, the dyspnæa increased terribly, and he died. A post-mortem examination was made, and a sarcomatous tumor weighing one and a quarter pounds was found occupying the mediastinum. The growth surrounded the trachea, aorta, and other large bloodvessels, and there were secondary deposits ranging in size from that of a bean to a chestnut upon the diaphragm and posterior wall of the thorax. The post-mortem examination does not appear to have been very thoroughly made, for there is no mention of metastases to any of the organs, though such almost certainly must have existed, nor was any investigation of the brain or eyes made. It is much to be deplored that sections from the eyes and their appendages could not have been thoroughly examined with the microscope, for the disease had almost certainly invaded them. That which was observed in this case, imperfect as the investigation was, when taken in connection with the one more fully described, makes it desirable that metastases to the ocular apparatus in cases of mediastinal sarcoma should be sought for. It may be, too, that it occurs in cases of sarcoma arising in other situations than the mediastinum. The presence of the sarcomatous deposits in the ocular apparatus might readily be overlooked, for there are hardly any gross appearances to be seen. It is reasonable to suppose that there was more sarcomatous deposit somewhere in the brain than that in the pia mater of the cerebellum which has been described, and which could only have been discovered by careful microscopical examination.

As already indicated, a large measure of interest centres in the distribution of the sarcoma cells within the eyes, optic nerves, oculo-motor (third) nerves, and the orbital muscles. Both third nerves are extensively infiltrated throughout their length, especially upon the right side. In the branches of the nerves in the left orbit no exactly similar appearance was found, except in those supplying the inferior rectus, which, while not themselves infiltrated, are densely surrounded by cells. Again, in the right orbit, of the muscles apparently identified, a portion of the internal (or inferior) rectus is contaminated, as also are the nerves supplying it, not merely in the form of surrounding areas of cells, but also by a separation of the individual fibres with the elements of the new growth, exactly as this occurs in the parent stem. Therefore, if the appearances seen in the left superior oblique are not accepted as certainly sarcomatous, we may infer that one pathway of the morbid process was along the oculo-motor nerves, and through them to two, possibly three, of the muscles which they supply.

The optic nerves within the skull are extensively diseased, but the process of infiltration grows less marked as they approach the eyes themselves. Indeed, even in the crosssection in the orbit scarcely any diseased tissue is evident, while in the portions of these nerves examined in connection with the posterior halves of the eyeballs, save for some slight cellular infiltration around the capillary vessels and in the intervaginal space, evidence of sarcoma is lacking. Therefore it may be inferred that a second pathway of the morbid process was via the optic nerves, and a striking and interesting feature of the case at once becomes apparent, viz.: that the disease was more advanced and extensive in degree within the skull than in the orbital and ocular termination of the third and second nerves. In other words, this indicates that the disease travelled along these pathways from the brain forward toward the eyes.

The deposits of sarcoma cells in each choroid, but particularly in that of the left eye, give this case importance in the

literature pertaining to sarcoma of the uveal tract. The fact that these deposits are limited to a certain area of the choroid, that they are surrounded by comparatively healthy tissue not contiguous with infiltrations elsewhere located, and that the bloodvessels within them and in their immediate vicinity contain cells apparently of the same character, affords evidence that they should be regarded as metastatic nodules, probably of embolic origin.

Fuchs, in his admirable monograph, Das Sarcom des Uveal Tractus, Wien, 1882, having analyzed the entire literature to date, states that metastatic choroidal sarcoma is unknown, and quotes Virchow's well-known sentence: "Those organs which exhibit a great tendency to protopathic tumor formation present a very slight inclination to metastatic deposits." Fuchs refers to, but rejects, Broemser's case¹ of supposed metastasis of a melanotic growth of the cheek to the choroid, for the excellent reason that no microscopic evidence is at hand that either the ocular or the facial growth was sarcomatous, and reiterates his belief that up to the date of his writing sarcoma metastasis to the choroid had not been observed.

Pflüger,² of Bern, contributes a case of sarcoma in a young woman, aged thirty years, which developed from a congenital nævus in the region of the right parotid gland, and which was followed by secondary sarcoma of the glands, with metastasis into the skin of the back and head, into the right choroid, and probably into the cerebrum. Three years and a few months elapsed between the period when the congenital pigment-patch began to enlarge and the death of the patient. Autopsy was refused, and the facts reported are based upon clinical observation alone. Ophthalmoscopic examination revealed a tumor occupying the medial half of the eyeground. Pflüger refers to another case of intra-ocular metastatic sarcoma reported by Schiess-Gemuseus,³ the primary growth being a sarcoma originating from a congenital nævus in the parotid region.

¹ Ueber einen Fall v. secundär Melanom. d. Choroid. Diss. Inaug., Berlin, 1870.

² Archives of Ophthalmology, vol. xiv. p. 185.

³ Graefe's Archiv, Bd. xxv., Abth. 2.

Ophthalmoscopic examination was impossible, owing to opacities in the media, but the microscope showed that the secondary growth had originated from the optic papilla. Hence the case is not properly classed with choroidal growths.

In the case forming the basis of this paper, unfortunately ophthalmoscopic examination is wanting, but the anatomical studies are sufficiently detailed to demonstrate secondary choroidal sarcoma. It is scarcely conceivable that the choroidal growth under these circumstances could have been the primary one, although, as is well known in a few instances, extremely small and totally unsuspected growths in this situation have been followed by very extensive metastasis; in one case quoted by Fuchs, a melanotic mass was found in the heart secondary to a small sarcoma in a shrunken eyeball, which had existed in this condition for more than twenty years.

Independently of the fact that the sarcomatous deposits in the eye were confined within the scleral walls, and were both clinically and microscopically of the nature of secondary growths, the mediastinum rarely suffers from this form of tumor, save as a primary growth. Among ninety-eight cases reported by various authors and collected by H. A. Hare, but five were secondary and thirty-one were primary, the remaining number having no distinct reference in regard to this point. The interesting fact has been noted that so far as the optic nerves, third nerves, and orbital contents are concerned, the microscopic evidence is that the disease travelled from the brain forward toward the eyes along these pathways, but the localized character of the choroidal neoplasms and their failure to be in any demonstrable connection with other sarcomatous areas, seems definitely to indicate that they should be regarded as embolic deposits.

¹ The Pathology, Clinical History, and Diagnosis of Affections of the Mediastinum Fothergillian Prize Essay. Philadelphia, 1889.

