

WARTHIN (A.S.)

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*With Universal Metastasis and Forma-
tion of a Free Sarcomatous Mass in
the Right Ventricular Cavity.*

BY

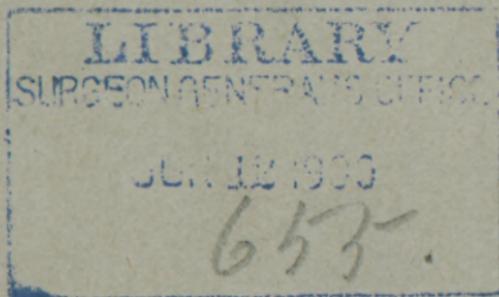
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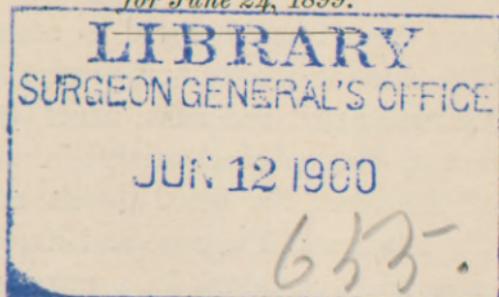
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A PRIMARY POLYMORPHOUS-CELL SARCOMA OF THE NOSE,

WITH UNIVERSAL METASTASIS
AND FORMATION OF A FREE SARCOMATOUS MASS
IN THE RIGHT VENTRICULAR CAVITY.

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THE reports of sarcoma of the nasal passages have multiplied to so great an extent during the last several years that the condition can no longer be looked upon as one of very rare occurrence. Bosworth, in 1889, had collected from the literature previous to that year reports of forty-one cases. In 1896 twenty-one cases were added to this list by Boylan, and I have been able to find in the literature since the latter's paper reports of twenty-seven additional cases. It is evident from this rapid increase of reported cases that sarcoma of the nose must occur with some degree of frequency.

The sarcomatous tumors described as being found in the nose present a wide variety in kind. Small and large round-cell, spindle-cell, lymphosarcoma, fibrosarcoma, myxosarcoma, osteosarcoma, osteoid sarcoma, angiomasarcoma, myxosarcoma, alveolar sarcoma, and mela-

notic sarcoma have been reported as occurring in this region. The site of the tumor presents also a wide range. The turbinated and nasal bones, the periosteum of these bones, the nasal cartilages, the sæptum, the muscles of the nose, the blood-vessels and connective tissue of the mucosa of the nose and nasopharynx have all given rise to sarcomata. In a number of cases an attempt has been made to prove their origin from non-malignant polypi. The evidence upon this point, however, is very slight, and there is no proof of any close relation between a benign polyp and sarcoma. From the cases reported they would seem to be of independent origin. The nasal sarcoma, because of its location and the conditions of its growth, often presents a polypoid form, and in those cases in which a myxoma was thought to have become sarcomatous it is more probable that the so-called polyp was malignant from the beginning. The possibility of the development of a sarcoma in a benign polyp need not be denied, but in those cases where this change was thought to have taken place the microscopic evidence is either entirely wanting or insufficient.

The opinion is quite generally held in the older literature that sarcoma of the nasal passages is not so malignant as sarcoma occurring in other regions of the body. Bosworth concludes from the result of his study of forty-two cases that "sarcoma of the nose does not apparently present the same malignant tendencies as it does when found in other locations." Warren, in his *Surgical Pathology*, says: "The disease does not appear to show the same malignant tendencies in the nasal passages that it does in other localities." And Boylan, from the study of his twenty-one cases, is inclined to

favor this opinion, since rapid recurrence took place after operation in the minority of cases, and in others there was a prolonged or permanent cure. From these points he concludes that the prognosis in nasal sarcoma is relatively favorable.

A study of the literature since Boylan's paper, however, leads to the conclusion that there is no justification for the assumption that sarcoma of the nasal passages is less malignant than in other regions. It is less malignant only in so far as it is in a situation where it may possibly be thoroughly removed. While many of the nasal sarcomata described have been of slow growth and slow recurrence, this is also true of sarcomata in other parts of the body. The slow growth of a sarcoma or carcinoma should never deceive us as to its possibilities of malignancy or lead us to delay in operative measures. Slow-growing sarcomata of the nose have sometimes taken on an extraordinarily rapid growth just as in other parts of the body. The possibility of a favorable prognosis in nasal sarcomata is based, therefore, purely upon the operative conditions, and not upon the character of the tumor.

The case which I present in this report is of value, first, in that it adds a new variety to the list of sarcomata found in this region; secondly, because of its great malignancy; thirdly, because of the great extent and interesting character of the metastases and the occurrence of a free sarcomatous mass in the right ventricular cavity. The history of the case is as follows:

Mr. F. E., aged thirty-nine years, was admitted to the University Hospital on the 1st of April, 1897. He was a lumberman, single, and gave a negative family history. Previous to the beginning of the present con-

dition his health had been good. A year and a half before admission his right nostril became partially occluded. By blowing his nose with some violence he could force out large "scabby, flaky masses." This condition lasted for a year, when a vesicular eruption becoming pustular gradually spread over the right side of the nose, extending to the left. Three months before admission he had had a number of "polypoids" removed from his right nostril. The patient did not know whether a microscopical examination of these had been made, but was told that they were ordinary nasal polypi. From the treatment of the case it is evident that the operator had regarded them as benign growths, as when the patient entered the hospital no suspicion had been raised as to the malignant nature of his disease.

He had been under treatment with a number of physicians who had diagnosed his condition as eczema, syphilis, and lupus. He had no history of acquired syphilis, and under specific treatment his condition had grown steadily worse.

A month before admission he had noticed numbness over the left side of the nose, left cheek, upper lip, and forehead to the median line. Diplopia, left-sided ptosis, and dilatation of the left pupil soon followed.

On admission the general condition of the patient appeared fair. He complained of weakness, nervousness, insomnia, and of dull pain in his forehead. His appetite was poor, and bowels were constipated. He passed about one litre of urine daily, very highly colored, and with specific gravity of 1.024. His nostrils were completely occluded, his breathing being entirely by the mouth and very shallow in character. His nose was symmetrically enlarged; the skin covered with yellowish, opaque crusts, with scattered pustules. Around this and extending slightly into the skin of each cheek there was redness with firm induration. The nostrils were filled with grayish-red masses. There was no odor.

The sense of smell was entirely lost. There was complete anæsthesia over the distribution of the supraorbital

and infraorbital branches of the fifth nerve. There was some atrophy of the muscles in this area. Ptosis of the left lid was present, with complete paralysis of the muscles of the left eyeball. Sight was diminished in the left eye. The retinal examination showed a marked degree of choked disk. The patient's mind was clear.

A clinical diagnosis was made of malignant tumor of the nose with secondaries at the base of the brain, involving the first, second, third, fourth, the first and second branches of the fifth motor fibres of the fifth and the sixth cranial nerves. The condition of the patient gradually became worse. No operation was attempted. On the 11th of May he had attacks of nausea and vomiting, followed by great disturbance of respiration and circulation. The extremities became œdematous, the patient sank into coma and died on the 17th of May. The necropsy was performed by me in the university laboratory of pathology four hours after the patient's death. The gross findings were as follows:

Section-protocol.—Body of medium height and slender build. The musculature good, slightly flabby. Fair amount of panniculus. No œdema. Skin sallow, nutrition fair. Marked hypostasis, amounting to cyanosis over the upper part of thorax, head, and back. Rigor mortis present in all muscles. Body heat present.

Head: Face cyanotic. There is a subcutaneous growth extending over the entire nose and a short distance into each cheek. The skin over this is thickened, rough, scaly, with numerous minute vesicles. The nostrils are completely closed by masses of soft, grayish-red tissue. The growth does not extend into the mouth. Over the bridge of the nose there is a small ulcer covered with surgical dressings. The nasal bones and cartilage seem completely replaced by the growth.

Brain: A small, soft growth, of the size of a cherry, is found on the inner surface of the dura near the longitudinal sinus. The pia is congested; all of the sinuses are distended with fluid blood. The brain substance is hyperæmic and œdematous. There is a large amount of

clear fluid in the lateral ventricles, which are somewhat distended. The pineal body is replaced by a tumor nodule, of the size of a large cherry. Otherwise the brain seems normal. The hypophysis is replaced by a tumor growth. The left third nerve is surrounded by a thick mass of new growth which is partly colloid in appearance. The left Gasserian ganglion is greatly enlarged and completely surrounded by new growth. The nasal fossa is completely filled with a soft tumor mass, showing extensive mucous degeneration. This mass is directly continuous with tumor masses filling up the frontal sinus, the sphenomaxillary fossa, and with the mass in the nostrils. The left cavernous sinus is also filled with tumor tissue. All of these masses are very soft, homogeneous, and show myxomatous change. The right third nerve and Gasserian ganglion are normal.

The examination of mouth, larynx, and trachea is negative.

Thyroid enlarged, and shows colloid degeneration.

The main incision shows marked venous congestion everywhere. The tissues bleed freely. The muscles are red, moist, and soft. There is a moderate amount of abdominal fat. The position of the abdominal organs is normal. There is no fluid in the peritoneal cavity.

Diaphragm extends to the fourth intercostal space on the right, to the fifth interspace on the left.

No remains of the thymus are present. The mediastinal tissue contains a number of enlarged lymph glands.

Pericardium: The pericardium contains about one hundred cubic centimetres of cloudy fluid in which there are small flakes of fibrin. The surface of the pericardium is dull and clouded. There are no new growths in the pericardial layers.

Heart: Of about twice the normal size, and very irregular in shape. The surface is irregularly nodular, the nodules appearing yellowish as seen through the epicardium. They are elevated, firm, and do not show any umbilication. A thick ring of new growth extends

around the auriculo-ventricular groove. On section the heart muscle is almost entirely replaced by homogeneous yellowish-white areas, contrasting strongly with the deep red of the remaining heart muscle. These areas project as rounded nodules into the cavities of the heart, and form the nodules seen on the surface beneath the epicardium.

Many of these areas are surrounded by a zone of hyperæmia or hæmorrhage. The centre of some of the nodules is soft, in others there is a colloid appearance. The endocardium appears unchanged, and in no place does it give any evidence of a breaking-through of the tumor. In the left ventricular cavity there is a large jelly clot with some fluid blood, and in the auricles and great vessels are large white clots. The right ventricle contains some fluid blood and a large firm mass, about the size and shape of a large English walnut. It is grayish-red in color, and has a ribbed and furrowed surface suggesting the appearance of brain coral. Its surface presents no appearance of any previous union with the heart wall, nor can any evidence of such connection be found in the endocardium of the right heart.

Lungs: There are about five hundred cubic centimetres of turbid fluid in each pleural sac. The surfaces of the pleuræ are cloudy and are covered with numerous flakes of fibrin. All over the surfaces of both parietal and visceral pleuræ are scattered numerous small growths, varying in size, but for the most part of the size of a small pea. In the parietal pleura they are arranged in rows corresponding to the direction of the ribs. The right lung shows extreme congestion and œdema. There is a moderate anthracosis. Throughout its substance there are many small growths, most abundant about the bronchi and under the pleura. These tumors are soft, white, and perfectly homogeneous. The left lung presents a similar appearance, but shows fewer of the growths. There are several small deep-red areas in the lower lobe just under the pleura. These are triangular in shape, with their bases beneath the pleura.

Bronchial glands: These contain large masses of new growth. On section they are soft, white, and homogeneous, and show a colloid appearance in their central portions.

The examination of the thoracic vessels and œsophagus is negative.

Spleen enlarged, very soft, cyanotic. On its anterior margin near the deepest fissure are two cavernous tumors about the size of small hickory nuts. On section the pulp is deep red, very soft, flows readily. The follicles are not visible and the stroma is unchanged. There are a number of depressed areas, grayish-red in color, with deep-red borders, and of firm consistence.

Adrenals show no change.

Kidneys: Both enlarged and cyanotic. The fat capsule is rather thick. The fibrous capsule is not adherent, except in areas corresponding to small white nodules in the capsule. On section both kidneys present practically the same appearances. The cortex is increased in thickness, deep bluish-red, of increased consistence. The cut surface bleeds very freely. The glomeruli can not be made out. The pelvis is filled with large tumor masses extending up between the pyramids into the kidney substance, and also into the pyramids themselves. The new growth is very soft, white, homogeneous, and in many places myxomatous. The chief portion of the new growth seems to be in the cavity of the pelvis, which is greatly dilated. It is not adherent to the mucosa of the pelvis, as it can be easily separated from this, leaving the surface free and apparently unchanged. The growths extend out around the renal vessels into the retroperitoneal tissues. The retroperitoneal glands are replaced by large masses of new growth of the same character as described above. The ureters are dilated, the mucosa is thickened.

Bladder: The walls are thickened, and there is a small area of hyperæmia with fibrinous exudate on the posterior wall.

Genitals: The external genitals are apparently un-

changed. The right testis is slightly enlarged. The body of the testis is replaced by tumor growth of the same nature as that described above. The left testis contains a growth of the size of a walnut. It is of the same character as that described above. The prostate is enlarged, but appears normal.

Intestines: Appendix normal. The mucosa of the small and large intestine is injected. In the serous coat are several small nodules of new growth. The mesenteric glands contain also tumor nodules.

Stomach: On the floor of stomach about the middle of the greater curvature there is a round ulcer, of about the size of a dollar, with sharp clean edges, extending to the muscular coat. Near this are two irregular areas of infiltration of new growth in the mucosa and submucosa. They are flat and do not extend into the muscularis. On section they present the same appearance seen in all of the other tumor masses, and show a beginning central degeneration. In other parts of the mucosa there are small erosions with thickened bases and indurated edges.

Pancreas: The head of the pancreas is replaced by a large tumor mass. On section this shows the same appearance as seen elsewhere.

Liver: The size is about normal; the left lobe is very long and thin. On section, the surface is dark-red and cyanotic, and bleeds freely. In some areas there is a distinct nutmeg appearance; the connective tissue is somewhat increased. No growths can be perceived by the naked eye. The examination of the gall bladder and biliary passages is negative.

Lymph glands: The cervical glands on the left side contain large tumor masses.

Microscopical Examination.—An abundance of material was taken from all parts of the body and fixed in alcohol, mercuric bichloride, and Müller's fluid. Both paraffin and celloidin imbedding methods were employed, and the sections were stained with various stains, hæmatoxylin and eosin and Van Gieson's method being most commonly used. The microscopical examination of the

sections taken from the primary tumor and from the metastases revealed such a variety of pictures that at first sight it seemed impossible that the different growths could be of the same origin. A careful study of these, however, made plain the fact that the differences in appearance were due to differences in the age of the growths and to the conditions in the tissues where they were located.

Primary growth: Section taken from the periphery of the primary tumor in the nasal fossa and from the infiltration of the skin and subcutaneous tissue of the nose present the appearance of a small round-cell sarcoma. The mass of the structure is composed of small round, deeply staining cells; there is a very scanty reticulum, with numerous large and thin-walled blood-vessels lying in intimate contact with the cells. The deeper parts of the nasal tumor give varied pictures. There the cells for the greater part are not of the small, round-cell type, but are much larger and very irregular in shape. Division figures are very numerous, and many of the cells have large and very irregularly shaped nuclei possessing a great excess of chromatin. "Grape-cluster" nuclei are very common, and many giant cells are found. In these older parts of the growth there is a greater amount of intercellular substance than in the peripheral portions. The cells are separated by a clear, slightly refractive substance, which does not stain with eosin or acid fuchsine, but gives the reactions for mucin. In the fresh tumor the intercellular substance must have been fluid. As in these older parts of the growth the number of cells is not nearly so great as in the areas of more recent development, it is probable that the intercellular substance has arisen from the degeneration or solution of part of the cells. Support is given to this view by the fact that the central part of all the larger masses is filled with a similar mucoid substance, the cells having entirely disappeared. In the fresh tumor these areas presented a colloid appearance, sometimes firm in consistence, at other times more watery. The posterior part of the

nasal fossa was completely filled with this jellylike mucin. In many places these cystlike spaces are surrounded by a capsule of granulation tissue. It would seem that the tumor in its growth had reached a certain height in these areas, the cells had completely degenerated, and there had been an attempt at encapsulation. No typical mucous tissue was found in any part of the original tumor or in any of the metastases.

Dura: The small growth taken from the dura presents the appearance of a small round-cell sarcoma.

Pineal body: The growth here is polymorphous-celled and shows myxomatous degeneration in the central part. The peripheral portion has the appearance of a small round-cell sarcoma.

Hypophysis: This is almost entirely replaced by a central tumor mass which is of the type of a polymorphous-cell alveolar sarcoma. The central part shows a marked myxomatous change. Many giant cells are present here, and the irregularity in the size of the nuclei is very marked. In the periphery are nodules of small round cells.

Gasserian ganglion: The sections of the mass taken from the region of the left Gasserian ganglion show a beautiful picture of the infiltration of large nerve trunks and ganglion by sarcoma cells. There are many of the ganglion cells preserved, surrounded by small, round cells, from which they stand out in sharp contrast. They are swollen and granular, but their nuclei and nucleoli can be distinctly made out, and their nucleated capsules appear unchanged. The nerve fibres of the large nerve trunks are widely separated by tumor cells and in many places have a knotted, swollen appearance. In the sections stained by Van Gieson's method these knotted fibres have a greenish color. The tumor cells here, like those in the central portions of the primary growth, are very irregular in size and shape. There are many giant cells with large nuclei showing marked hyperchromatosis. Many of the nuclei are star-shaped, others are ragged in outline. Caryomitotic and amitotic division

forms are abundant. There are many ectatic blood-vessels. The central portion of the growth shows also a myxomatous change. Throughout the trunk of the left third nerve there is an infiltration of sarcoma cells. The colloid mass into which the third nerve passed is a cavity filled with a colloidlike mucin surrounded by a capsule of granulation tissue. Outside of this capsule the tumor cells are of more uniform size and there are not so many giant cells. The blood-vessels are very numerous and large.

Heart: The entire heart wall is infiltrated with tumor cells. The muscle in many areas is wholly replaced by nodules of polymorphous cells. The larger nodules show myxomatous change and in every way present an appearance similar to that of the original growth. The remaining muscle cells are greatly atrophied and are widely separated by small round cells. Many of the muscle fibres show simple and waxy necrosis. The entire endocardium is infiltrated with small round cells, and in one area in the right ventricular wall the tumor cells have broken through the endothelium and form a small flattened growth on the wall of the ventricular cavity. This could not be seen in the naked-eye examination.

The sections of the free mass in the right ventricular cavity show it to be of sarcomatous structure. There are many cells larger than leucocytes and possessing large vacuolated nuclei. A few giant cells are found, and many cells with large, irregular, deeply-staining nuclei. The majority of the cells are of the small round variety. At one side of the mass there is a collection of red blood-cells and fibrin. A very scanty reticulum can be made out and a few small blood-vessels can be seen. The origin of the mass seems very evident after the microscopical study of the endocardium of the right ventricle. It is undoubtedly a polypoid nodule that, projecting from the endocardium, grew until it was too large to pass out of the ventricle, and then breaking loose continued to grow as a free body. The mass shows no necrosis or degeneration.

Lung and pleura: The small growths in the pleura are of the type of a small round-cell sarcoma. The larger ones show a polymorphous variety of cells and myxomatous degeneration. The small nodules throughout the lung consist of small round cells, the larger ones of polymorphous cells. There is hardly a blood-vessel throughout the lung that has not a circumvascular growth of sarcoma cells. Numerous emboli of sarcoma cells are found in the capillaries. In many of the smallest growths the cells are irregular in size and shape and show great excess of chromatin. The lung shows extreme œdema and congestion, and there are several hæmorrhagic infarcts and small areas of broncho-pneumonia. Many of the larger tumor nodules show a healing process and the formation of scar tissue in the central part of the nodule. This can be seen in all stages, from a beginning formation of granulation tissue around the myxomatous portion of the tumor to nodules made up of scar tissue alone.

Spleen: Small nodules of tumor cells are found throughout this organ. There are also a number of anæmic infarcts.

Liver: A number of small nodules of small round cells are found in the periportal connective tissue.

Kidneys: There is an acute degenerative nephritis present, and the greater part of both kidneys is replaced by masses of sarcomatous tissue of the same structure as described above. Many of the smaller nodules are made up of the polymorphous cell type.

Pancreas: The head of the pancreas is almost entirely replaced by a sarcomatous mass, which is made up chiefly of small round cells, but contains also many polymorphous cells.

Stomach: The base of the round ulcer and the flat infiltrations of the mucosa consist of nodules of sarcoma. The ulcer is apparently caused by the mucous degeneration of a large nodule projecting through the mucosa. The structure of these nodules in the wall of the stomach is the same as that found in the other tumors.

Intestine: The small nodules in the serosa are of the same type of sarcoma as that described above.

Testis: The tumors here present the appearance of a small round-cell sarcoma. Areas of mucous degeneration are abundant, and the blood-vessels are very numerous and ectatic.

Prostate: The prostate contains localized areas of small round cells.

Lymph glands: The cervical, peribronchial, mesenteric, and retroperitoneal lymph glands contain large nodules of polymorphous or small round-cell sarcoma. The majority of these show mucous degeneration.

Summary.—All of the growths are of the nature of sarcoma. The majority of the smaller nodules and the periphery of all the larger ones are made up of small, round, deeply-staining cells having but little intercellular substance and lying in intimate contact with the blood-vessels. In the central part of all the larger nodules, and in some of the small ones, the cells are larger, polymorphous, and there is an increase in the intercellular substance, which is myxomatous in character. In many of the nodules the entire central part of the growth has undergone a mucous degeneration, and early stages of this degeneration are seen in all of the growths. The tumors are further characterized throughout by the number and size of the blood-vessels. From the structure of the growth the diagnosis of the tumor as a myxomatous polymorphous-celled sarcoma would seem most appropriate.

That the growth in the nasal fossa is the primary one there can be no reasonable doubt. The history of the case, the development of the symptoms, the size and structure of the nasal growth all support this view. The exact site of origin can not be determined. The patient affirmed that it appeared first in the right nostril upon the right side of the septum. Moreover, the relation of the sarcoma to the polyps stated to have been removed can not be settled in the absence of any definite microscopical evidence concerning their structure. The

fact that the tumor everywhere shows a marked tendency to a mucous degeneration of its cells and the formation of a myxomatous intercellular substance might be taken as an evidence of an inherited tendency on the part of its cells tending to show a descent from a myxomatous polyp. This, unfortunately, will not admit of further confirmation.

The points of special interest in this case are the widespread metastases and the intracardiac growth. Secondaries were found in the dura, pineal body, hypophysis, cavernous sinus, lungs, pleura, heart, liver, spleen, kidneys, pancreas, stomach, intestines, peritonæum, testicles, prostate, and the cervical, bronchial, retroperitoneal, and mesenteric lymph glands. The richness of the growth in cellular elements, the scanty stroma, the numerous large thin-walled blood-vessels, the smallness and shape of the cells, all contributed to the facility of the rapid dissemination of the tumor. The numerous metastases throughout both venous and arterial systems are easily explained by the above-mentioned factors.

The free sarcomatous body in the right ventricular cavity forms the most important feature of the case. Intracardiac and intravenous growths are very rare both in carcinoma and sarcoma, but have been described in both, more frequently in the case of the latter. Kanthack * has described a case of carcinoma of the testis in which there was a metastatic mass upon the tricuspid valve extending through the auricle into the inferior vena cava and through the tricuspid orifice into the cavity of the right ventricle. The origin of this seemed to have been from an intravenous growth in the inferior

* *Jour. of Path. and Bact.*, January, 1898.

vena cava, a fragment of which must have become separated and grafted upon the tricuspid valve, where it continued to grow.

The probable origin in my case is that suggested above—namely, the breaking loose of a polypoid nodule from the endocardium, its retention in the ventricle, and its subsequent growth. Microscopically the endocardium was infiltrated with sarcoma cells, and in one place there was found the thin, flattened growth on the surface of the endocardium. This may have been the origin of the mass, or, on the other hand, it may have arisen from a primary embolus of tumor cells retained in the heart cavity. The numerous emboli of tumor cells found in the lung vessels and the hæmorrhagic infarcts of the lung may have resulted from the breaking loose of portions of this intracardiac growth. The anæmic infarcts in the spleen were also probably caused by emboli of sarcoma cells, as masses of these cells could be seen growing in dilated blood-spaces of this organ.

Another point of interest in the growth of this tumor is its tendency to self-healing. As mentioned above, this could be seen in all stages, from the beginning of the formation of a granulation-tissue capsule around the area of degeneration to completely formed nodules of scar tissue completely replacing the tumor.

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