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Spinal ganglioneuroblastoma – complete response to chemotherapy alone

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Summary: Ganglioneuroblastoma in the spinal region is rare, the treatment of choice being surgical excision. We present a 21 year old male who was diagnosed to have this condition in the dorsolumbar spinal region. The tumour was extending intraspinally and was unresectable. Combination chemotherapy with Adriamycin® (doxorubicin hydrochloride), vincristine, cyclophosphamide, etoposide, ifosfamide and cisplatin resulted in histologically proven complete remission. No radiotherapy or curative resection was done. The patient is alive without evidence of disease 24 months later. Never before has chemotherapy been successfully used as the sole modality of treatment in this condition. Our report raises important questions about the management of this rare condition, particularly in a situation of unresectability.

Introduction

Neuronal tumours of the central nervous system (CNS) are rare. They are classified as ganglioglioma, ganglioneuroma, ganglioneuroblastoma and neuroblastoma. These related tumours have a common origin from primordial neural crest cells and reflect different maturation patterns of a common neoplasm. Neuroblastoma is the least differentiated containing primitive neuroblasts, ganglioneuroblastoma possesses both primitive neuroblast and ganglion cells, while ganglioneuroma is a fully differentiated form containing mature Schwann cells and ganglion cells.¹ The

treatment of choice for both cerebral and spinal ganglion cell tumours is surgical excision.^{2,3} Radiotherapy is given for residual disease, recurrence or progression.² Although adjuvant chemotherapy has been used in ganglioneuroblastoma with variable results^{4,5} there is no report of the use of chemotherapy as the sole modality of treatment. We report a 21 year old man who achieved complete remission following combination chemotherapy.

Case report

A 21 year old man was referred to the medical oncology department of this hospital in November 1990. He was earlier admitted to the orthopaedics ward for backache, wasting and weakness of his

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right leg of 3 months duration. He was immobilized because of severe pain, there was wasting and weakness (Power grade 2/5) of hip flexors and extensors. Blood pressure was normal and there was no lymphadenopathy. His haematological and biochemical parameters, chest X-ray and electrocardiography were normal. A computed tomographic (CT) scan of the spine revealed a soft tissue mass 3 cm wide extending from the dorsal 10 to lumbar 4 vertebra. The mass extended intraspinally and up to the chest displacing the right crus of the diaphragm. There was also the destruction of lumbar 2 and 3 vertebral bodies. A True-cut biopsy of the mass revealed ganglioneuroblastoma (Figure 1). Urinary vanillylmandelic acid was elevated marginally to 2.5 ng (normal 2.4 ng). The tumour was considered unresectable by the orthopaedic surgeons and it was therefore decided to try chemotherapy, to be followed by surgical resection in the event of reduction of the size of the tumour. The chemotherapy given was as follows.

(A) Adriamycin® (doxorubicin hydrochloride) 50 mg/m² on day 1, cyclophosphamide 1 g 700 mg/m² on day 1, vincristine 1.4 mg/m² on day 1 all intravenously. Three such courses at 3 week intervals were followed by:

(B) etoposide 100 mg/m² on days 1, 2, 3, ifosfamide 1 g/m² on days 1–5 along with mesna, cisplatin 20 mg/m² on days 1–5 all by slow infusion and appropriate hydration. (Three courses at 3 weeks intervals).

Assessment after two courses of chemotherapy revealed complete disappearance of pain and return of good power. The patient was able to walk without help. A repeat CT scan at this stage revealed a partial response (more than 50% reduction) in the tumour mass. In view of the fact that the patient tolerated chemotherapy very well and there was a good response, chemotherapy was con-

tinued. Drugs were selected based on stray reports of response as seen from the literature. The aim was to give the patient a broad spectrum exposure to anti-cancer drugs. A follow-up CT scan and T₁-weighted magnetic resonance image revealed near-complete clearance of the tumour except for a small residual opacity (very good partial response, defined as more than 90% reduction in tumour mass). The patient was surgically explored at the end of the chemotherapy and a small 1 × 1 cm residual lesion completely removed. Histopathology of this revealed fibrous tissue. There was no tumour. The patient remains well 24 months later and a recent follow-up CT scan has not shown any abnormality.

Discussion

Ganglioneuroblastoma is predominantly encountered in older children and adolescents. The commonest site is the adrenal medulla and the most common extra-adrenal site is posterior mediastinum.⁵ The most common site in the brain is the temporoparietal lobe followed by the cerebral hemisphere, the floor of the third ventricle, the brain stem, the cerebellum and the spinal cord.¹ Ganglion cell tumours of the spinal cord are extremely rare. So far only 16 cases have been reported.^{6,7} The standard treatment of ganglioneuroblastoma is complete surgical excision.⁵ Radiotherapy is given in an adjuvant setting if the patient is over 12 years old, if there is incomplete excision, or if the tumour is of a composite pattern. Information regarding the use of chemotherapy as the major mode of treatment of ganglioneuroblastoma is limited. In a large series of 80 patients of posterior mediastinal ganglioneuroblastoma, Adam treated two unresectable ganglioneuroblastoma with chemotherapy and radiotherapy.¹ A 10 year old patient treated with cyclophosphamide and 1,810 cGy radiation therapy was alive for 5 years post-treatment. Another one year old patient treated with cyclophosphamide and 2,500 cGy radiation therapy achieved complete remission and had no evidence of disease for 16 years. Since both these patients were given both radiotherapy and chemotherapy, it is difficult to pinpoint the source of benefit. Kilton reported two patients, one patient with stage IV disease received cyclophosphamide 15 mg/kg and vincristine 0.025 mg/kg without any response and the other patient with paraspinal ganglioneuroblastoma received three courses of similar chemotherapy following a laminectomy, without any change in the size of the tumour.⁴ To the best of our knowledge ours is the first ever case of ganglioneuroblastoma in which complete remission has been achieved with chemotherapy alone.

Figure 1 Histopathology of the Trucut biopsy of the tumour before chemotherapy showing typical features of ganglioneuroblastoma (H & E, × 400).

Ganglioneuroblastoma may infiltrate locally as well as metastasize by way of haematogenous and lymphatic channels, as does neuroblastoma. Ganglioneuroblastomas are slow growing tumours and long-term postoperative survivals have been reported in many clinical series.^{2,3,8} The prognosis is generally favourable with 2 year survival of 92% and 5 year survival of 88% in a large series.¹ Spontaneous regression of neuroblastoma is well documented and there is evidence in the literature that many of the so-called cures in neuroblastoma are in fact spontaneous regression. In our patient no mature ganglioneuroma was found on excision and response occurred only after chemotherapy, too close a coincidence for spontaneous regression.

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Is clubbing a feature of the anti-phospholipid antibody syndrome?

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Summary: A patient with the anti-phospholipid antibody syndrome and digital clubbing is described. No recognized cause for the clubbing was found. It is suggested that platelet aggregation and microthrombi formation as a result of anti-phospholipid antibody may be involved in the pathogenesis of the digital clubbing. This may be a new feature of the anti-phospholipid antibody.

Introduction

Digital clubbing is a recognized feature of many respiratory, cardiac and gastrointestinal diseases. We describe a case of clubbing in a man with the anti-phospholipid antibody syndrome, with no

other recognized cause for his clubbing, and suggest that this may be a feature of this condition.

Case report

A 48 year old retired safe-maker was referred for investigation of abnormal liver function tests. In

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