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ROENTGEN SENSITIVITY OF CEREBRAL TUMOURS AND SO-CALLED LATE IRRADIATION NECROSIS OF THE BRAIN

by

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The effects of ionizing irradiation on the glioblastoma multiforme concern the changes in the tumour itself and the possibility of damage to the surrounding brain tissue. The question arises as to whether an effect is brought about through prevention of growth of individual cells or by necrosis of the whole tissue, perhaps as a result of interference with the blood supply. The mechanism of this irradiation effect may be caused by a disturbance of the barrier, with exudation of certain substances from the vessels. These may either directly (dysorie of Schurmann), or indirectly through an allergic process, destroy the tissue. Hypoxia of the tissue, on the other hand, may be produced by the exudation of an albuminous substance; this is particularly the case in connection with radiation damage of the normal brain and spinal cord.

We feel there is some justification for assuming that the ideal effect of irradiation, namely the destruction of growing tumour cells, occurs only in two neuroepithelial tumours: the medulloblastoma and pinealoma. The possibility of a cure of such tumours by irradiation, in spite of the usual diffuse spread of metastases to the sub-arachnoid spaces, will be discussed.

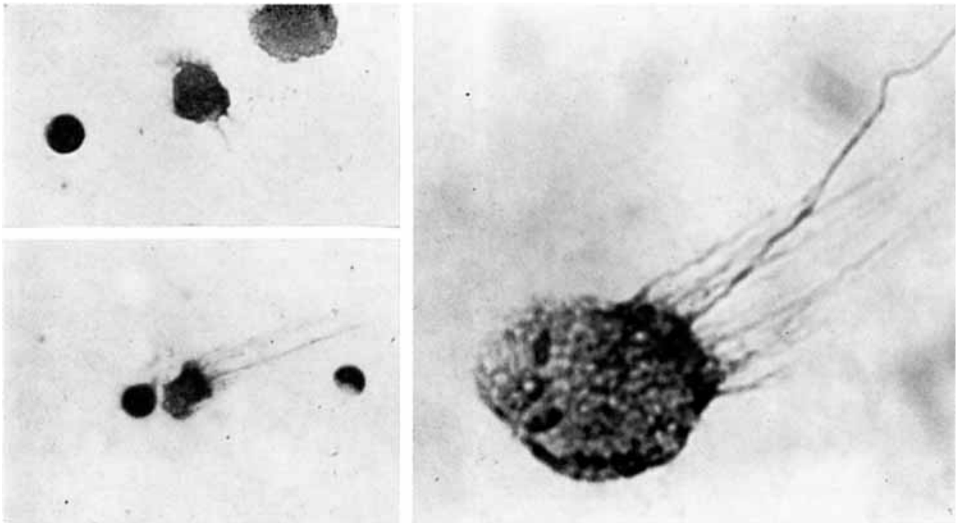

Fig. 1. Cells in the cerebrospinal fluid, typical of pineal parenchyma (cf. Del Rio Hortega), showing the nature of the blastoma. ×500 and 1250, respectively.

The irradiation effects upon the more important types of intracranial neoplasms will first be considered, with emphasis upon the treatment of the glioblastoma multiforme.

Gangliocytoma. We have had no experience with irradiation of this tumour of the brain and know of no convincing report in the literature.

Oligodendrocytoma and astrocytoma. We have had one case of oligodendroglioma which was followed for eight years. Neither of the operation specimens revealed evidence of definite radiation effects on the cells or vessels. An irradiation effect cannot be deduced with certainty from the 8-year survival, as similar biologic behaviour after re-operation on an oligodendroglioma has often occurred. The total irradiation dose in this case was 16 000 rad.

In another case of oligodendroglioma (8 000 rad to the temporal region) a severe radiation effect on the temporal white matter with cystic changes in the latter were observed. This led to marked internal decompression. The tumour, about 5 cm in diameter, persisted, and its cells were unchanged (Zülch 1956, Fig. 94).

In a further case, a man, aged 52, with a fronto-medial oligodendroglioma, four series of irradiations to 5 fields were given, each series lasting about 4

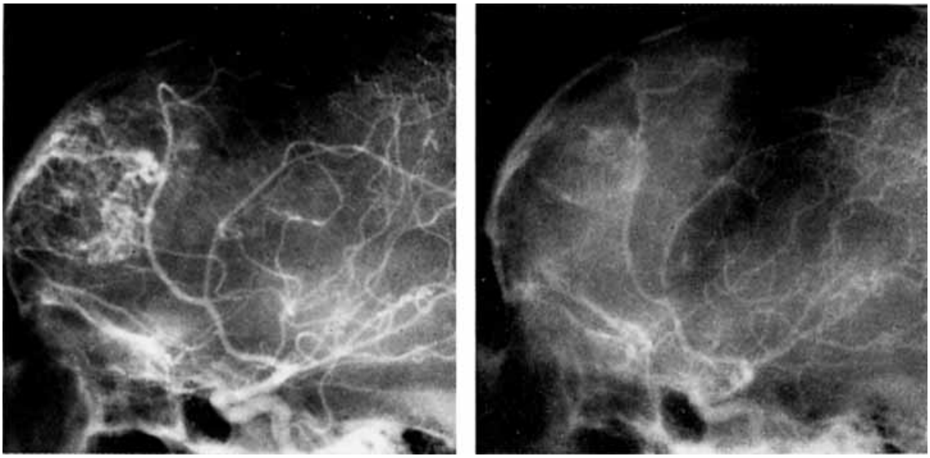

Fig. 2. Two angiograms of a midfrontal metastasis of a mammary carcinoma, the second taken after irradiation with 9 200 rad over two frontal fields.

to 5 weeks, with a total of 30 000 rad. The patient survived for 5 years and 3 months from the beginning of the first treatment. At autopsy, the tumour lay over a wide area of the cortex. Mild demyelination was present in part of the white matter. This could not be definitely attributed to the irradiation because peritumoral oedema may also produce this change. Careful examination of the specimen revealed no deviation from the normal appearances of an oligodendroglioma.

Finally, we may refer to a case reported in the literature (EICKE 1952), which after a total irradiation of 23 200 rad developed gross late necrosis of the white matter. The tumour remained about 3 cm in size and only in the crossfire of the different fields was there acute tissue necrosis with scarring. This agrees with the universal results reported in the recent monography of BOUCHARD (1966). Oligodendrogliomas must therefore, like astrocytomas, be regarded as relatively radiation-insensitive tumours.

Consideration of the astrocytomas will be omitted from this communication (see Zülch 1963).

Polar spongioblastoma. A young boy, aged 15, with a polar spongioblastoma of the posterior part of the third ventricle with extension into the mid-brain, was given 4 600 rad to 5 fields over 3 months. The number of sessions is unknown. The spongioblastoma by the presence of several mitoses was recognized as being of a polymorphous, rapidly growing type. There were no signs of an irradiation effect, while the surrounding brain tissue clearly indicated commencing late ir-

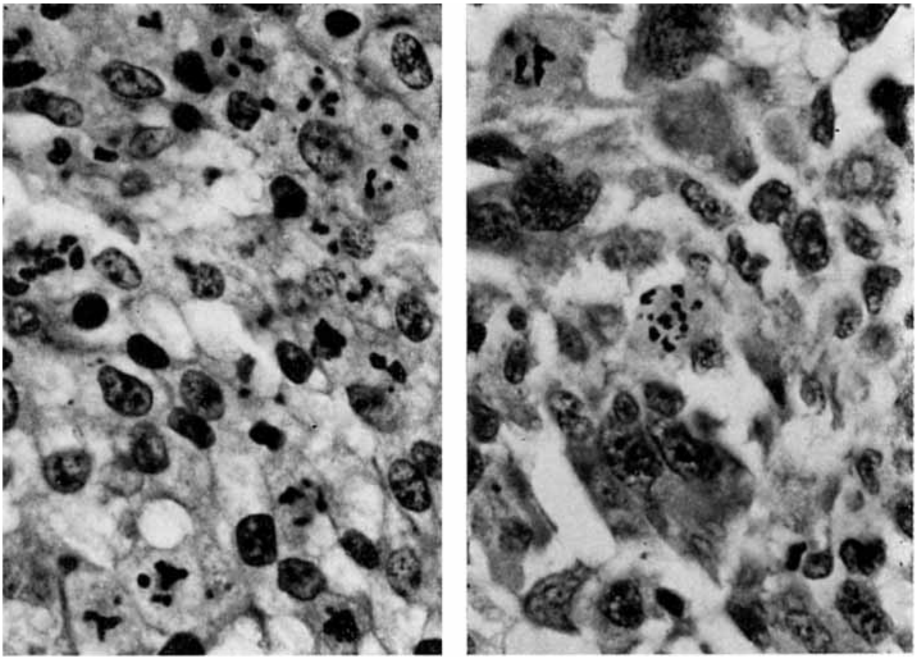

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Fig. 3. a) Glioblastoma. Enormous number of often very atypical mitoses. b) Fibrosarcoma, 9 years after irradiation, probably around 8 000 rad over one parietal field after excision of an extraventricular ependymoma. × 100.

radiation necrosis. The total survival period after the irradiation was seven and a half months.

Gross focal late irradiation necrosis was observed in a second case of spongioblastoma of the pons, but the margins of the tumour had continued to grow.

No indication appears to exist for irradiation of the polar spongioblastoma (according to our definition), i.e. the juvenile pilocytic astrocytoma of Dorothy Russell (Russell & Rubinstein 1963). This is in accordance with the experience of Bouchard. This author refers to the 'glioma of the fasciculus opticus', closely related to the above mentioned piloid astrocytoma, whereby again obviously the polar spongioblastoma is meant. These tumours have a very slow growth, a fact that must be remembered when irradiation effects on such tumours are considered. Bucy (1946) reported a case of a so-called astrocytoma of the cerebellum, a spongioblastoma in which a cyst was emptied, which was followed for 12 years, with remission of the symptoms. After this a massive residual tumour was visible which again was operated upon, and again there was prolonged

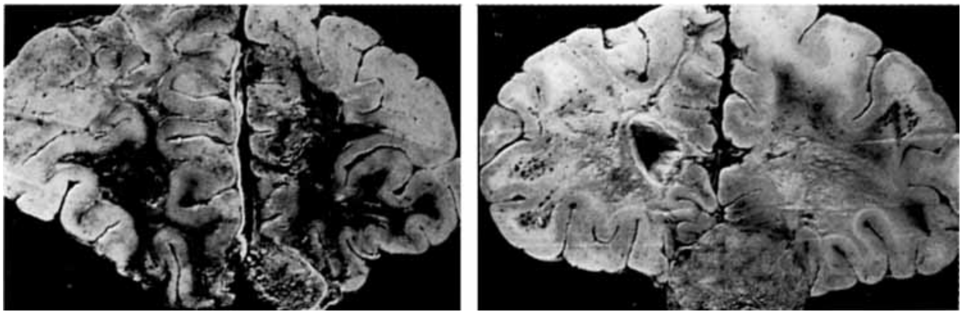

Fig. 4. Complete destruction of the white matter of both frontal lobes in an olfactory groove meningioma in a patient, aged 50 years, having received irradiation with 9 000 rad in 2 series with an interval of one month. (Death occurred 5 years later from intercurrent disease.)

healing. In view of the markedly slow and favourable growth of this type of tumour it is difficult to analyse statistically the irradiation effect. If these tumours are operated upon it will only be in instances of unfavourable site, admittedly frequent, such as when a short-circuit (shunt) has to be performed. Irradiation is indicated only in the presence of obstruction of the cerebrospinal fluid.

Medulloblastoma. Frequent reports have appeared in recent years of a very good effect of irradiation upon medulloblastoma. RICHMOND (1953), for example, in 43 % of his series of children with medulloblastoma, after irradiation obtained a survival period of 5 years. KAHN (1955), whose cases the present author himself examined histologically, had a 15-year survival. Most of the remaining reports do not include such a successful irradiation effect even when combined with operation. This is confirmed by BOUCHARD in his survey. The detailed description of LINDGREN (1958) must be recognized as the first report on the necrosis of the tumour tissue. Most of his success was obtained at the expense of damage of both occipital lobes (late irradiation necrosis), which can now be avoided with an appropriate technique.

Pinealoma. HORRAX & WYATT (1947) have reported on the good results with conventional roentgen irradiation.

The present author can report a case of dramatic improvement as a temporary effect in one of our cases. This was an 8-year-old girl with a very small pinealoma and a large metastasis in the infundibular region (so-called ectopic pinealoma), demonstrated by pneumography as being 3 cm in size. There was a gross diencephalic and endocrine as well as optical and ocular syndrome. The subarachnoid space was not obstructed. The pinealoma could be diagnosed with

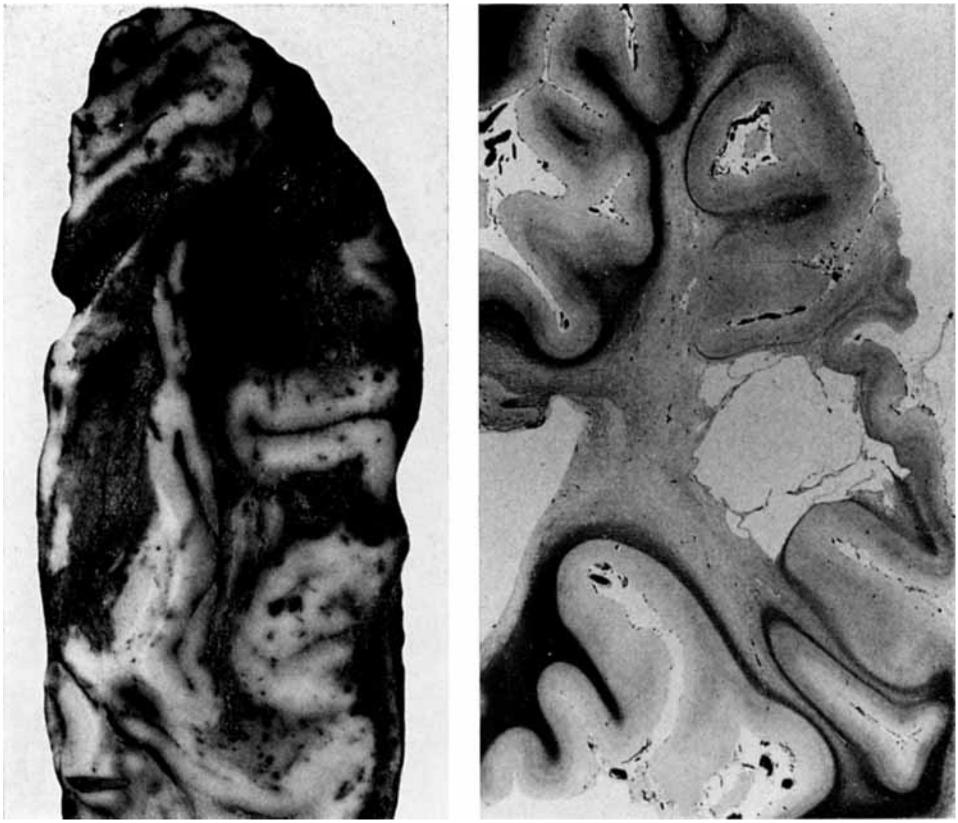

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Fig. 5. a) A 200 g specimen of a 'growing' late radionecrosis (operation for parietal 'recurrence'). b) Case of delayed radionecrosis. Demyelination with preservation of the U-fibers; formation of a great cystic necrosis in the center. Heidenhain-Wölkes myelin stain.

certainty by the shape of the cells in the cerebrospinal fluid (Fig. 1). The child was cachectic (weighed 12.7 kg) and had to be artificially fed. She was irradiated through 4 fields with 9 000 rad over 6 weeks. There was good recovery and the hypothalamic and midbrain symptoms as well as those due to the ocular muscle paralysis disappeared. The child could as a result go to school and was active for a long time as a completely healthy individual. She survived altogether 5 years. Because of recurrences, a total dose of 23 500 rad through 4 fields to the chiasma region had to be given. The child finally died with severe cerebellar signs, an increasing tetraparetic syndrome and, towards the end, a quadrigeminal syndrome (Zülch 1963, Figs 1—3).

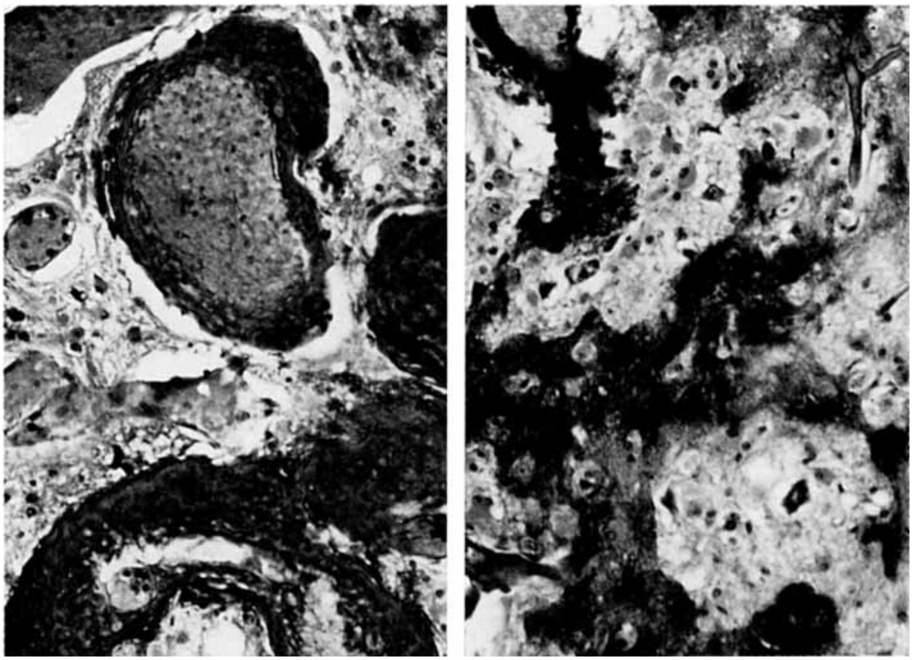

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Fig. 6. a) 'Para-amyloid' transudation around great veins in delayed radionecrosis. b) Diffuse spreading of the 'para-amyloid' substance into the brain tissue. ×120.

This final phase may be related to the growth of the primary pinealoma in the mid-brain, which was not irradiated, rather than to an irradiation effect on the brain during the irradiation of the ectopic metastasis. Repeat encephalography 2 years and 3 months after the first irradiation disclosed that the metastasis in the chiasma region had disappeared. The base of the anterior horn and the third ventricle were completely free from indentation. Further encephalography shortly before death was prohibited by the parents. Autopsy was not possible. The anisomorphic pinealoma should therefore also be irradiated with modern techniques.

Ependymoma. Only a slight irradiation effect has been observed in these growths. Para-amyloid substance, but scarcely any change in the tumour tissue, was seen in one case. In another case there was a certain degree of sclerosis but this could not be definitely classified as an irradiation effect.

Glioblastoma multiforme. The irradiation effect on the glioblastoma multiforme forms the focal point of this communication.

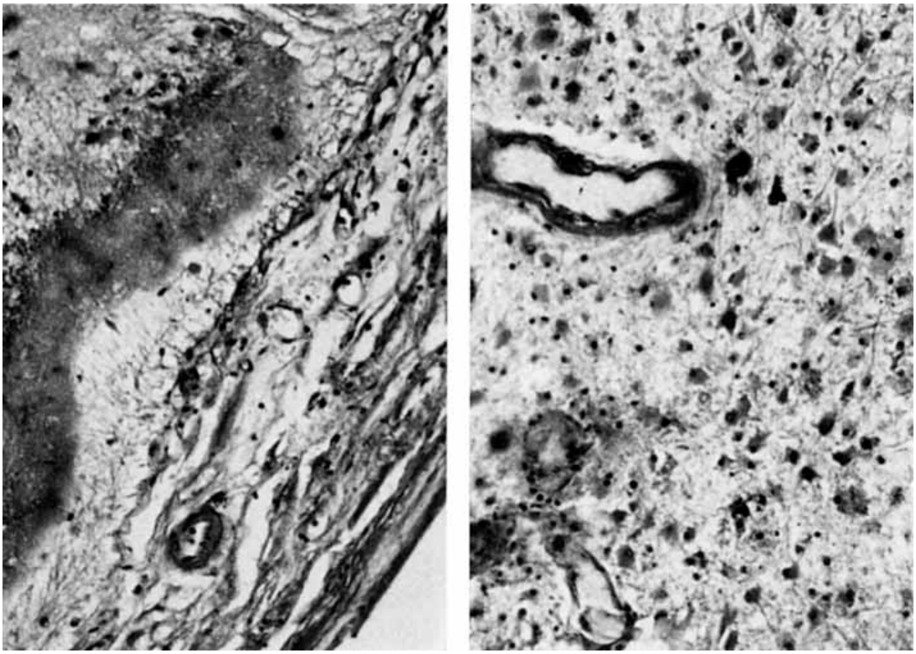

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Fig. 7. a) Para-amyloid zone bordering the upper layers of the cortex towards the leptomeninges. b) Proliferation of fibrillary astrocytes, partly of a pleomorphic character, in a demyelinated zone of radionecrosis. ×120.

An early effect was noted in a 55-year-old patient with an angiographically proved right temporo-occipital tumour who was given an irradiation series of 1 600 rad over 9 days. The patient died with raised cerebrospinal fluid pressure. Inside the tumour and vessels lay para-amyloid exudations, readily distinguishable from other vascular changes in glioblastomas. The necroses that were present could certainly not be interpreted as an irradiation effect because they belong to the morphologic ensemble of the glioblastoma. The survival period, as well as the irradiation dosage, was probably too small to have produced such an effect.

Another patient, aged 59, with a glioblastoma multiforme of the temporal pole, was irradiated with 6 700 rad to 2 fields over 21 days. The patient died 42 days later. At autopsy, early para-amyloid deposits were seen in the vessels. Amoeboid glia, e.g. around the capillaries, represent early changes that may also be seen in the transudation zone of the para-amyloid material.

A third patient, aged 56, with a right temporo-medial glioblastoma multiforme received 10 600 rad to 6 fields over 31 days. At autopsy, 16 days following

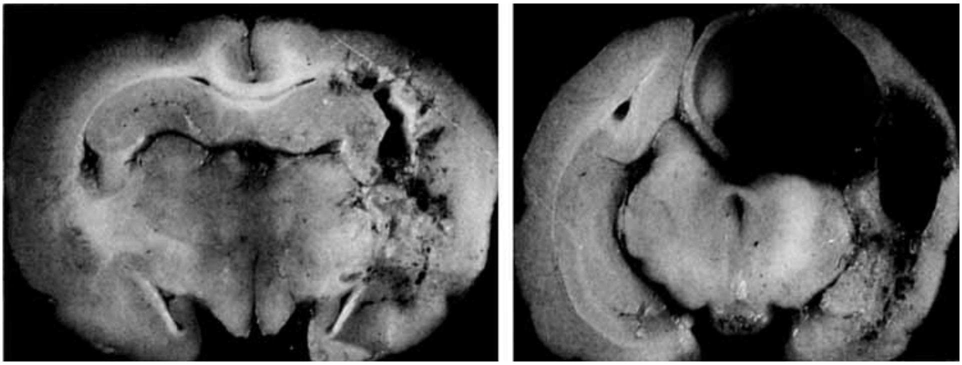

Fig. 8. Experimental radionecrosis in a rabbit, 10 months after a single-dose irradiation with 3 000 rad conventional roentgen rays. a) Radionecrosis and formation of cyst. b) Space-occupying cyst.

the treatment, massive necrosis in the interior of the tumour, a possible irradiation effect, was evident. The surrounding brain showed no deviation from the normal; no change in the tumour cells could be recognized. The irradiation effect was in this case uncertain.

Finally, in a patient with a left fronto-basal glioblastoma, cortical necrosis occurred 14 days after an operation in which radiocobalt pearls were placed in the wound cavity for 24 hours (cf. KLAR et coll. 1954). These had not destroyed all parts of the tumour; there was transudation of material similar to the para-amyloid substance in late irradiation necrosis. No comparable case has so far been encountered.

In summary, the earliest irradiation effects occurred 31 days after irradiation with 10 600 rad to 6 fields. This, however, is not quite definite, because gross central necrosis is not rare in glioblastomas, and because no change was noticeable in the tumour cells. Perhaps, and the para-amyloid extravasation present in two further cases speak for this, a change in the vessel wall may have actually taken place, e.g. an increased tendency to spontaneous thrombosis. This is the principal irradiation effect in glioblastoma. An effect on the cells, such as has definitely been demonstrated in the pinealoma, were not present in the glioblastomas.

The results are in agreement with those reviewed by BOUCHARD though it cannot be denied that in individual cases a prolongation of life may occasionally be obtained. The object must be to necrose the glioblastoma massively but obtain relative preservation of the surrounding cerebral tissue. How far this is possible technically is open to discussion. The problem by irradiation is to determine the quantity of irradiation to be given: whether to give a dose sufficient for com-

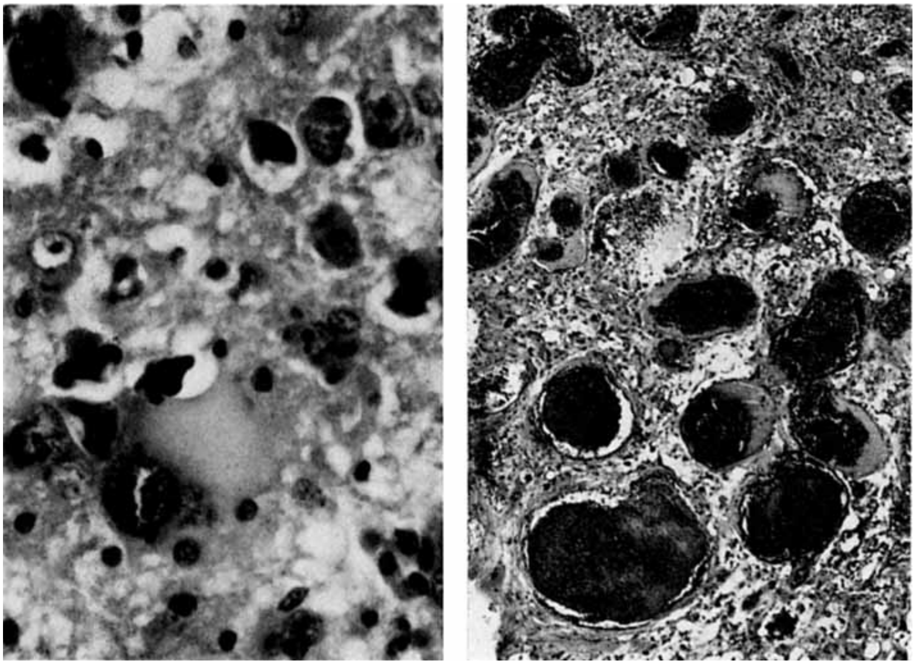

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Fig. 9. a) Multinucleated and giant astrocytes in experimental radionecrosis. ×500. b) Angioma-like proliferation of new vessels in experimental radionecrosis. ×50.

pletely destroying the tumour and run the risk of late necrosis occurring in adjacent cerebral tissue, or to give a lower dose, in which case there will be less damage to cerebral tissue but the tumour may not be completely destroyed.

Metastases. Extensive experience of the irradiation of metastases and follow-up of the degeneration of the vascular structures angiographically have led us to believe that the irradiation effect was produced by thrombosis which caused massive necrosis. Small malignant foci often escaped notice, however. The danger of increased malignancy will be discussed later (Fig. 2).

Extracranial tumours: meningioma and neurinoma. Scarcely any indication for the irradiation of these tumours exists. A case in which because of war conditions irradiation was carried out conventionally, probably with 9 000 rad over one month in 2 series, concerned an olfactory groove meningioma; the irradiation was obviously given with a bilateral fronto-temporal approach. The tumour was practically unchanged although perhaps a little more hyalinised than usual. On the other hand, the entire frontal region (ZÜLCH 1960) was destroyed by bilateral irradiation necrosis, the myelin sheaths were lost, and the tissue had been changed into a cystic gelatinous mass. This resulted in an increased intracranial space due to marked internal decompression. The patient developed a parallergic reaction suggesting encephalitis. He passed into status epilepticus with a fatal outcome (Fig. 4).

Malignant mesodermal tumours. We could follow a patient, aged 52, with a monstrocellular sarcoma in the left parietal region, who received in three irradiation series a total of 22 400 rad, made up of 3 700 over 15 days, followed 14 days later by 11 400 rad over 27 days, and finally 3 years and 4 months later 7 000 rad over 25 days. The operation specimen 8 days after the last irradiation and 4 years and 3 months after the beginning of the first irradiation disclosed an obvious necrotizing effect. An actual and statistically favourable irradiation effect had been obtained.

A post-operative survival as long as two and a half years has been encountered in an exceptional case of a small sarcoma which was completely removed at operation. These tumours usually possess the same malignancy as the glioblastoma multiforme.

Of the remaining sarcomas the reticulo-sarcoma of the brain and the spinal epidural space are particularly irradiation-sensitive (BINGAS & ZÜLCH 1964).

Undesirable effects of ionizing irradiation: increased malignancy

Foci of increased malignancy with a higher number of mitoses than previously encountered in any other human tumour were observed in the vicinity of large necroses in two irradiated glioblastomas (Fig. 3a). The number of mitoses was practically the same as that of the cells (ZÜLCH 1960). It would appear that this was due to an increase in the rate of growth, similar to that reported by NETSKY (1956) in the irradiation of cell cultures. This author reported a depression of growth, later followed by so-called biphasic growth with a speeding up; the original slower rate of growth was thus again achieved and later exceeded.

A similar experience dates from before the Second World War, and came from Tönnis's Clinic in Berlin where prolonged survival was attempted by the introduction of radium needles (LORENZ 1949). It was perhaps scarcely a coincidence that in both these two cases the tumour growth was speeded up to a degree not previously encountered. Within six months, gigantic recurrences, almost the size of a fist, were removed six times by operation (ZÜLCH 1940).

Development of irradiation cancer

A young female, aged about 14 years, had an ependymoma of the cerebral hemisphere which was radically removed. Six years later a true fibrosarcoma occurred in the ring scar of the dural flap and led to death (ZÜLCH 1952). Late irradiation necrosis was evident deep down in the brain substance but there was no trace of the primary ependymoma. The irradiation was conventional and had involved up to 8 000 rad (LORENZ) without any unusual features (Fig. 3b).

Cases of NÖTZLI & MALAMUD (1962), MANN et coll. (1953), RUSSELL & RUBINSTEIN (1963), and TERRY et coll. (1959), as well as a case of WENDE (1962) appear in the literature. It is interesting that the tumours were always fibrosarcomas, which histologically are similar or identical. BERG & LINDGREN (1958), in their experimental work with irradiation of normal rabbits, have observed osteosarcomas developing in the region treated.

Indications for irradiation based on morphologic experience

1. Medulloblastoma and pinealoma: cells can definitely be killed.
2. Metastases: thrombosis of the neoplastic vessels can be produced and necrosis thus be obtained. The effect under (1), i.e. destruction of tumour cells, may also apply.
3. Similar considerations apply to the sarcomas and especially the reticulosarcoma which appears to have cells that are particularly sensitive.
4. A relative indication is the irradiation of a glioblastoma where the type of effect and the results have not yet been fully reviewed.

Irradiation of the polar spongioblastoma, ependymoma, astrocytoma and oligodendroglioma is not recommended; operation only, and, in cases of recurrence, re-operation followed by irradiation are preferred.

It is necessary to emphasize that it is difficult to establish irradiation effects by a purely statistical investigation without biopsy. In the above review of the morphology and biology of glioblastomas it was stated that there are two types of malignancy, true malignancy of growth of the tumour and clinical malignancy which can be deduced only from statistics. The collection of series of morphologically controlled cases, such as LINDGREN has been able to present in his monograph, is of course just as important as large statistics.

Two special conditions produced by ionizing irradiation must be considered under clinical malignancy. Late irradiation necrosis may lead to a space-occupying or an atrophic process. This will be described below in detail. Both possibilities lessen the value of any purely statistical observation because an apparent recurrence may be an expanding late irradiation necrosis of the white matter, while a loss of volume of the white matter by irradiation necrosis may produce an internal decompression space and thereby simulate post-irradiation healing.

Late irradiation necrosis

This has received particular attention in the last decade (ARNOLD et coll.; BAILEY et coll.; BOUCHARD; LINDGREN; LÖHR & VIETEN; SCHOLZ et coll.; ZEMAN; ZÜLCH 1956, 1960, 1963). It appears that the first case of irradiation late necrosis in man was described by FISCHER & HOHLFELDER (1930). The case was later described in more detail by KALBFLEISCH (1946). SCHOLZ & HSU (1938) described the brain of a schizophrenic who was given irradiation elsewhere in an experimental study of the blood cerebrospinal fluid barrier. SCHOLZ (1934) tackled the condition by experimental work and MARKIEWICZ (1935) reported these findings in detail. The observations of PENNYBAKER & RUSSELL (2 300 rad to a rodent ulcer of the skin) are well known. The present author encountered late irradiation damage of the brain in 26 autopsies of his material. These included 6 oligodendrogliomas and astrocytomas, 1 spongioblastoma, 3 ependymomas, 8 glioblastomas, 2 metastases, 2 meningiomas, 3 monstrocellular sarcomas and 1 unclassified process. Since 1956 he has repeatedly referred to the danger of late irradiation necrosis of the white matter (1960, 1963) and emphasized its peculiar susceptibility and on the other hand the relative immunity of the grey cortex.

Time-dose relationships have been defined by BERG and LINDGREN. These authors encountered late irradiation necrosis of the white matter only in some of their cases; this was however observed after doses that up to then were lower than those used in conventional therapy. COCCHI reported a case in which a focal dose of 3 500 R to a pituitary adenoma produced late irradiation necrosis which destroyed the overlying temporal lobe on the non-operated side.

I mentioned earlier that late irradiation necrosis can lead either to an increased or a decreased volume of the intracranial space. The olfactory groove meningioma (Fig. 4) exemplifies how the gelatinous scarred and shrunken white matter may lead to a loss of space.

In contrast to the above mentioned feature I may relate a case of a 24-year-old woman, earlier reported upon (ZÜLCH 1960, 1963) in whom a right parieto-occipital tumour was partially resected. Post-operative irradiation with 6 000 rad was followed after 3 years and 4 months by a second series of 2 500 rad, and a few months later by a third series of about 3 700 rad, a total of over 10 000 rad. One year after operation the normal birth of a daughter was followed in the next year by normal birth of a boy. Five years after operation there were signs of raised intracranial pressure and epileptic attacks indicating the necessity of further operation, at which a 200 g mass was removed. The patient has since remained free from symptoms. Investigation of the large portion of cerebral tissue excised revealed total necrosis of all the white matter but no blastoma infiltration; the cortex was unaffected (Fig. 5a).

A similar case was described by LÖWENBERG-SCHARENBERG & BASSET (1950) (6 000+3 600 rad 22 months later) which also presented 'signs and symptoms of a space-occupying process'. At operation the irradiation-damaged area appeared macroscopically like a glioma (similar to the appearances described by SCHOLZ & HSU).

DUGGER et coll. (1954) have also described a case in which space-occupying necrosis occurred 26 months after irradiation. This case also seemed to be one of a glioma and the records indicated that irradiation doses of 6 000 rad over 12 days, 3 600 rad over 24 days and 2 340 rad had been given. The patient died 9 years later when localized gliosis with atrophy, principally affecting the white matter, was revealed.

The pathogenesis of late irradiation necrosis. Clarification of the pathogenesis may be obtained from the morphology or experimental late necrosis in animals. The data that follow were derived from observations in man and in a series of experimental irradiation injuries in rabbits by the method of BERG & LINDGREN, which HARDER (1965) published in a doctorial thesis. It was possible in these experiments with animals also to produce expanding necrosis cysts (ZÜLCH 1963, Figs 8 to 11) perhaps to some extent similar to the expanding space-occupying late irradiation necrosis described. We believe, with SCHOLZ, to have established that damage of the permeability of blood vessels underlies the lesions and that this produces a substance designated as para-amyloid (ZÜLCH 1960, 1963). We do not think that the conclusion of SCHOLZ can be maintained, however, viz that because of a change in vascular permeability, ischaemia develops in the tissues and causes secondary necrosis because the vessels are no longer patent for gases and nutritive material, so that the tissue becomes anoxic. HARDER's experimental work repeatedly demonstrated that quantitatively a para-amyloid change in the vessels remained in the background and that destruction of the myelin sheaths and particularly an early and gross change in the glia were the outstanding features. The astroglia, for example, proliferates in a manner which results in the formation of multinuclear giant cells, as evident otherwise only in malignant tumours (Fig. 9).

Animal experiments reveal damage only in the white matter. The cortex is damaged only if, just as in man, it lies in the cross-fire of the irradiation of many fields receiving excessive doses, as in EICKE's case. This occurred in a small circumscribed region in the case of the olfactory groove meningioma; the cortex remained otherwise intact. These findings thus differ from those of WACHOWSKI & CHENEAULT (1945). A working hypothesis might be that an allergic auto-immune process occurs, with primary damage of the myelin sheaths, similar to that which MARKIEWICZ, and BERG & LINDGREN have envisaged as a basic process. According to this concept, a substance which damages the myelin sheaths escapes from the vessels. The changed myelin then forms an antigen which evokes antibodies against the myelin, leading to its partial destruction. An auto-immune disease in which the glia also plays a certain but obscure role thus occurs. Proliferation of dysmorphic astroglia is a prominent feature in animal experiments. Our findings in man suggest that this process of demyelination may lead to a kind of autonomous disease, perhaps even progressing in the non-irradiated parts.

In spite of all this, certain questions relating to the pathogenesis remain unanswered. In many instances human subjects remained free from late irradiation necrosis in spite of high dosages. Moreover, the condition is almost always confined to the white matter. Late irradiation necrosis may be a result of peritumoural oedema but in animal experiments never appears to arise in this form. The same time intervals and similar morphologic appearances as in man may apply but in about a fifth of the animals no late irradiation damage occurs (BERG & LINDGREN). Constitutional factors may perhaps first set this auto-immune process in action. This variable latency in the occurrence of late damage may extend from the 7th to the 9th month (the predilection time) (e.g. the case of PENNYBAKER & RUSSELL), but also up to 5 years. In one of the cases beyond 5 years slight extension of the process in the cortical region was evident (ZÜLCH 1956, Fig. 24).

The extensive white matter of the spinal cord is as radio-sensitive as that of the brain. The irradiation effect is particularly prominent (KRISTENSSON et coll. 1967) because the concentration of so many white tracts in a thin segment usually produces a transverse lesion after irradiation of external organs, e.g. hypopharyngeal carcinoma. Care in the clinical diagnosis, as in the statistical evaluation of irradiation effects in cerebral tumours, must however be exercised.

A case of post-irradiation damage of the spinal cord that clearly indicated the difficulties of a roentgen therapist was recently reviewed. An operation had been performed on an unclassified tumour of the arachnoid and the dura of the spinal cord. The material was reported as unclassified but a similarity with some thyroid neoplasms and certain meningiomas was emphasized. The tumour grew in an infiltrative manner and was malignant. It was finally irradiated in a conventional manner with 5 500 rad. A transverse symptomatology, apparently as a result of late irradiation necrosis, developed a few months later.

The patient survived fourteen and a half years, when the morphologic changes indicated that the spinal cord in the irradiation zone had become partially strangled by surrounding scar tissue, several millimetres thick. No signs of a para-amyloid substance could be recognized histologically. The spinal cord was softened from a ring-scar originating in the leptomeninges and dura which obviously had led through constriction to liquefaction of the spinal cord. In addition there was probably thrombosis of the anterior spinal artery which had become recanalised. It is probable that all the malignant cells had been destroyed by the irradiation, i.e. the desired effect had been achieved. The presence of tumour cells in the leptomeninges and dura concentrically around the spinal cord had led to scarring of the infiltrated region, secondarily causing strangulation of the spinal cord. The patient had thus been protected from growth of the malignant tumour (for 14 years and 6 months), an effect at the cost however of softening of the spinal cord. This did not arise from late irradiation necrosis but through scarring of the primary tumour (a detailed report will follow).

This case clearly indicates the discrepancy between the purpose of therapy and the actual effect of the irradiation. The goal can often only be achieved at the expense of secondary damage but how far this occurs with the glioblastoma should be discussed.

SUMMARY

The effects of conventional irradiation on different types of intracranial tumours are described and indications for radiotherapy are given on the basis of morphologic observations. The possibilities of late irradiation damage to the brain and spinal cord are emphasized; such damage may suggest either recurrence or give a false impression of cure. In the absence of correlation with autopsy and isotope data and operative and angiographic findings, these facts should be taken into account in all statistical evaluations of the results of irradiation therapy.

ZUSAMMENFASSUNG

Die Wirkung konventioneller Röntgenbestrahlung auf die einzelnen intrakraniellen Geschwulstarten wird besprochen und aufgrund morphologischer Beobachtungen werden Folgerungen für die Indikation zur Röntgenbestrahlung gezogen. Die Möglichkeit der Strahlen-Spätschädigung des Gehirns und Rückenmarkes wird betont. Diese Spätnekrose kann entweder ein Recidiv oder Heilung vortäuschen. Dies ist bei allen statistischen Untersuchungen über Strahlenwirkung, ohne autoptische, operative, angiographische und Isotopenkontrolle, zu berücksichtigen.

RÉSUMÉ

L'auteur décrit les effets de l'irradiation par les moyens classiques sur différents types de tumeur intra-crâniennes et définit les indications de la radio-thérapie sur la base des signes morphologiques. Il insiste sur la possibilité de radio-lésions retardées du cerveau et

de la moelle; ces lésions peuvent faire penser soit à une récidive, soit donner une fausse impression de guérison. En l'absence de corrélation avec les données de l'autopsie et par les isotopes, et avec les constatations opératoires et angiographiques, ces faits doivent être pris en considération dans toutes les études statistiques des résultats du traitement par les radiations.

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