Paraplegia 27 (1989) 394–401

0031-1758/89/0027-0394$10.00

Neuroblastoma in an Adult causing Spinal Cord Compression: Report of a Case and Review of the Literature

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Summary

Adult neuroblastoma (ANB) is an uncommon malignancy, there being only 42 reported cases in the world literature. The purpose of this report is to present a case of ANB with spinal cord compression by an intraspinal component, and review methods of diagnosis and treatment.

NB is one of the most frequent childhood malignancies (90% of the patients are less than 10 years old) and both pathologists and clinicians tend to exclude it from differential diagnosis when the patient is an adult.

When the tumour is located in the paraspinal region, local extension through the intervertebral foramen into the spinal canal can occur in a dumbbell fashion, a pattern of growth first described by Weber in 1856.

Key words: *Adult neuroblastoma, Dumbbell neuroblastoma; Spinal cord compression.*

NB is an embryonic tumour of neural crest origin. This explains three notable features (1) the spectrum of histologic forms (2) the diverse location of primary foci, and (3) The ability to produce catecholamines.

The incidence of paediatric cases is only 500 per year in the USA. Adult cases are even rarer (Simone *et al.*, 1982). Within the last few years, a number of reports dealing with ANB have appeared in the literature, and we can now say that this neoplasm occurs in all age groups (Mackay *et al.*, 1976).

The anatomical distribution of NB reflects that of the sympathetic nervous system.

There are published reports on ANB that suggest a predilection for sites of involvement which differ from those seen in childhood NB, e.g. head and neck (13.3%) or lower extremities (10%) (Mackay *et al.*, 1976; Aleshire *et al.*, 1985). Other authors have reported ANB with primary disease sites similar to those seen in paediatric neuroblastoma (PNB), e.g. thorax 20% (PNB cases 20.3%) and abdomen 50% (PNB cases 63%) (Kaye *et al.*, 1986).

Based on histopathologic observations it was assumed that NB seen in children (PNB) and adults (ANB) have similar cell origin (neuroectodermal origin) (Aleshire *et al.*, 1985; Eto *et al.*, 1986; Vinores *et al.*, 1984).

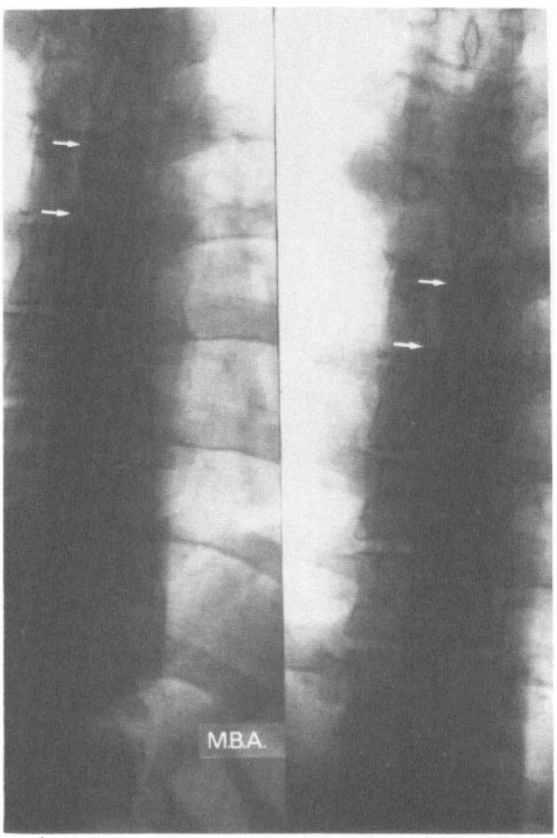

Figure 1 Myelography showing an extrathecal compression at T6–T7 level (Arrows).

Neurogenic tumours are among the most common neoplasms of the mediastinum and are seen in the posterior mediastinum in the paravertebral area, whence local extension through the intervertebral foramen in a dumbbell or hourglass fashion into the spinal canal can occur. In most instances this cancer presents signs and symptoms of spinal cord compression. Mediastinal tumours have a greater tendency to extend into the spinal canal than retroperitoneal tumours (Holgersen *et al.*, 1983).

Case Report

In December, a 30-year-old man presented with a month's history of thoracic back pain, of moderate to severe intensity, radicular in distribution and accompanied in the last 10 days by lower-limb weakness and numbness.

Clinical examination showed weakness of the lower limbs with clinical signs consistent with cord compression at T6 neurological level. A chest X-ray was normal. Myelography showed an extrathecal compression at T6–T7 level (Fig. 1). Because of the history,

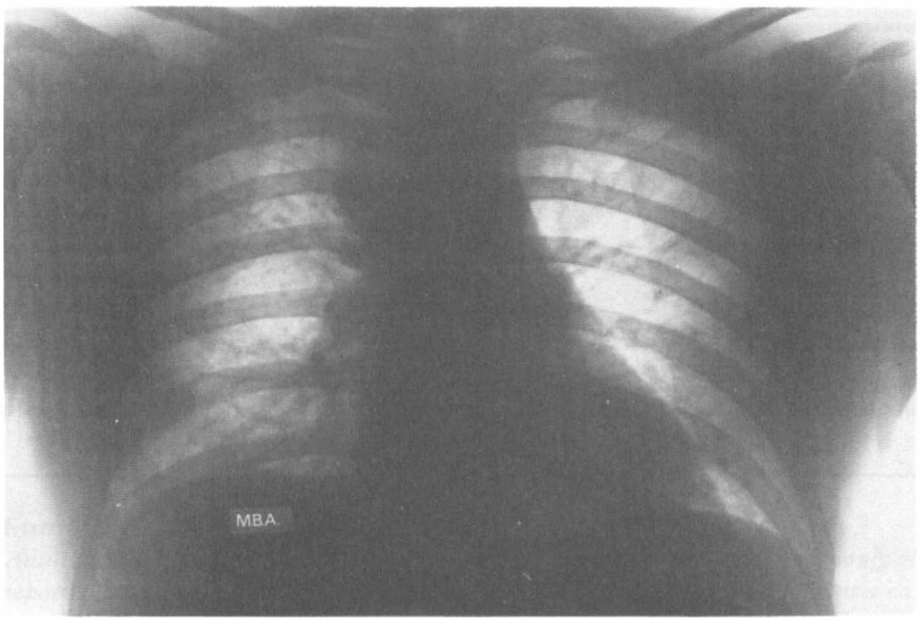

Figure 2 Chest X-ray showing a broad mediastinum and a right paraspinal mass.

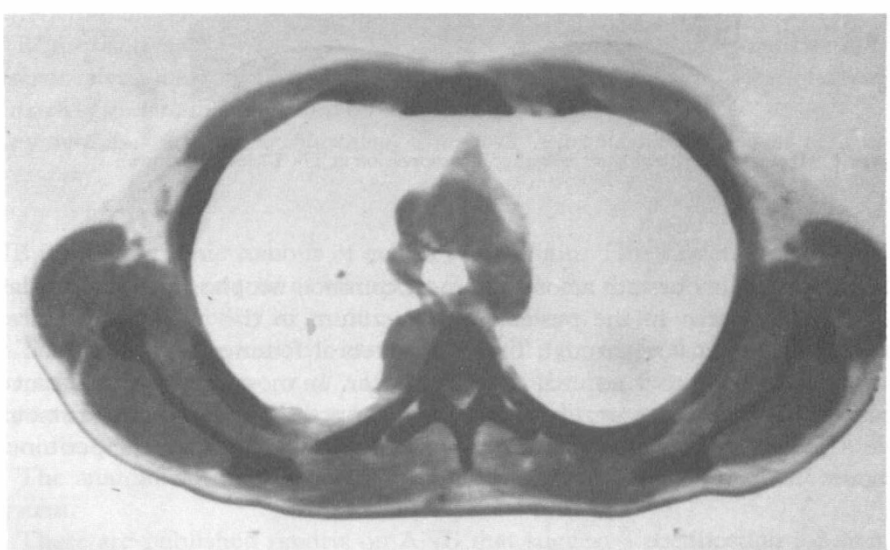

Figure 3 CT Scan showing a right paraspinal mass and a little pleural effusion.

clinical signs and radiological findings, a T6–T7 laminectomy was done. The biopsy only showed normal epidural fat.

The patient did not improve after surgery and more exhaustive radiological studies were done. A chest X-ray now showed a broad mediastinum (Fig. 2). Spinal X-rays and

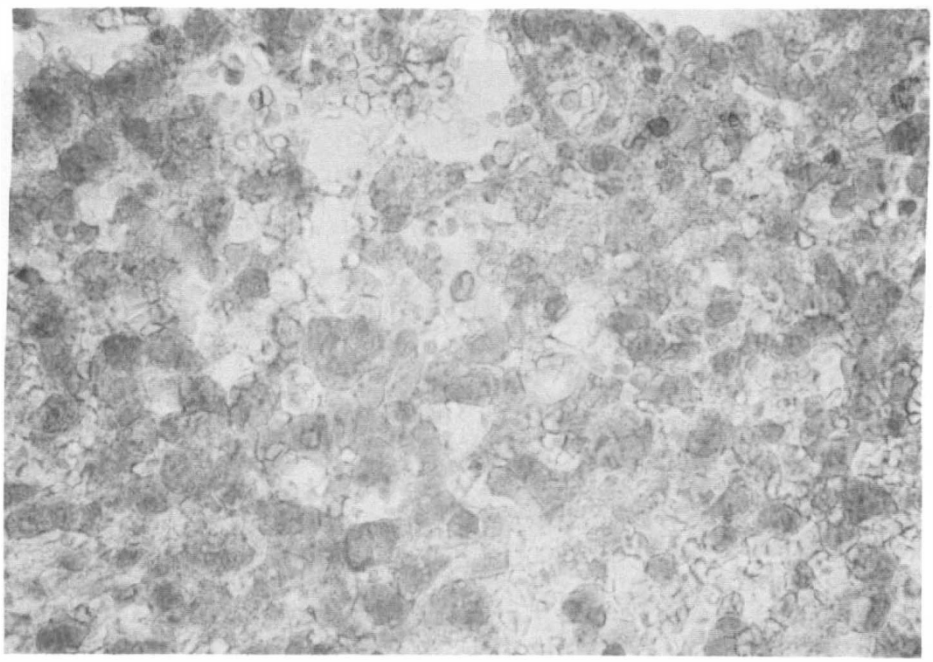

Figure 4 Histological features: small dark cells with round to oval hyperchromatic nuclei and scanty cytoplasm. NSE positive (red).

a radionuclide scan were normal. A CT scan showed a right paraspinal mass and a small pleural effusion (Fig. 3).

In April, 5 months after the onset of symptoms at the T6 level, severe pain of a radicular nature and clinical signs consistent with cord compression at the T1 level developed. Therefore an exploratory thoractomy was done. There was a pleural effusion, a dilated, thrombosed vena azygos and a paraspinal mass with local extension through the fourth right thoracic intervertebral foramen.

The biopsy showed an undifferentiated tumour consisting of small dark cells defined by round to oval hyperchromatic nuclei and scanty cytoplasm. Various sized islands of small round cells were found. Immunocychemistry was carried out and Neuron Specific Enolase (NSE) was positive; S-100 protein was also positive (Fig. 4). Common Leucocyte Antigen and Epithelial Membrane Antigen were negative.

Because of the location and the histological and immunocytochemistry characteristics we can say that this tumour exhibited features of NB.

Examination of the sternal bone marrow showed infiltration with round cells bearing scanty cytoplasm which were described as nonhematopoeitic. Catecholamines in the blood and urine were normal. Electron microscopy studies were not done; there was no autopsy. The patient began treatment, first with radiotherapy (4000 rads) over the cervical and thoracic spine. After one dose of radiotherapy, chemotherapy was started with dexamethasone plus cyclophosphamide and adriamycin. After the first cycle the neurological situation was stable, but he developed an abscess in the gluteal region and therefore the treatment was discontinued. Ten months after beginning treatment, there was radiological evidence of disseminated disease, and a month later, 16 months after the onset of illness, the patient died.

Discussion

The difficulty of establishing a diagnosis of ANB is a reality (Mackay *et al.*, 1976; Reynolds *et al.*, 1981; Kaye *et al.*, 1986; Eto *et al.*, 1986). NB in general occurs with spinal cord compression in only 1 to 4% of cases (Punt *et al.*, 1980; Reyne *et al.*, 1986). The symptoms of onset may include pain, particularly radicular pain, limb weakness, urinary retention and constipation or loss of sphincter control and paraplegia. The average age at presentation was 34 (range 16–75) in the world literature. The duration of symptoms before the diagnosis could be made and surgery carried out has been between 6 weeks to 84 months in the various reports (Akwari *et al.*, 1978; King *et al.*, 1976).

When involvement of the bladder and rectal sphincters was observed, this were associated with severe and irreversible compression of the spinal cord.

It is evident that early and accurate diagnosis can prevent severe neurological changes and prolonged morbidity (Balakrishnan *et al.*, 1974; King *et al.*, 1975; Punt *et al.*, 1980, Massad *et al.*, 1985).

Because osseous metastases are frequent, spinal cord compression is common in the terminal stages of NB in general (Punt *et al.*, 1979). Most NB arise in an adrenal gland, but 16% originate in the sympathetic ganglia (Siegel *et al.*, 1986). The pathologist must consider ANB in the differential diagnosis of all small cell neoplasms affecting the adult population (Reynolds *et al.*, 1981; Aleshire *et al.*, 1985; Kaye *et al.*, 1986).

There is difficulty in establishing a diagnosis of ANB, especially if conventional light microscopy alone is used. ANB is among the histological group of 'small dark cell tumours' defined by cells that are 12 μm in diameter with round to oval hyperchromatic nuclei and scanty cytoplasm which often exhibit Homer-Wright rosette formation (Aleshire *et al.*, 1985). Electron microscopy helps to establish an exact diagnosis of ANB. Long cytoplasmic processes resembling axons or dendrites and synaptic junctions are two findings which indicate ANB with electron microscopy (Misugi *et al.*, 1968; Mackay *et al.*, 1976; Hashimoto *et al.*, 1983; Aleshire *et al.*, 1985; Kaye *et al.*, 1986.). Dense core neurosecretory granules, microtubules and intermediate filaments are other characteristics of ANB, but they are nonspecific findings.

In adults there is liable to be confusion with lymphomas and undifferentiated small cell carcinomas (In these cases common leucocyte antigen and epithelial membrane antigen are respectively positive). The diagnosis of these tumours should be made by a combination of methods.

NB resulted in excretion of elevated quantities of catecholamines and their by-products. Because measurement of these metabolites is not reported in many of the published cases on ANB, it is unclear whether they are elevated. In 25% of cases there is no increase of catecholamine excretion. (Gitlow *et al.*, 1970; Dosik *et al.*, 1978.).

Many NB tumour markers are reported like gangliosides, sialic acid containing glycosphingolipids (Ladish *et al.*, 1985); Tetanus toxin (TT) (Berliner *et al.*, 1984); Serum ferritin (Hann *et al.*, 1980); Neuron Specific Enolase (Vinores *et al.*, 1984); S-100 protein and bombesin (Kay *et al.*, 1986), but they are also found in other 'Small dark cell tumours' (Seeger 1982; Beemer *et al.*, 1984) and other tumours of neuronal origin.

Although the final diagnosis always rests on surgical exploration and histological examination of the tumour, there are multiple radiological studies for evaluating a patient with known or suspected NB (Fagan *et al.*, 1974; Resjo *et al.*, 1979).

If the tumour is paraspinal and the patient has spinal cord involvement myelography and/or a metrizamide CT scan are essential, MRI is a noninvasive procedure which appears to have clinical advantages in evaluating intraspinal neoplasms and their response to therapy. It provides excellent differentiation of soft tissue planes without the need for ionising radiation or contrast injection (Cohen *et al.*, 1984; Siegel *et al.*, 1986; Dietrich *et al.*, 1986). It has been our practice to care for these patients as a team in a multidisciplinary Spinal Cord Injury Unit.

Knowledge of the site of the primary local tumour, its extent, histological degree according to the criteria of Shimada, as well as a precise knowledge of the stage of the disease are essential for proper treatment and prognosis (Evans *et al.*, 1976; Coldman *et al.*, 1980; Shimada *et al.*, 1984; Evans *et al.*, 1987).

Surgery is the mainstay of treatment for patients with localised disease (Akwari *et al.*, 1978; Massad *et al.*, 1985; Allan *et al.*, 1986; Kaye *et al.*, 1986), and chemotherapy for those with metastatic spread (Dosik *et al.*, 1978; Lopez *et al.*, 1980). Radiation therapy is used to treat gross residual disease and may sometimes render an inoperable tumour operable (Massad *et al.*, 1985; Allan *et al.*, 1986; Holperin *et al.*, 1986). Surgical intervention is urgently indicated once an intraspinal component has been defined. There is no assurance that symptoms and signs of compression of spinal cord or other vital structures, e.g. respiratory tract (Akwari *et al.*, 1978) will be resolved after extirpation of the tumour.

Despite the common presentation of adult NB as stage III or IV, in 40% of cases of ANB, initial aggressive surgical therapy is best (Mackay *et al.*, 1976; Dosik *et al.*, 1978; Lopez *et al.*, 1980; Aleshire *et al.*, 1985). It is essential to search for evidence of disease in other areas. Bone marrow aspiration is essential, regardless of the findings in the peripheral blood.

The prognosis of patients with metastasic NB is poor but may be improved with chemotherapy (Kinnier *et al.*, 1974; Lopez *et al.*, 1980). For those patients who have had aggressive surgery, the median survival is 20.5 months compared with 12.5 months for those not receiving surgery. The median survival of those also receiving chemotherapy was 18 months compared with 13 months in those not receiving chemotherapy (Salaskrishnan *et al.*, 1974; Lopez *et al.*, 1980; Allan *et al.*, 1986; Kaye *et al.*, 1986).

Physical therapy, bracing when necessary and frequent re-evaluation will provide the opportunity for maximal functional rehabilitation. Development of spinal deformity after destruction of spinal components is not a problem in adults although pre-existing deformity may progress. The achievement of complete remission and/or prolongation of survival are realistic aims in the management of NB in adults.

Dedication

To my Father.

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