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# Early Diagnosis of Metastases in the Epidural Space

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## Summary

Examination of the cerebrospinal fluid (CSF), and myelography, were performed in most of 89 consecutive patients with X-ray evidence of vertebral metastases to test the value of these examinations in the early detection of neoplastic involvement of the epidural space. Patients were divided into 3 groups. In 7 cases (group I), the vertebral metastases were asymptomatic. Fifty-nine (group II) had symptoms or signs of radicular lesions but not of spinal cord compression. Twenty-three showed various stages of spinal cord or cauda equina compression (group III).

Involvement of the epidural space was demonstrated on myelography in almost 50% of patients from groups I and II by a partial (29%) or complete (19%) arrest of the opaque medium. In addition, five patients in group II with normal myelograms had increased levels of CSF protein. Leucocyte counts were within normal limits in all patients. Neoplastic cells were found in two cases.

It is suggested that in patients with only radiological evidence of neoplastic involvement of the epidural space and complete myelographic blocks, laminectomy, followed by radiation therapy, should be performed. Patients showing partial blocks should receive radiation therapy only.

## Introduction

Epidural compression of the spinal cord is a serious complication of malignant disease. With the exception of lymphomas[1, 2] surgery, often followed by irradiation, is a recommended treatment, despite a high percentage of disappointing results[3, 4, 5, 6, 7]. Several authors have stressed, however, that the milder the neurological impairment and the earlier the diagnosis the better are the therapeutic results[7–13].

In most neoplasms, the involvement of the epidural space by neoplastic tissue originates from bone metastases. This relation is demon-

strated by the high frequency of vertebral metastases shown by X-rays in patients with extradural metastatic compression of the spinal cord[7, 9, 11, 13]. Thus patients with vertebral metastases appear as a high risk group with respect to epidural spinal compression.

The purpose of this work was to test the value of lumbar puncture and myelography in early diagnosis of the epidural space involvement in unselected patients with vertebral metastases, in the absence of clinical signs of spinal cord compression.

## Material and Methods

Examination of the cerebrospinal fluid (CSF) and myelography were performed in 66 patients who had evidence of vertebral metastases on plain X-ray, confirmed by bone scanning, but no clinical signs or symptoms of medullary compression. All these patients were examined during a three year period by the same physician at the Institut Jules Bordet, a general cancer hospital.

Patients were divided into 3 groups according to neurological status. In 7 patients (group I), the neoplastic vertebral involvement produced no symptoms and was discovered on routine X-ray examination. The 59 patients in Group II complained of radicular pain in the dermatomes corresponding to the involved vertebra. Twenty-four of them had, in addition, objective signs of radicular compression such as changes in sensation, depression or loss of tendon reflexes, or weakness or muscular wasting in the distribution of affected roots. Twenty-three patients who were admitted to the hospital during the same three year period and had objective clinical signs of spinal cord or cauda equina compression are also reported in the study. They were placed in group III.

CSF was obtained by lumbar puncture and analysed for protein by the method of Lowry et al.[14]. The cells were counted in the chamber of a haemocytometer. Examination for neoplastic cells was performed on the deposits obtained by centrifuging CSF at 1,000 G for 5 minutes. Myelograms were performed with 5 ml of Etiodant (ethyl iodophenyl undecanoic acid, Glaxo Co, Brussels). The myelographic findings were classified as normal, showing partial block, or showing complete block.

## Results

*Distribution of patients*

The distribution of patients according to site of primary neoplasm and clinical grouping is shown in Table 1. The most frequent primary cancers were breast and lung carcinomas which accounted for 44 and 15 per cent respectively of the patients studied. Other types of primary tumours were represented by small numbers of cases and were considered together in a "miscellaneous" group. Neurological symptoms were less frequent and less severe in patients with breast carcinoma in comparison with other types of cancers. Six out of the 7 cases without neurological complaints (group I) had breast carcinoma whereas in group III

Table 1. *Distribution of Patients According to Clinical Groups and Primary Tumours*

| Primary tumor | Breast | Lung | Pro-state | Mela-noma | Colon | Lym-phoma | Lar-ynx | Blad-der | Kid-ney | Ovary | Thy-roid | Ewing sarc. | Oeso-phagus | Undeter-mined | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group I | 6 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 |
| Group II | 30 | 7 | 5 | 1 | 3 | 1 | 1 | 2 | 2 | 1 | 1 | 0 | 1 | 4 | 59 |
| Group III | 3 | 6 | 2 | 3 | 1 | 3 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 23 |
| Total | 39 | 13 | 7 | 5 | 4 | 4 | 3 | 2 | 2 | 1 | 1 | 1 | 1 | 6 | 89 |

only 3 patients out of 23 who showed signs of spinal cord or cauda equina compression had breast cancer.

*CSF examination*

Figures concerning CSF protein are given in Table 2. All samples with blood contamination were discarded. The levels of protein were not related to the nature of the primary neoplasm but to the degree of neurological impairment, particularly to the presence of clinical symp-

Table 2. *Levels of Protein in Cerebrospinal Fluid*

| Primary tumour | Clinical group | Number of samples | < 50 mg per 100 ml | > 50 mg per 100 ml |
|---|---|---|---|---|
| Breast | I | 6 | 6 | 0 |
| | II | 25 | 19 | 6 |
| | III | 1 | 0 | 1 |
| Lung | I | 0 | 0 | 0 |
| | II | 6 | 3 | 3 |
| | III | 3 | 1 | 2 |
| Miscellaneous | I | 1 | 0 | 1 |
| | II | 17 | 9 | 8 |
| | III | 7 | 1 | 6 |
| Total | I | 7 | 6 | 1 |
| | II | 48 | 31 | 17 |
| | III | 11 | 2 | 9 |
| | Total | 66 | 39 | 27 |

toms of spinal cord compression. Thus in group I, with the exception of one patient who also had extensive involvement of the base of the skull, all patients had normal protein levels. In group II, pathological values were found in about one third of the patients, the figures ranging from 13 to 1,100 mg per 100 ml. In group III almost all showed abnormally high concentrations of protein ranging from 26 to 2,000 mg per 100 ml.

Leucocyte counts were not significantly increased. Neoplastic cells were found in two patients.

*Myelography*

The results of technically satisfactory myelographies, obtained in 75 patients, are shown in Table 3. As with the protein levels, myelographic abnormalities were related to the severity of the neurological

symptoms. The most striking result was the frequency of abnormal myelograms in patients without signs of compression of the spinal cord or cauda equina (groups I and II). Thus a partial block was found in 2 cases in group I and 15 in group II. There was a complete block in 11 patients out of the 52 in group II. On the other hand, 5 patients in group III had normal myelograms. Three of these showed clinical symptoms of cauda equina lesions and 2 had incomplete pyramidal syndromes.

Table 3. *Results of Myelography*

| Primary tumour | Clinical group | Number of performed myelographies | Normal | Partial block | Complete block |
|---|---|---|---|---|---|
| Breast | I | 5 | 4 | 1 | 0 |
| | II | 26 | 16 | 7 | 3 |
| | III | 1 | 0 | 0 | 1 |
| Lung | I | 0 | 0 | 0 | 0 |
| | II | 7 | 4 | 2 | 1 |
| | III | 4 | 0 | 0 | 4 |
| Miscellaneous | I | 1 | 0 | 1 | 0 |
| | II | 19 | 6 | 6 | 7 |
| | III | 12 | 5 | 2 | 5 |
| All cases | I | 6 | 4 | 2 | 0 |
| | II | 52 | 26 | 15 | 11 |
| | III | 17 | 5 | 2 | 10 |
| | Total | 75 | 35 | 19 | 21 |

The Queckenstedt test was normal in all patients whose myelograms were either normal or showed only partial blocks. The test was abnormal in about half of the 21 patients with complete blocks.

*Correlation between CSF protein level and myelography*

Comparisons between clinical examination, CSF protein level and myelography are given in Table 4. These show essentially that in a number of patients with metastatic involvement of the epidural space, CSF protein determination and myelography are complementary examinations. Thus, in 26 patients where myelography was considered as normal, 7 had increased levels of protein ranging from 56 to 308 mg with a mean value of 115 mg per 100 ml. On the other hand, 10 patients out of 15 with myelograms showing partial blocks and 4 out of 18 with complete blocks had normal concentrations of CSF protein.

Table 4. *Correlation Between Levels of CSF Protein and Myelography*

| Myelography | Normal | | Partial block | | Complete block | |
|---|---|---|---|---|---|---|
| Protein (mg per 100 ml of CSF) | < 50 | > 50 | < 50 | > 50 | < 50 | > 50 |
| Group I | 4 | 0 | 1 | 1 | 0 | 0 |
| Group II | 14 | 5 | 9 | 4 | 3 | 8 |
| Group III | 1 | 2 | 0 | 0 | 1 | 6 |
| Total | 19 | 7 | 10 | 5 | 4 | 14 |

*Results of treatment and outcome in patients from groups I and II*

No treatment was given to patients from group I who were free of neurological symptoms and signs. In group II, 38 patients received only X-ray therapy (2,200 to 2,500 rads). Pain was relieved in 23 but only one showed an objective regression of radicular deficit. Five patients from group II underwent laminectomy in addition to receiving

Table 5. *Follow-up of Patients from Groups I and II*

| Myelography | Normal | Partial block | Total block |
|---|---|---|---|
| Number of patients | 21 | 14 | 8 |
| Mean duration of the follow-up (months) | 10 | 9 | 3 |
| Outcome: | | | |
| Death without spinal compression | 13 | 11 | 5 |
| Death with spinal compression | 2 | 0 | 1 |
| Alive without spinal compression | 6 | 3 | 2 |
| Alive with spinal compression | 0 | 0 | 0 |

X-ray therapy, and pain was relieved in two. Follow-up results are given in Table 5. Adequate follow-up was available for 43 patients of whom 11 are still alive without signs of spinal cord compression. In 32 patients who died, 3 developed paraplegia 1, 15 and 20 months after the first neurological examination.

## Discussion

The most unexpected and not previously investigated aspect of this study was the high rate of abnormal myelograms found in patients without signs of compression of the spinal cord or cauda equina. On

58 myelograms performed in such patients, partial block was found in 17 cases (29%) and total block in 11 (19%). Thus, of patients with vertebral metastases and no clinical signs of spinal cord compression the presence of neoplastic tissue in the epidural space may be demonstrated by myelography in about one half. The involvement of the epidural space is more likely to be demonstrated in patients with symptoms of radicular compression (group II) than in patients where the vertebral metastases cause no complaints. The frequency of abnormal myelograms seems to be related to the nature of the primary tumour. For instance, it was considerably lower in patients with breast carcinoma than with lung cancers or with melanomas. This difference, however, could be due to the fact that routine radiography of the skeleton was performed in patients with breast carcinoma more often than in those with many other types of neoplasm.

Whereas leucocyte counts and searches for neoplastic cells in the CSF appeared unhelpful in the early diagnosis of metastatic involvement of the epidural space, increased protein levels were found in 7 patients out of 32 with normal myelograms. In all these patients neoplastic compression or involvement was the only explanation for the increase in CSF protein concentrations. Conversely, levels of protein lower than 50 mg per 100 ml were found in 4 out of 18 patients with complete blocks. Similar observations have already been reported[8, 9]. It is also known that, as in this study, manometric blocks may be absent in patients with complete blocks in their myelograms[9]. Thus myelography and determinations of CSF protein should be considered as complementary examinations when epidural metastases are suspected.

The last point to consider is whether the establishment of the diagnosis of epidural metastases before the appearance of clinical symptoms of spinal cord compression benefits patients.

It is possible to avoid the development of paraplegia and, if so, how?

The purpose of the present study was not to answer this question. In most of our patients, the treatment consisted in the administration of relatively low doses of X-ray therapy. This treatment frequently improved the radicular pain but failed to prevent spinal cord compression in about 10% of the cases. In view of the unanimous opinion that the best results are obtained in cases where the neurological deficit is mild[7, 8, 9, 10, 11, 12, 13], it appeared reasonable to adopt a more aggressive therapeutic attitude in patients in good general condition and without signs of spinal cord compression. Thus cases with partial myelographic blocks are now treated by irradiation (4,500 rads). Myelography is repeated to evaluate objectively the effect of the treatment. Laminectomy may be performed later if there is radiological or clinical deterioration. When there is a complete block, laminectomy followed

by radiotherapy is carried out. A preliminary non-controlled study is now in progress in this hospital to test this therapeutic approach and determine whether a cooperative and randomized trial is worth undertaking.

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