Oligodendroglioma with extraneural metastases

KURT JELLINGER, MARGARETE MINAUF, AND MECHTHILD SALZER-KUNTSCHIK

From the Neurological Institute and the Department of Pathology, University of Vienna, Austria

Remote metastases of glial tumours are in general rather rare and only few instances of extraneural metastases of oligodendroglioma have been found in the literature (James and Pagel, 1951; Spataro and Sacks, 1968). We are reporting a case of an operated oligodendroglioma, in which metastases to the lumbar vertebrae were found at necropsy.

CASE REPORT

A 58-year-old woman (NI 249-67) had first experienced the sudden onset of severe headache, vomiting, and right-sided hemiparesis about 3½ years before death. These symptoms subsided within a few hours and recurred several months later intermittently, at this time associated with disturbances of speech. About 10 months after the onset of the illness, the patient suffered an almost complete right-sided hemiparesis, loss of speech, and grand mal seizures. A left carotid angiogram revealed a space-occupying lesion in the frontal region, compatible with a meningioma. At operation, a well-demarcated tumour, superficially and deeply located, was found and partially removed.

BIOPSY SAMPLE This included two specimens. The superficial one was a cherry-sized, greyish-red and solid mass well demarcated by a small rim of greyish tissue. The deep specimen was a 4.5 × 4.0 cm solid and also well demarcated mass of bluish-grey colour with many small haemorrhages and central necroses.

TUMOUR HISTOLOGY (N 46-65) There were densely packed tumour cells growing mainly within the meninges showing some variability in their architecture. In part the tissue was composed of solid groups of small cells with round to oval nuclei, rich in chromatin, and with faintly eosinophilic, poorly outlined cytoplasm. Other parts were reminiscent of 'alveolar' or 'trabecular' formations. The nests or clusters of cells were separated by fine septa and a rather dense vascular stroma (Figs 1a and b). Several regions showed a rather loose architecture and were rich in fibrous tissue and blood vessels. Although small parts of the tumour showed the features of an oligodendroglioma (Fig. 1b), a metastatic lesion possibly from a bronchial carcinoma or renal cell carcinoma could not be fully excluded because of the sharply defined borders of the blastomatous tissue, as well as of the cell pattern and the high vascularity in large parts of the tumour.

A thorough examination in search of a possible primary blastoma elsewhere in the body yielded no positive findings. Post-operatively the patient felt well throughout the following 2½ years.

Two weeks before death complete aphasia and right-sided hemiplegia again occurred suddenly. The patient became comatose and remained so for the last few days.

GENERAL NECROPSY (P.Nr. 1434-67) This showed moderate bilateral cardiac enlargement and a left-sided pyelonephrosis due to an obstructive stone in the renal pelvis. There were sclerotic changes of the body of the 4th and 5th lumbar vertebrae and a focal, sharply defined sclerosing lesion with the greatest diameter of 1 cm within the body of the 3rd lumbar vertebra. Careful macroscopic examination did not reveal any evidence of neoplasm in the adrenals, lungs, pleura, lymph nodes, genitals, heart, blood vessels, glomus caroticum, thyroid, spleen, liver, kidney, pancreas, and breasts, or elsewhere in the body. There were no pigmented naevi in the skin. Also, histologically, there was no evidence of tumour in the lungs, genitals, liver, kidney, and thyroid.

BRAIN Macroscopically, the entire brain, especially the left hemisphere, appeared swollen and showed signs of increased intracranial pressure. The surgical defect within the left fronto-central region was surrounded by greyish-white, rather firm tumour tissue. Tumour growth of similar appearance was also seen within the meninges of the opposite gyrus cinguli, where a rather hard nodule was present. In the left frontal region numerous small and several larger haemorrhages of different age were found.

SPINAL CORD The cord and its meninges were grossly unremarkable.

HISTOLOGY OF INTRACRANIAL TUMOUR Several sections of the right gyrus cinguli and left frontal lobe were examined on paraffin-embedded and frozen material stained with the routine methods of neuropathology, including silver impregnation techniques.

The highly cellular tumour nodule was mainly located within the interhemispheric fissure, above the corpus callosum, and infiltrated the cerebral parenchyma. The cortex of both cingulate gyri as well as the corpus callosum were mainly involved. The tissue consisted of small, round cells with round to oval nuclei, rich in chromatin. With Hortega's silver carbonate method, the
FIG. 1. A. Surgical specimen; tumour growing in the meninges. Small round tumour cells with chromatin-rich nuclei, showing no specific structure or arrangement. H & E x 110. B. Surgical specimen; tumour growing in the meninges. Groups of cells with round nuclei and poorly stained, hardly visible cytoplasm, separated by stroma, reminiscent of 'trabecular' formation. H & E x 110. C. Cerebral tumour found at necropsy (right gyrus cinguli) showing the typical structure of an oligodendrogloma with some degree of pleomorphism. H & E x 140. D. High power view, H & E x 560.
small, round tumour cell nuclei were commonly argyrophilic. There was often a halo around the nucleus and the cytoplasm appeared 'empty' or poorly stained and hardly visible. The tumour cells formed nests, clusters, and columns, which were separated by more or less dense stroma (Figs 1c and d). They grew along the surface of the cerebral cortex and infiltrated the meninges diffusely (Fig. 2). They were closely packed near the surface, and became less dense as they infiltrated deeper regions. In some areas, long spindle-shaped cells were arranged in dense sheets or bundles. With the Cajal-method, no astrocytes were demonstrated within the tumour nodule.

The tumour surrounding the surgical defect in the left frontal lobe also grew towards and into the meninges. It showed essentially the same structure, but with a remarkable degree of pleomorphism with numerous, sometimes bizarre cell-elements and regressive changes, such as small necroses, haemorrhages or lymphoid infiltration. To some extent this must have taken place before operation, since the surgical specimen also revealed tumorous growth within the meninges. Oligodendrogliomas are known to invade the meninges (Kwan and Alpers, 1931; Kernohan, Woltman, and Adson, 1933; Löwenberg and Waggoner, 1939; Zülch, 1941; Blumenfeld and Gardner, 1945; Trowbridge and French, 1952; Zülch, 1956; Russell and Rubinstein, 1963; Bestle, 1969) and, in doing so, occasionally display considerable variability in architecture. In a personal series of 65 histologically verified cases of oligodendroglia we observed tumour growth within the meninges in 19 instances (29.2%). This was encountered in seven out of 42 surgical specimens (16.6%), and in 12 of 23 necropsy cases (52%). In four of the latter surgery was not performed.

Seeding along the cerebrospinal pathways is also well known (Cairns and Russell, 1931; Greenfield and Robertson, 1933; Kwan and Alpers, 1931; Martin, 1931; Blumenfeld and Gardner, 1945; Polmeteer and Kernohan, 1947; Earnest, Kernohan, and Craig, 1950; Trowbridge and French, 1952; Zülch, 1956; Strang and Nordenstam, 1961; Russell and Rubinstein, 1963; Minauf and Jellinger, 1968; Bestle, 1969), but extraneural metastases are

**BODY OF 3RD LUMBAR VERTEBRA** The sclerotic appearance was due to massive new bone formation in the marrow spaces and along pre-existent bone spiculae. Tumour cells similar to those described in the cerebral tumour (Fig. 3c) infiltrated the fibrous marrow diffusely. They formed cell nests of varying size and density, and possessed chromatin-rich, round, oval, or polygonal nuclei surrounded by scant indistinct cytoplasm (Figs 3a and b). No reticulin fibrils could be impregnated between the tumour cells. Unfortunately, Hortega's silver impregnation could not be performed on the material available.

**FINAL DIAGNOSIS** Oligodendroglia with extensive invasion of the meninges, seeding along the cerebrospinal pathways, and extraneural osteoblastic metastases to the 3rd to 5th lumbar vertebrae.

**DISCUSSION**

The clinical course of this patient's illness with intermittently occurring symptoms of sudden onset can be explained by repeated haemorrhages within the tumour, which was confirmed at biopsy and necropsy. At operation, the tumour was found partly growing within the meninges. It did not, therefore, show all the typical diagnostic features of an oligodendroglia and caused some diagnostic difficulties. This problem was recently discussed by Minauf and Jellinger (1968). At necropsy, the cerebral tumour could be definitely diagnosed as an oligodendroglia; large parts of it showed the typical 'honeycomb' pattern. In other areas, a marked degree of pleomorphism with numerous rather large, sometimes bizarre cells, eosinophilic stained cytoplasm, and occasional mitotic figures were encountered. The tumour could thus also be called an 'oligodendroblastoma'.

The extensive invasion of the meninges was remarkable. To some extent this must have taken place before operation, since the surgical specimen also revealed tumorous growth within the meninges. Oligodendrogliomas are known to invade the meninges (Kwan and Alpers, 1931; Kernohan, Woltman, and Adson, 1933; Löwenberg and Waggoner, 1939; Zülch, 1941; Blumenfeld and Gardner, 1945; Trowbridge and French, 1952; Zülch, 1956; Russell and Rubinstein, 1963; Bestle, 1969) and, in doing so, occasionally display considerable variability in architecture. In a personal series of 65 histologically verified cases of oligodendroglia we observed tumour growth within the meninges in 19 instances (29.2%). This was encountered in seven out of 42 surgical specimens (16.6%), and in 12 of 23 necropsy cases (52%). In four of the latter surgery was not performed.

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**FIG. 2. Tumour in right gyrus cinguli and meninges. H & E \times 110.**
FIG. 3. A and B. Osteoblastic metastasis within the 3rd lumbar vertebral body: groups of small cells with round chromatin-rich nuclei and poorly stained cytoplasm; newly formed trabeculae (arrows). H & E x 115. B. High power view of tumour cells within the marrow spaces. H & E x 560. C. Tumour in the left frontal lobe (for comparison) showing identical appearance. H & E x 560.

extremely rare and so far have only been reported after surgery:

James and Pagel's (1951) patient had had three operations for a left parietal oligodendroglioma. Several months before death, this patient developed metastatic nodules to the scalp and later to cervical lymph nodes. At necropsy, extensive metastases were found in the right femur, skin of the scalp, lymph nodes, and lungs. In the patient of Spataro and Sacks (1968), four craniotomies for a left parietal oligodendroglioma had been performed. The necropsy revealed extensive involvement of the cerebrospinal pathways, skeleton—especially vertebrae—and liver. We would like to mention that metastases to the skeleton were osteoblastic in all so far known observations. It seems of interest that Bailey and Bucy (1929) had already mentioned the possibility of extracranial metastases of oligodendroglioma in a patient who had developed an extension in the neck after four operations.

It is our opinion that the tumour found in the lumbar vertebral bodies in our case represents a distant metastasis of the cerebral oligodendroglioma. It meets the criteria postulated by Weiss (1955) for an acceptable case of metastasizing central nervous system glioma: (1) the presence of CNS tumour has been proved; (2) the clinical history indicates that the initial symptoms were due to this tumour; (3) a complete necropsy did not yield any suggestion of a primary tumour elsewhere in the body; and (4) the morphology of the distant growth was consistent with the cerebral tumour.

SUMMARY

A 58-year-old woman suffered from a left parietal oligodendroglioma. At craniotomy one year after the onset of clinical symptoms the tumour was found to invade the overlying meninges. The patient died 2½ years after surgery. Necropsy revealed...
extensive meningeal spread of the tumour as well as metastases in the body of the 3rd to 5th lumbar vertebrae. This tumour conformed to Weiss's criteria of acceptable extraneural metastases of gliomas and represents the third case of extra-
neurally metastasizing oligodendrogliomas noted in the literature.

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