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Abstract

1. When chicken sarcoma virus is serially inoculated on the mouse brain, it loses its carcinogenecity, but when it is inoculated on young chicken, granuloma develops in the liver and lung. When this granuloma is transplanted on adult chicken, a transplantable fibrosarcoma is obtained. 2. According to literature, the originaltumor of the Brown-Pearce cancer is a basal cell cancer, but that imported to Japan in 1953 presented a histological picture of carcinosarcoma. The metastasized tumor of the eye presents a purely cancer tissue, but when this is inoculated on the testis, carcinosarcoma is reproduced. It is therefore considered that the mother cell of the sarcoma is of host origin. 3. MY sarcoma is not a sarcoma, but is a spindle cell cancer. It might be a sarcoma which transformed into a cancer during serial transplantation, but perhaps it was originally a cancer but had been erroneously diagnosed as sarcoma. 4. The tumors we obtained by means of the feeding tests of Yoshida tumor all developed at organs other than those of the digestive tract. They are chiefly reticulo-sarcoma, but others which develop are malignant granuloma in the liver and lung, malignant adenoma in the kidney, papilloma of pelvis, and ependymoma in the cerebral ventricle. Since the discovery of the Yoshida tumor in 1943, serial transplantation has been conducted for 19 years with this tumor not only in Japan but also in foreign countries, but there has been no report to this date that a transformed strain has developed by cell transplantation. It therefore must be considered that the carcinogenesis observed in our feeding tests is a carcinogenesis due to a mechanism completely unlike that of cell transplantation. It has been confirmed by electron microscopy that in the early stage of transplantation of this tumor into the abdominal cavity there was an additional tumor growth due to the anaplastic proliferation of serous cells. 5. During the serial transplantation of viral tumors and/or virus dependent tumors, the tumor sometimes undergoes a morphological change. Though the cause of this is not yet sufficiently elucidated, it is suspected that there is some relationship with virus in the wide sense.

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ON THE HISTO-MORPHOLOGICAL CHANGES OF TRANSPLANTABLE TUMORS

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The histo-morphological changes of tumor cells are often met with in the course of serial transplantation of malignant tumor cells, especially in those of high rate in transplantability. And the transformation of cancer cells into sarcoma cells is not infrequently observed, while the reports dealing with the transformation of sarcoma into cancer are rare. It is assumed in these cases that virus has some relationship with neoplastic proliferation (DURAN-REYNALS[1], SCHMIDT[2], *et al.*).

Such a transformation occurs in serial transplantation in homologous animals, but it is also often noted in serial transplantation in heterologous animals.

Polyoma virus was discovered in 1956[3], and it has revealed the ability to induce more than 20 varieties of tumors. Thus an epoch-making revolution was introduced into the concept of tumor viruses. Similar biological activity has also been observed in chicken sarcoma virus as reported by DURAN-REYNAULS[1] in 1950, i. e. if chicken sarcoma virus is inoculated on ducks and other birds after the serial transplantation on pigeons, various types of tumors can be induced. A report will be made next about the morphological changes of transplantable tumors (including virus dependent tumors) which we have been dealing with for past ten odd years.

1. Chicken sarcoma

A virus was isolated by means of successive inoculation of Chiba-strain chicken sarcoma virus on the brain of mouse or guinea pig[4]. When this virus is inoculated into the brain of mouse or guinea pig, they only develop slight meningitis in the brain, but there are a proliferation of mesenchymal cells and an infiltration of monocytes, lymphocytes and eosinophilic leukocytes in the liver, lung and spleen. The findings in the lung correspond with the histological picture of viral interalveolitis. Tumor never develops when this virus is inoculated on adult chicken. However, when repeated inoculations are conducted, response similar to the foregoing appears in the visceral organs and a strong immunity develops against the transplantation of chicken sarcoma. This virus has been named by HAMAZAKI NN chicken sarcoma virus (non neoplastic chicken sarcoma virus).

It is noteworthy that, when serial transplantation of this virus is performed on young chicken weighing 300—600 grams, some of the animals will die after developing hemorrhagic inflammation accompanied by necrosis of the liver, lung and spleen, but granuloma develops in the surviving chicken[5]. This granuloma appears scatteringly and is a nodular in shape. Histologically, degeneration and necrosis of the parenchymal cells, proliferation of spindle- and stellate mesenchymal cells, and infiltration of monocytes, lymphocytes, and some eosinophilic leucocytes can be observed (Fig. 1). In the tissue specimen, well demarcated necrotic foci of various sizes are seen around which the proliferation of mesenchymal cells is especially marked, being mixed with multinucleated giant cells. This finding resembles that of so-called sarcoidosis. It closely resembles the tumor which has been developed by BORGES and DURAN-REYNAULS on duck, when Rous virus changed by passing though pigeon has been inoculated into the duck. Mucus was observed in the granuloma by Muci-Carmin staining and from such tissue virus can be isolated by the same procedure mentioned above. Furthermore, by transplanting this granuloma on adult chicken a transplantable fibrosarcoma is obtained.

The majority of the virus dependent tumors cannot be produced at ease only by virus inoculation, because they require a second factor. This applies not only to HST virus[7] but also to Bittner virus and Gross virus. Non-neoplastic chicken sarcoma virus is a transformed strain which develops after Rous virus loses its second factor by successive inoculation on heterologous animals. By successive inoculation on young chicken, it must have reabsorbed its second factor to gain carcinogenesis.

2. Brown-Pearce cancer

Brown-Pearce cancer is a rabbit cancer reported by BROWN and PEARCE[8] in 1921. It has been diagnosed as basal cell cancer originating in the epidermis of the scrotum inoculated with syphilis spirocheta. The photographs in the author's original report has certainly indicated that it is cancer[8], but detailed histological studies by us (H. E., Mallory-, Giemsa-, RNA-staining, Silver impregnation, TPT reaction*) of the Brown-Pearce cancer imported to Japan from the United States in 1953 have revealed it to be carcinosarcoma[9]. Cancer cells are uniformly arranged, showing a beam shape, and sarcoma cells are diffusely proliferated among these to form composition tumor (Fig. 3) or sometimes cancer cells and sarcoma cells separately proliferate to form collision tumor (Fig. 2). It is interesting to note that if this tumor metastasized into the eyeball, it shows the picture of carcinoma simplex, but when transplanted to the testis of other rabbits it is transformed into carcinosarcoma.

*Triphenyl tetra-zoliumchloride reaction.

It has been often reported (EHRLICH-APOLANT[10], C. LEWIN[11], etc.) that cancer during serial transplantation transforms into carcinosarcoma and sometimes into sarcoma, but views are divided on the origin of sarcoma cells. Three possible origins of sarcoma cells are:

1. Metaplasia of cancer cells
2. Malignancy arising from the transplantation of the connective tissue of the stroma of the original tumor.
3. Development of sarcoma from the host mesenchymal cells *in loco* stimulated by transplantation of a carcinoma.

From the standpoint of existing information on histogenesis, the probability of (1) is weak. On the possibility of (2) it is usualy said that in the transplantation of tumor only the parenchymal cells are transplantable and the cells of the stroma die within a short time, while a new stroma is produced by the mesenchymal cells of the host. (3) In order to produce tumor by stimulation it is necessary to continue stimulation for more than several months, but in this case the transformation was completed within a short time.

By transplanting the metastasized tumor in the eyeball which is made up only of cancer cells into the testis of another rabbit, again we have been able to reproduce carcinosarcoma in the testis. Therefore, there is no doubt that in this case the part of the newly produced sarcoma tissue has originated from the host tissue.

3. MY sarcoma

This tumor spontaneously developed in So strain mice at the National Institute of Genetics in Mishima, Japan and it has been serially transplanted by YOSHIDA with the use of D103 strain mice[12].

Histological structure is not a sarcoma but a spindle cell cancer, which was decided by H. E. and Azan staining, silver impregnation, TPT reaction and electron microscopic examination conducted by OHMORI[13]. That is, the tumor cells in the metastasized foci in the lung sometimes construct a glandular-like structure and the formation of argentophil fiber was not noted in the parenchyma of the tumor (Fig. 4). Electron microscopically, the cell membrane is smooth and strong and between the cell membrane desmosome and septate desmosome can be demonstrated, elucidating it to be epithelial in origin (Fig. 5). In the case of the so-called MY sarcoma, no statement can be made whether it changed into cancer during serial transplantation or whether it was originally a cancer but was erroneously diagnosed as sarcoma, until careful examination is made on the original tumor. As YOSHIDA has reported that a histological picture resembling cancer was noted in part of the original tumor and as it is rare that sarcoma transforms into cancer, the original tumor perhaps must have been cancer. If this assumption is correct, it was not a morphological change but actually the

diagnosis was erroneous. Among those tumors considered in the past to be morphological changes, a case such as this may in rare instances be included.

4. Yoshida tumor

When young white rats are experimentally fed on fresh Yoshida tumor, no tumor develops in the digestive tract, but in about 26 per cent of the test animals reticulosarcoma develops in the liver, lung and spleen, moreover granulomatous sarcoma in the spleen (Fig. 9) and lung, also hepatoma develops in the liver with rare development of ependymoma from ependyma (Fig. 12). In a small number of cases malignant adenoma is seen in the kidney with the development of papilloepithelioma and/or clear celled tumor (WILLIS) in the epithelium of the mucous membrane of the pelvis (Fig. 11). When such papilloma develops, the animal dies before the tumor becomes enlarged due to the development of urination disturbance and purulent pyelonephritis brought about by ascending infection. Such cases are often (10%) seen in serial feeding of Yoshida tumor or tumor homogenate. In following the neoplastic change of the dura mater with the lapse of time[14], it was noted that hemorrhage at first developed around the blood vessels, nerves, and lymph spaces and thereafter an infiltration of monocytes and lymphocytes appeared. Next, proliferation of fibrocytes began from the peripheral area of the foci and as the proliferation advanced into the interior of the foci, inflammatory wandering cells gradually decreased and many young fibrocytes proliferated diffusely. By this time almost all of the inflammatory charateristics had disappeared and neoplastic characteristics appeared.

Anaplasia of the cells became conspicuous and it was especially noteworthy that the proliferated fibrocytes could suitabley be called as undifferentiated mesencymal cells with their arrangement disorganized to such an extent that they appeared like leaves scattered in the wind[14]. If they were non-neoplastic cells, even if their proliferation were so vigorous, they would never grow in complete disregard of the arrangement of normal cells at this position. This is due to the loss of "contact inhibition"[15] which regulates the arrangement and the position of non-neoplastic cells. This loss is considered to be characteristic of tumor cells. At this stage the cells might be already transformed into malignant cells, but the histological structure is not sufficient to establish a definite diagnosis. It is considered to resemble sarcoma, but no further detail could be determined. However, the tumor cells thereafter suddenly change to a star or spindle shape, showing a reticular or sometimes a sinusoid structure and thus the characteristics of reticulosarcoma could be evidently recognized (Fig. 7).

On the other hand, in pursuing the changes of the peritoneal serous cells with the lapse of time after transplanting Yoshida ascites tumor into the abdominal cavity of white rat, it was found that this cell enlarges and proliferates

in the process of cancerization[16]. In our observation with supravital staining with the use of neutral red, it was noted that normal peritomeal serous cells do not respond to supravital staining at all, but after 48 hours following tumor transplantation, this cell markedly enlarged and proliferated. Giant nucleolus appears in the large nucleus and the cytoplasm is deeply stained in red granular shape. As the cell body protrudes on the surface of the serous membrane, the tendency for detachment becomes apparent. HAMAZAKI named this the second tumor cell of Yoshida tumor. With complete detachment, the neutral red staining of the cytoplasm is lost and showing yellow-brown neutral red granule group (rosette) adjacent to the nucleus, they become typical Yoshida tumor ascites cells.

TSUTSUMI has recently pursued the foregoing changes through electron microphotography[17]. In the vertical sections of the normal omentum the serous cells appeared very thin with the cytoplasm connected in streaks, while the structure of the organellas could hardly be ascertained (Fig. 13). However, there was a peak-like protrusion of the cell body can be seen at the part of nuclear position. In the vertical section of the omentum 72 hours after the transplantation of Yoshida ascites tumor, the cell body reached a thickness of about 6.0 μ and the development of rough endoplasmic reticulum and Palade's granules was remarkable. The thickness of the nucleus reached 4.6 μ and the nucleolus was remarkable (Fig. 14). This corresponds to the period of the second tumor cell formation. Thereafter, the number of organellas decreased and the cytoplasma became clear, while the nucleus transformed to produce 2—3 deep inlets. These cells show neoplastic change definitely and it is noteworthy that at the contact parts between these cells desmosomes are observed, which demonstrate that these cells are of mesothelial origin (Figs. 15 and 16). In this early stage of cancerization TSUTSUMI has recently discovered virus particles which never appear in the later stage. (Details will be published in another article.) From the foregoing findings Yoshida tumor is a malignant coelothelioma from the standpoint of histogenesis, but as far as the purely morphological viewpoints are concerned, it might be called mesothelial sarcoma. In test feeding with this original tumor to young white rats, reticulosarcoma develops, but it is a strange phenomenon that in a few cases epithelial tumors (malignant adenoma, papilloma of pelvis and ependymoma) develop.

DISCUSSION

While making serial transplantation of breast cancer which developed spontaneously in male mice in 1914, WOGLONS[18] found this cancer to be transformed into sarcoma in 1919. This is mouse sarcoma 180 but subsequently this has also been called Crocker sarcoma. It is not clearly known whether the cancer cells

themselves became sarcomatous or whether the connective tissue of the stroma after transforming into sarcoma replaced with vigor the cancer cells.

In contradiction of the heretofore reported opinion where the author stressed that the cancer was replaced by sarcoma during serial transplantation, there is another theory, i. e. no relationship exists between the original tumor and the tumor developed by transplatation, but it is a tumor spontaneously developing at the transplanted site. However, it is quite evident that between the two a relationship does exist from the standpoint of both time and space. Many workers believe that the development of sarcoma following cancer transplantation is due to malignant effects arising from the stimulation given to the connective tissue of the stroma by cancer cells (APOLANT[19], etc.). Although it is considered rare for cancer to develop by the transplantation of sarcoma, the same explanation is provided as the cause. Connective tissue is liable to develop tumor by various stimulations. Not infrequently stroma cells do become malignant during serial transplantation of sarcoma, but a great difficulty is involved in its recognition.

According to APOLANT[19], cases of sarcoma transforming into cancer during serial transplantation are more frequent than reported in literature. However, when sarcoma and cancer are intermixed, it is said that the proliferation of sarcoma is as a rule more rapid, resulting compression atrophy of cancer. It appears that a logical solution is available to the question whether the origin of the mother cells for the new development of sarcoma is the stroma of the original tumor or the connective tissue of the host. In the transplantation of tumor, the grafting of stroma did not take hold and only the parenchymal cells were transplanted. Accompanying this proliferation, the stroma is produced by the connective tissue originating from the host and therefore the newly developed sarcoma must be of host origin. The most important problem is whether or not the development of transformed tumor subsequent to transplantation has any special relationship with carcinogenesis from the viewpoint of non-specific stimulation and sub-cellular inductor. It goes without saying that it is impossible to elucidate this phenomenon by the stimulation due to a foreign material alone and thus from the past, various theories postulating the existence of a special factor have, from time, to time been presented based on extensive observation and experience. Though this assumption is void of a satisfactory criterion, there is sufficient reason to accept it as a working hypothesis with subcellular inductor as basis. The weakness of the non-specific theory lies in the fact that latent period needed for the transformation of the grafted tumor is very short, because the development of cancer through irritation requires a long period of time. For example, with Benzpyren a latent period of at least 70 days is needed. In the case of tumor transplantation the animal usually dies within several weeks and

Table 1. Homologous Transplantation

	Original tumor	Newly developed tumor
Ehrlich-Apolant (1906)	Carcinoma (mouse)	Carcinosarcoma→Sarcoma
Sticker, E. (1906)	Sarcoma (dog)	Carcinoma
Flexner-Jobling (1907)	Pleomorphic cell sarcoma (rat)	Carc. simplex→Adenocarcinoma
Bashford, E. F. (1907)	Sarcoma (mouse)	Carcinoma
Russell (1910)	Carcinoma	Sarcoma
Bashford, E. F. (1911)	Adenocarcinoma mammae (mouse)	Sarcoma 37
Lewin, C. (1912)	Adenoma (rat)	Spindle cell sarcoma
Woglom (1918)	Breast cancer	Sarcoma 180 (Crocker)
Lubarsch (1919)	Sarcoma (guinea-pig)	Epithelioma
Fibiger & Bang (1920)	Tar-carcinosarcoma (mouse)	Spindle cell sarcoma
Lewin, C. (1928)	Sarcoma (rat)	Carcinoma
Andervont (1937)	Dibenzanthracene carcinoma (mouse)	Sarcoma
Ludford, R. J. & Barlow, H. (1945)	Breast cancer (mouse)	Sarcoma
Hamazaki, *et al.* (1953—1961)	Malignant coelothelioma (rat)	Reticulosarcoma, granulomatous sarcoma, malignant adenoma of kidney, papilloma of pelvis, ependymoma, hepatoma
〃	Basal cell carcinoma (rabbit)	Carcinosarcoma
〃	MY sarcoma (mouse)	Spindle cell carcinoma

Table 2. Heterologous Transplantation

	Original tumor	Newly developed tumor
Auler, H. (1927)	Breast cancer (human)	Endothelioma (rat)
Kritochewski, et al. (1929)	Melanoblastoma	Myxosarcoma (rat)
Purdy (1933)	Fujinami snrcoma emulsion	Duck cell sarcoma, in adult duck
〃	Rous virus No. 1	Tumor from original tumor cells, in young duck
〃	Fujinami sarcoma emulsion	Mixed tumor from both cells, in young duck
Duran-Reynauls (1950)	Rous virus of pigeon	Histiocytoma, lymphocytoma, leukosis, in duck, etc.
Sanford, *et al.* (1952)	Hepatoma (mouse) in tissue	Sarcoma by back transplantation to mice
Stewart (1957)	Culture, polyoma virus (parotid tumor)	Mice of different strains: salivary gland tumors, subcutaneous & kidney sarcomas, mammary carcinomas, skin tumors, osteosarcomas, etc. Hamster: sarcomas of kidney, skin, heart, intestine, etc. Rat: sarcomas of kidney & skin, hemangioma of liver

therefore this characteristic is highly evaluated. Here the latent period is short and does not exceed several days.

In the case of Rous sarcoma in which a filtrable factor has been demonstrated, a tumor with an identical histological structure can be produced when its cells are injected or when its virus is inoculated. As far as viral tumors are concerned, it is very rare that a transformed tumor can be produced by the transplantation of its cells. However, if the conditions of transplantation are remarkably changed, histological structure of the tumor is also changed.

By serial inoculation of Rous virus on pigeons, DURAN-REYNALS (1950)[1] successfully produced a different type of virus, which developed histiocytoma, lymphocytoma, leukemia, others if it inoculated on ducks. Thus reported, that it was no longer necessary to consider the existence of virus specific to each cancer. With reference to this assumption, further definitive experimental evidence was added with the discovery in the later years of polyoma (Table 2). The results of our feeding tests with Yoshida tumor reported in this paper have also suggested that many types of tumors can be produced by a single factor. It was in 1943 when the Yoshida tumor was discovered[20], but in spite of the 19 years of serial transplantation of its cells no transformed tumor could be produced. By transplanting the emulsion of Fujinami sarcoma on mature duck, causing a proliferation of duck cells, PURDY (1933)[21] experimentally produced a sarcoma. When the emulsion of No. 1 Rous sarcoma is inoculated on young ducks, the transplanted tumor cells proliferate to form sarcoma. Moreover, when the emulsion of Fujinami sarcoma is transplanted on young ducks, a tumor is produced by the host cells as well as by the transplanted tumor cells.

The question whether the transformation of tumor during serial transplantation is due to metaplasia of transplanted tumor cells or not still remains unclarified. At present there is no firm evidence to either confirm or deny this question. Nonetheless, the existence of direct metaplasia is generally doubted and inasmuch as indirect metaplasia requires a considerable length of time, it does not conform with the existing situation. Since it has been recognized that the cancer as well as sarcoma arising from transformation respond completely differently to staining and that there is a great difference in resistance to cold between cancer tissue and sarcoma tissue, the question involved between the two is more than that of morphological transition (J. KLINKE)[22].

It is exceptional that a successful heterologous transplantation of tumor can be made. When heterologous transplantation is successful without prior treatment with cortisone, it should be considered that a tumor was newly developed by the transplantation of a sub-cellular inductor and not in fact by cell transplantation. This is because heterologous transplantation of cells is impossible. For example, MOTOLSCY achieved a 100 % success in heterologous transplantation in his experi-

ment with Ehrlich Putnokey tumor on Brazilian black rat. As a black pigment was discovered in the tumor cells of the new host, it is evident that this cell originates from the host cell[28].

SUMMARY

1. When chicken sarcoma virus is serially inoculated on the mouse brain, it loses its carcinogenecity, but when it is inoculated on young chicken, granuloma develops in the liver and lung. When this granuloma is transplanted on adult chicken, a transplantable fibrosarcoma is obtained.

2. According to literature, the original tumor of the Brown-Pearce cancer is a basal cell cancer, but that imported to Japan in 1953 presented a histological picture of carcinosarcoma. The metastasized tumor of the eye presents a purely cancer tissue, but when this is inoculated on the testis, carcinosarcoma is reproduced. It is therefore considered that the mother cell of the sarcoma is of host origin.

3. MY sarcoma is not a sarcoma, but is a spindle cell cancer. It might be a sarcoma which transformed into a cancer during serial transplantation, but perhaps it was originally a cancer but had been erroneously diagnosed as sarcoma.

4. The tumors we obtained by means of the feeding tests of Yoshida tumor all developed at organs other than those of the digestive tract. They are chiefly reticulo-sarcoma, but others which develop are malignant granuloma in the liver and lung, malignant adenoma in the kidney, papilloma of pelvis, and ependymoma in the cerebral ventricle. Since the discovery of the Yoshida tumor in 1943, serial transplantation has been conducted for 19 years with this tumor not only in Japan but also in foreign countries, but there has been no report to this date that a transformed strain has developed by cell transplantation. It therefore must be considered that the carcinogenesis observed in our feeding tests is a carcinogenesis due to a mechanism completely unlike that of cell transplantation. It has been confirmed by electron microscopy that in the early stage of transplantation of this tumor into the abdominal cavity there was an additional tumor growth due to the anaplastic proliferation of serous cells.

5. During the serial transplantation of viral tumors and/or virus dependent tumors, the tumor sometimes undergoes a morphological change. Though the cause of this is not yet sufficiently elucidated, it is suspected that there is some relationship with virus in the wide sense.

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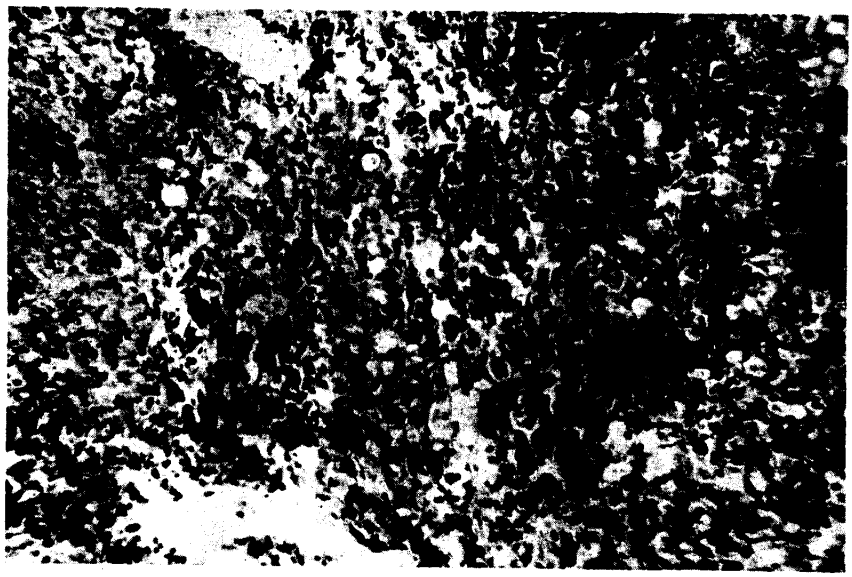

Fig. 1. Chicken sarcoma: Necrotising granulomatous focus of liver in chicken. Atrophic degenerating liver cells (a) and giant cells (b) are demonstrated.

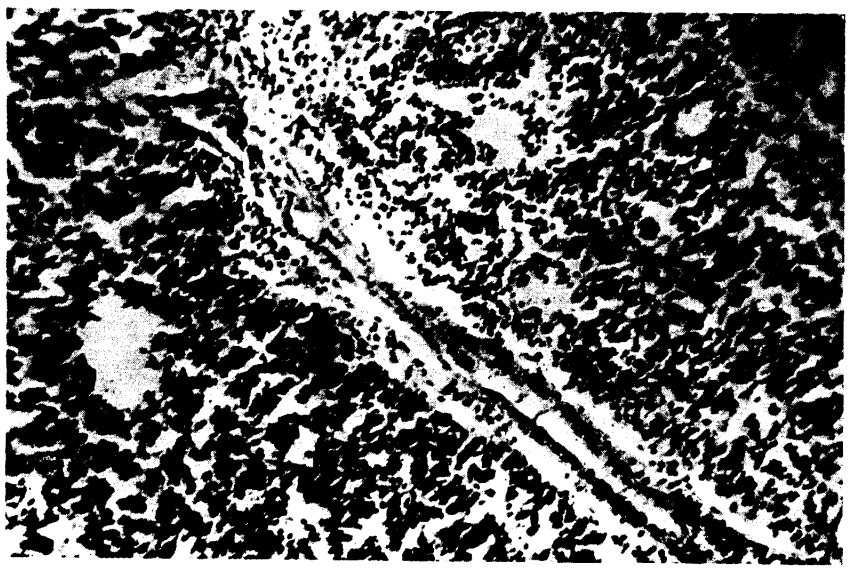

Fig. 2. Brown-Pearce carcinoma grown in type of "collision tumor". In lower left side there is a carcinoma simplex and in upper right side a round cell sarcoma. The border line between the two sides consisted of fibrous membrane.

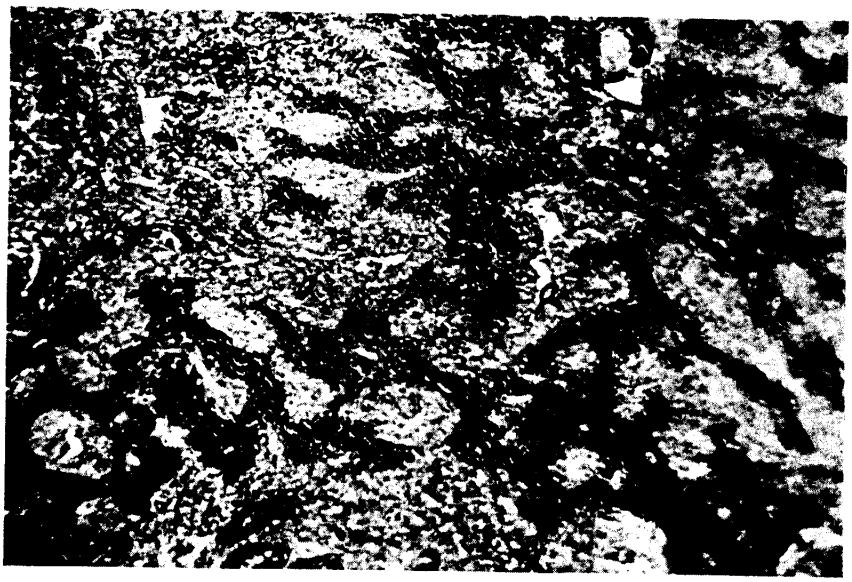

Fig. 3. Brown-Pearce carcinoma: Same tumor grown in type of "composition tumor". Mallory's stain. (a) Carcinoma tissue forming trabecular cell masses colored in brown red. (b) Sarcoma tissue constructing stroma of the tumor, stained dark blue in color.

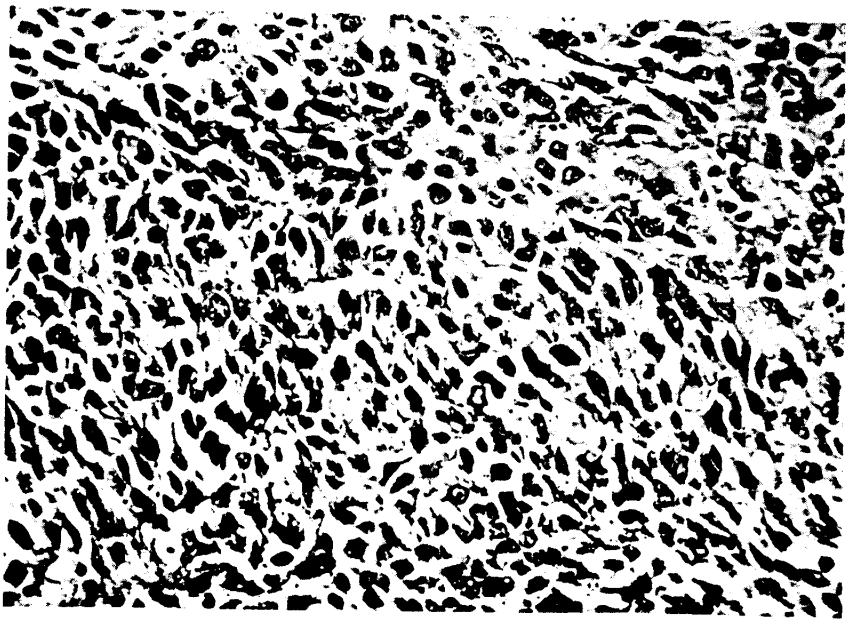

Fig. 4. MY sarcoma: Pap's silver impregnation. There is no clearcut- argyrophil fiber.

Fig. 5. MY sarcoma: Electron microscopic picture of the border line between two tumor cells. The cell membrane demonstrates desmosome as well as septate desmosome. × 7500

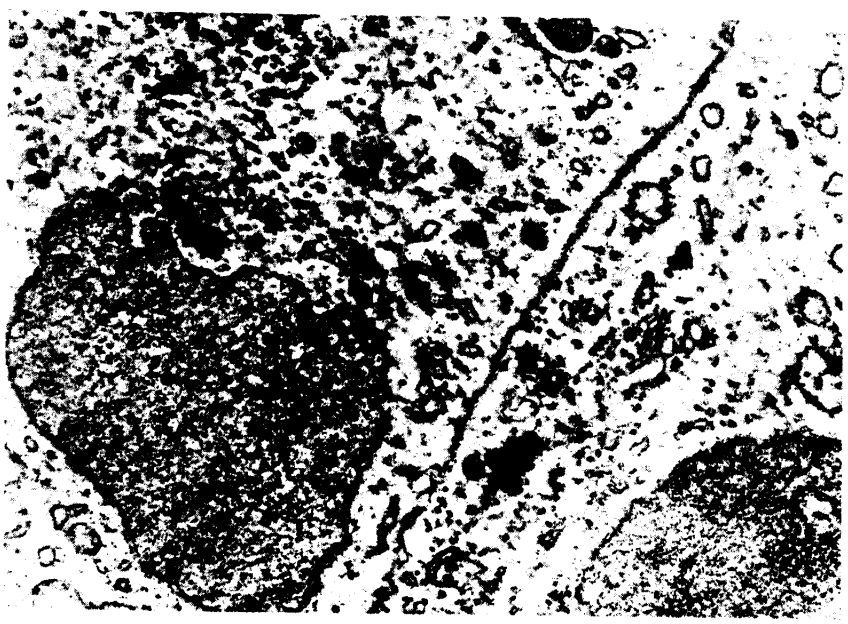

Fig. 6. MY sarcoma: Two tumor cells showing Golgi's field and centrioles. ×1300

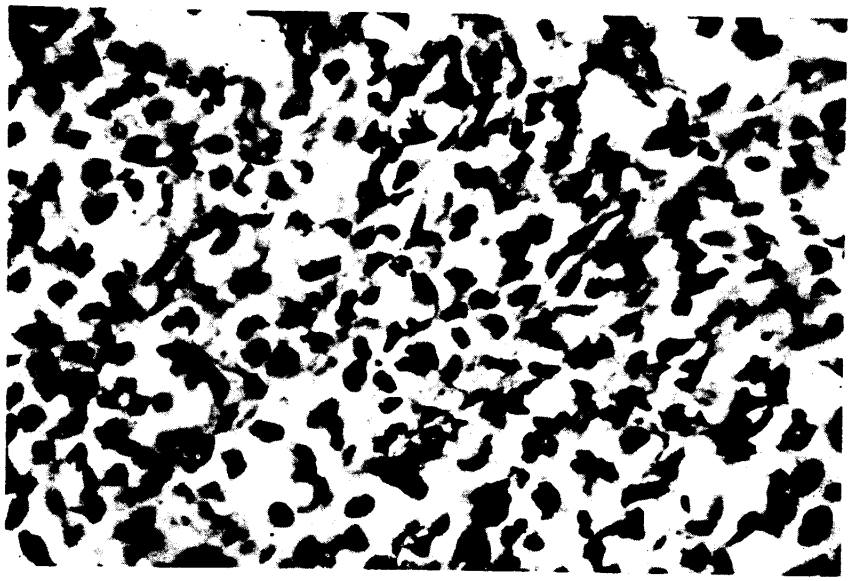

Fig. 7. Yoshida tumor: Reticulosarcoma of skull base induced by Yoshida tumor feeding.

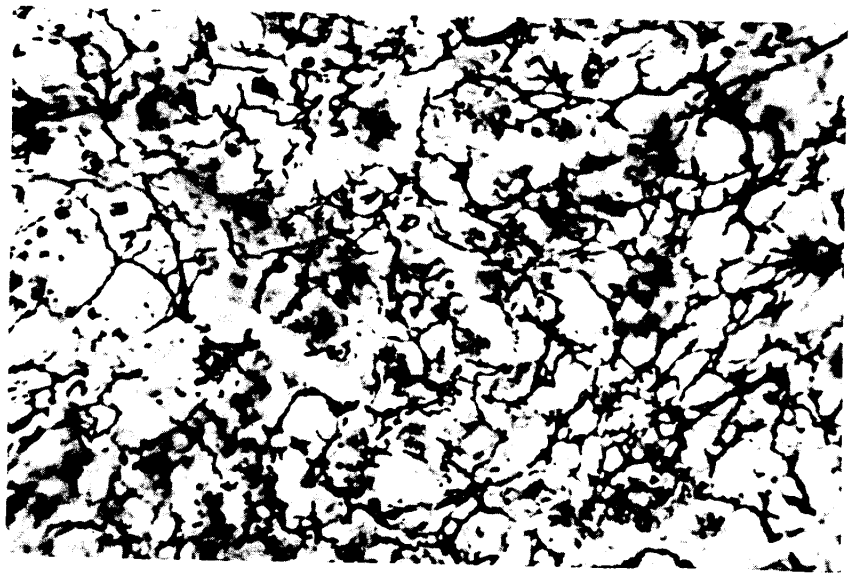

Fig. 8. Same specimen treated with Pap's silver impregnation.

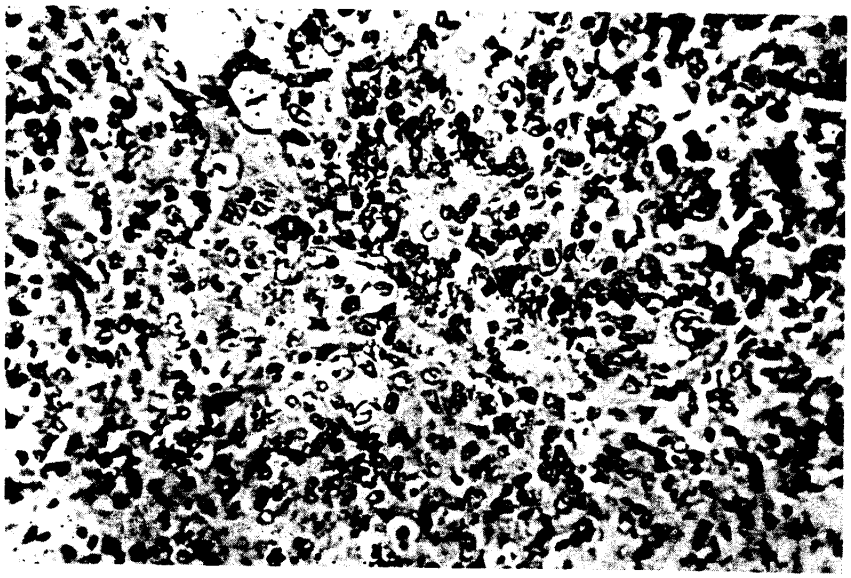

Fig. 9. Granulomatous sarcoma of spleen of rat. Tumor tissue consists of pleomorphic undifferentiated mesenchymal cells. Large nulear inclusion bodies (a, a') can be seen.

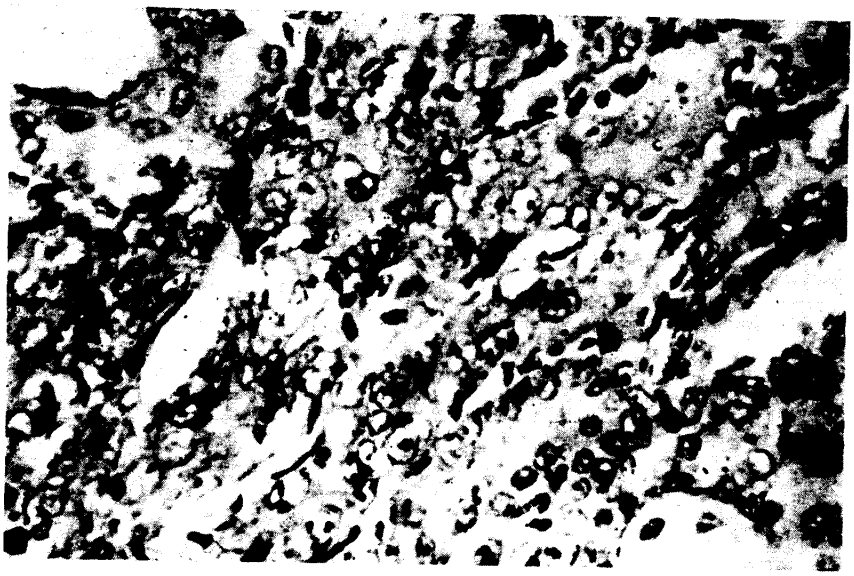

Fig. 10. Malignant adenoma of kidney. Epithelial cells of the convoluted ducts proliferated anaplastically demonstrating large and small nuclei which are piled up in epithelial layers.

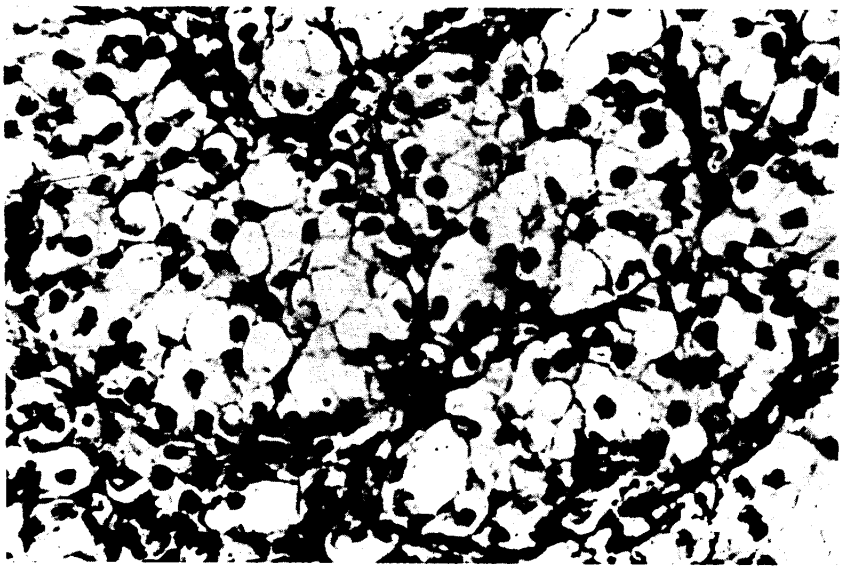

Fig. 11. Clear-celled tumor derived from the epithelial cells of pelvis by Yoshida tumor feeding.

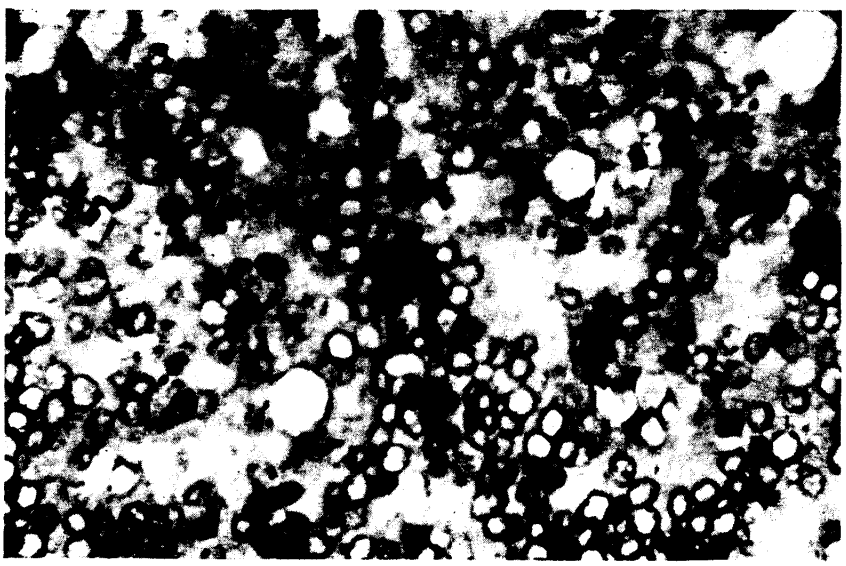

Fig. 12. Ependymoma developed in the lateral ventricle of brain by the feeding tests. The nuclei of tumor cells are as clear as vesicles.

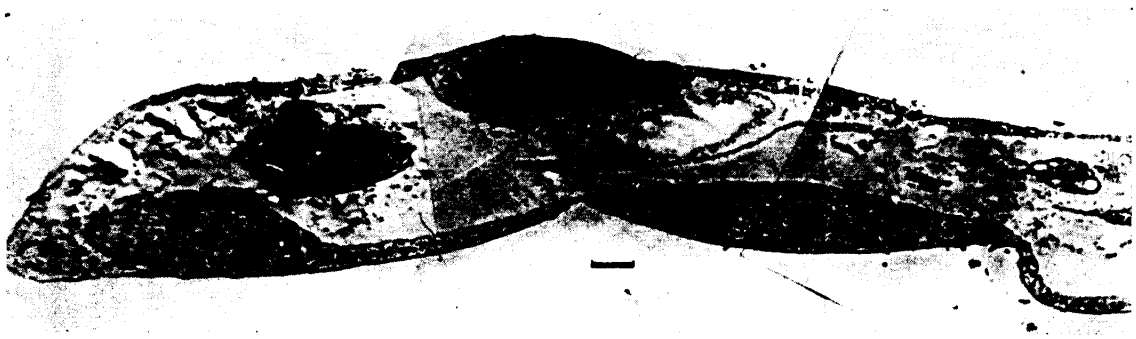

Fig. 13. Photo by electron microscope. Vertical section of omentum of normal rat. ×5500

Fig. 14. Vertical section of the omentum 72 hrs after intraperitoneal grafting with Yoshida ascites tumor in rat. Serous cells swelled enormously showing numerous organellas and giant nuclei with big nucleoli. ×3300

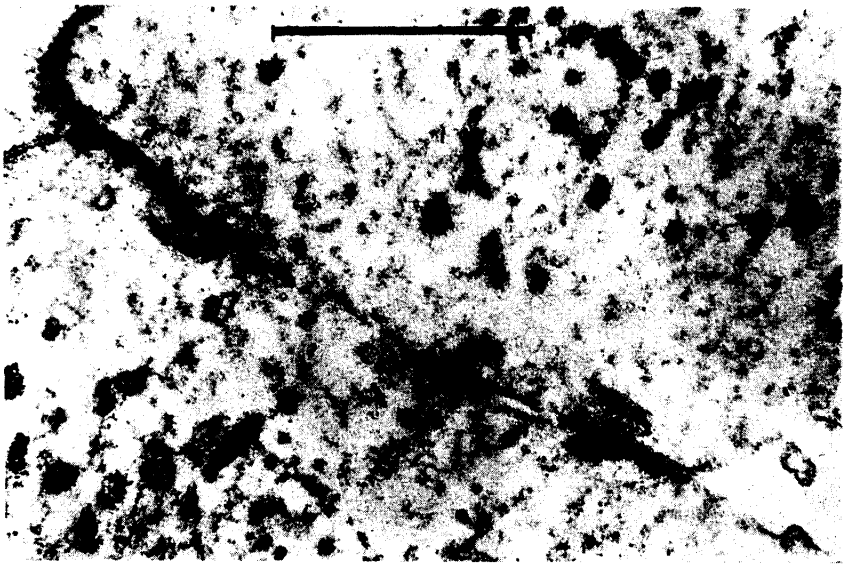

Fig 15. Same section. Rarefaction of orgenellae and polymorphy of nuclei indicate neoplastic change of serous cells. ×5500

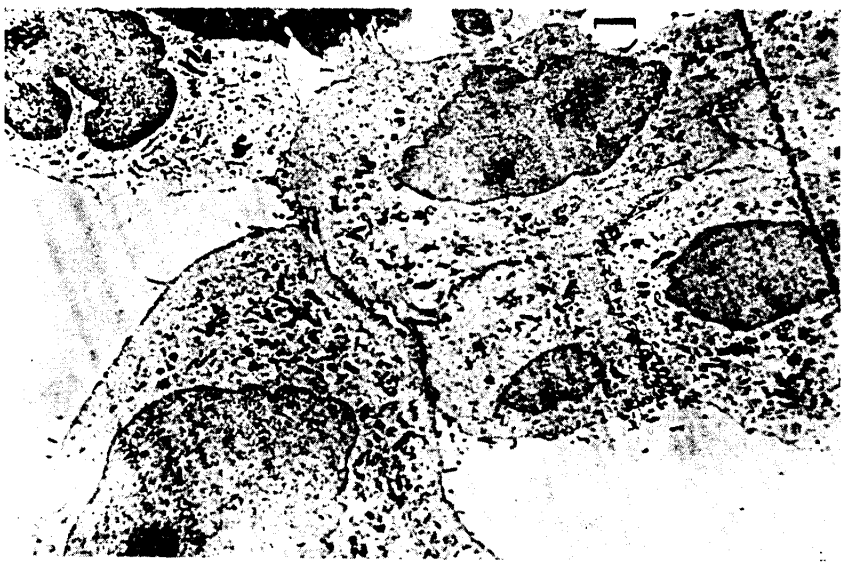

Fig. 16. Same section. Desmosome between the neoplastic cells suggesting their origin from mesothelial cells. ×33500