Vincristine Sulphate in the Treatment of Skeletal Metastases from Cerebellar Medulloblastoma

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The most common site for metastatic deposits from a cerebellar medulloblastoma is the spinal subarachnoid space; distant spread of this malignant tumor usually takes place via the cerebrospinal fluid pathways. Extracranial metastases may occur after surgery, but metastases outside the central nervous system are extremely rare. There are a number of reports of confirmed extracranial metastases of medulloblastoma.1,2,4-7,13,14,16,19,20,22,23,27

Weiss24 formulated four criteria to aid in the establishment of a definite relationship between the primary growth and the secondary deposits:

1. The proven presence of a single histologically characteristic tumor of the central nervous system,
2. A clinical history which demonstrated that this tumor accounted for the initial symptoms,
3. A complete necropsy to exclude the presence of another primary site,
4. Identical morphology of primary lesion and metastases with due allowances for difference of anaplasia.

We are describing two additional cases of skeletal metastases that meet these criteria.

The two patients have received cytotoxic drug therapy and are still living. Lassman et al.,9-12 have noted that many of the malignant intracranial gliomas of childhood may improve and the patients live longer when treated with vincristine sulphate (Onconvin*). These two cases of medulloblastoma became radio-resistant, developed bony metastases, and then responded to treatment with this drug.

Case Reports

Case 1. This girl was 7 years old when an extensive solid cerebellar tumor was partially excised on October 9, 1963. The histology proved it to be a medulloblastoma. The operation was followed by high voltage x-ray therapy. After the treatment had been completed, incoordination of movement was still present on the right side.

Nine months later, in July, 1964, the patient was readmitted; 4 months previously she had developed infectious hepatitis with headaches and severe ataxia. Two days before admission her headaches became much worse and she started to vomit. On the day of admission her speech had become slurred and she had lost the use of her right hand.

Examination. Although papilledema was not present, the patient had nystagmus on looking to the right, marked ataxia in all four limbs, and weakness in the right arm. Ventriculography showed evidence of recurrence of the posterior fossa tumor. She was given a second course of high voltage therapy; she improved and was discharged after 7 weeks in hospital.

However, within 6 weeks of discharge, she had to be readmitted due to increasing pain in the back, shoulders, and hips, loss of weight, and general malaise. A ventriculo-atrial shunt was performed to relieve the internal hydrocephalus; the plain x-ray film taken to check the position of the atrial catheter also revealed evidence of skeletal secondary deposits in the right scapula and humerus (Fig. 1). A skeletal survey was done, and this showed further evidence of osteolysis and osteosclerosis in the spine, pelvis, and femora (Fig. 2), resembling the metastases of neuroblastoma. A thorough clinical and x-ray search for such a tumor was made in the abdomen, pelvis, and thorax, but none was found. Intravenous pyelogram was normal.

Ten days after discovery of the metastases, a course of intravenous vincristine
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sulphate was started (0.05 mg/kg per week). Within 48 hours of the first injection of the drug, the bone pains had almost disappeared and her condition rapidly improved. Five months later a repeat skeletal survey showed progressive sclerosis of the previous osteolytic deposits (Fig. 3).

Pathology. The cerebellar tumor, biopsied in September, 1963, showed a cellular tumor formed of primitive and generally undifferentiated cells with hyperchromatic nuclei, scanty cytoplasm, and a moderate number of mitotic figures. In a few areas spongioblastic differentiation was discernable but definite neuroblastic differentiation or rosette formation was not found. The histological appearance was compatible with the diagnosis of medulloblastoma (Fig. 4).

Case 2. This 10 year old boy was first seen when 5 years old when in February, 1961, total removal of a histologically verified medulloblastoma of the fourth ventricle was attempted. The patient received almost immediate high voltage therapy. He made a good recovery except for left optic atrophy which caused poor vision in that eye.

For approximately 4½ years after high voltage therapy he did well, but he was readmitted on July 20, 1966, suffering from headaches, vomiting, and the presence of a soft fluctuating swelling on the forehead. Over the three days prior to admission his walking had deteriorated, he became ataxic, and on examination there was bilateral optic atrophy, horizontal nystagmus to the left, and weakness of the left foot. Recurrence of the posterior fossa tumor was suspected but ventriculography showed an extensive space-occupying lesion in both frontal lobes extending as far back as the thalami. The

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Fig. 1. Case 1. This chest film was taken to check the position of the atrial catheter of the Holter valve and incidentally showed new bone formation and sclerosis in the right scapula and metaphysis of the right humerus (October 10, 1966).

Fig. 2. Case 1. Lateral view of dorsal spine (upper) and anteroposterior view of pelvis (lower) showing patchy areas of osteolysis and osteosclerosis before treatment with vincristine sulphate (October 20, 1966).