Surgery Journal 2 (1): 1-4, 2007

Missed Diagnosis of Non-Hodgkin's Lymphoma in an Elderly Patient Presenting with Spinal Cord Compression

[1]T.O. Odebode, [2]I.A. Adigun and [3]M.O. Buhari
[1]Department of Surgery, Division of Neurosurgery,
[2]Department of Surgery, Division of Plastic and Reconstructive Surgery,
[3]Department of Pathology, University of Ilorin Teaching Hospital, Ilorin, Nigeria

Abstract: Spinal Cord Compression (SCC) occurring in an adult with Neurofibromatosis Type-1 (NF-1); is most readily attributed to a spinal neurofibroma or a metastasizing neurofibrosarcoma. Rare causes including Non-Hodgkin's Lymphoma (NHL) are seldom considered in the list of differentials. We report a 65-year-old man who had clinical features of neurofibromatosis type-1 since childhood. He first presented to our neurosurgical service two months after he developed weakness and anesthesia in lower extremities, incontinence of urine and faeces and progressive weight loss. He had developed a large painless midline mass in the lowback two years earlier. Examination revealed multiple café-au-lait macules, axillary frecklings, a subcutaneous nodule and a firm plexiform lumbosacral mass. A dorso-lumbar CT scan showed a large lobulated soft tissue mass over the lumbosacral segment involving the gluteal and the paraspinal muscles, with intraspinal extension causing L_{3-5} vertebral collapse and epidural compression. Lytic lesions were also apparent in the iliac bones and L_{3-5} vertebral bodies. A decompressive laminectomy and biopsy was done and subsequent histological findings were consistent with the diagnosis of mixed cell non-Hodgkin's lymphoma. He was commenced on steroid therapy but he refused planned radiotherapy and cytotoxic chemotherapy opting for a voluntary discharge. He died three weeks afterward. This case illustrates the grave consequence that accompanies a belated diagnosis of a treatable condition and that cord compression is not always due to NF1 related lesions in patients with NF-1. The significance of histological verification of mass lesions of NF-1 in avoiding missed diagnosis cannot be overemphasized.

Key words: Spinal-cord-compression, non-hodgkin's lymphoma, neurofibromatosis, paraspinal muscles, cytotoxic

INTRODUCTION

Although neurofibromatosis type-1 represents a major risk factor for the development of malignancy, it is rarely associated with non-Hodgkin lymphoma, with one case having been reported in the medical literature (Kim *et al*., 2003). When an adult patient with neurofibromatosis type-1 presents in with SCC, a malignant transformation of a neurofibroma to a neurofibrosarcoma with metastases to the spine or a spinal intradural neurofibroma is usually considered being responsible. Because Spinal Cord Compression (SCC) is a rare initial manifestation of Non-Hodgkin's Lymphoma (NHL) (Lu, 2005; Simiele *et al*., 2003; Acquaviva *et al*., 2003; Wei *et al*., 2001) occurring usually in the setting of progressive advanced disease, it is rarely suspected as a cause of cord compression especially in the setting of NF-1. We report an elderly man with NF-1 presenting with spinal cord compression due to a co-existing NHL, to illustrate the rarity of this association and the tendency of this association to result in missed diagnosis.

CASE REPORT

A 65-year-old elderly male had developed café-au-lait macules, axillary freckling and a subcutaneous nodule since childhood but took them for birthmarks (Fig. 1). Two years prior to presentation to our Neurosurgical service, he developed a painless lumbosacral mass, which progressively increased in size. This increase was exaggerated at two months before presentation when he also developed a low-back ache, weakness and numbness of both lower extremities, incontinence of faeces and urine, severe weight loss and low-grade fever. Examination revealed marked wasting, left cervical lymphadenopathy, twelve café-au-lait macules of varying

Corresponding Author: T.O. Odebode, Department of Surgery, Division of Neurosurgery, P.O. Box .5173, Central PO, Ilorin 24001, Kwara State, Nigeria

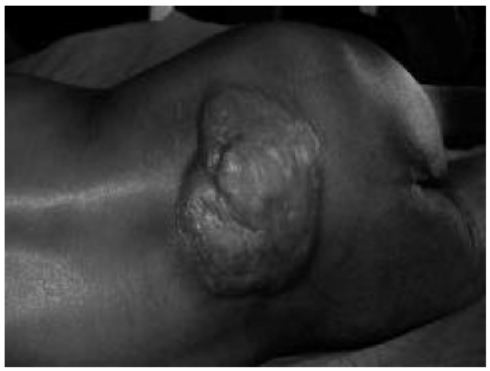

Fig.1: A 65-year-old man with non-hodgkin's lymphoma and neurofibromatosis type-1 showing a large lumbosacral mass

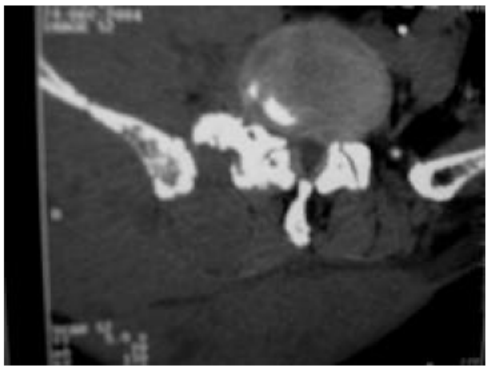

Fig. 2: Lumbosacral spinal computerized tomography scan showing a soft tissue mass infiltrating the gluteal and paraspinal muscles and causing collapse of L_3-L_5 vertebrae and epidural cord compression

sizes, left upper arm subcutaneous nodule, freckles in both axilla and a 25 by 20 cm firm plexiform lumbosacral mass spanning D_{12}-L_5 vertebral levels (Fig. 1). There were neither Iris lisch nodules nor bony abnormalities. He had a spastic paraplegia at L_2, neurogenic bladder and a rectal incontinence.

A lumbar puncture for CT myelography was technically difficult because of the location of the lumbosacral mass, a dorso-lumbar CT scan was done which demonstrated a large lobulated soft tissue mass over the lumbosacral segment involving the gluteal and the paraspinal muscles, with intraspinal extension causing L_{3-5} vertebral collapse and epidural compression (Fig. 2). Lytic lesions were also apparent in the iliac bones and L_{3-5} vertebral bodies. There was no evidence of

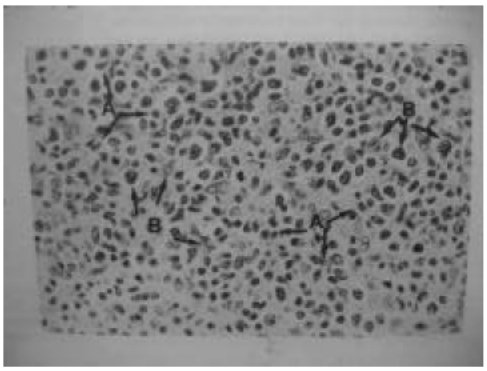

Fig. 3: Photomicrograph of surgical specimen of the patient shown in Fig 1, showing diffuse mixed small, medium and large lymphoid cells infiltrating the dermis, subcutaneous tissue and underlying muscle (H and sE×440)

intra-abdominal metastases (Fig. 2). The chest radiograph, blood chemistry, hepatic and renal functions were normal and peripheral blood smear was normo-cellular. ESR by Westergren was slightly elevated (35 mm h^{-1}). He was negative for HIV 1 and 2 by ELISA technique.

A decompressive laminectomy and excision of the lumbosacral mass revealed a highly vascular lesion. Histology of the excised lesion demonstrated diffuse sheets of mixed small, medium and large lymphoid cells infiltrating the dermis, the subcutaneous tissue and the underlying muscle, consistent with a diagnosis of diffuse mixed cell (small, medium and large cells) Non-Hodgkin's lymphoma (Fig. 3). He was commenced on prednisolone and planned for radiation therapy and chemotherapy. However the patient declined further treatment opting for a voluntary discharge and he died two weeks afterward.

DISCUSSION

Though NF-1 has been found to coexist with other tumours such as chodromyxoid fibroma (Odebode *et al*., 2005) ampullary carcinomas (Costi *et al*., 2001) mycosis fungoides (Broam *et al*., 2002) and central nervous system lymphomas, NHL (Kim *et al*., 2003) remains a rare association with NF-1. NHL presenting with initial spinal cord compression and coexisting with NF-1 in an elderly patient is extremely rare and the mechanism underlying the co-existence is unknown. It is possible that the association is serendipitous being due to chance but it could be familiar or genetic being due to some NF1 mutations, which increase the risk of malignancy (Bruce, 2000).

Apart from other skin lesions of NF-1, the lunbosacral mass in this patient mimicked a plexiform neurofibroma, thus strengthening the erroneous impression that cord compression in him was due to a spinal neurofibroma. A recent increase in size of the lesion also suggested malignant transformation to a neurofibrosarcoma. The flaws against these differentials are the patient's age and the rarity of neurofibrosarcoma in individuals with NF1. A plexiform neurofibroma occurs most commonly in childhood while neurofibrosarcoma occurs in only 3% of affected cases (Schneither and Dawson, 1994). Histological verification of excised lesion revealed features of NHL confirming a clinical missed diagnosis. This underscores the import of histological verification of NF-1 skin mass lesions earlier emphasized by Odebode *et al*. (2005).

Paraplegia resulting from spinal cord compression and radicular involvement are infrequent events in the natural history of NHL (Lu, 2005; Simiele *et al*., 2003) as well as the mimicked spinal neurofibroma and neurofibrosarcoma. When these occur in NHL, they are usually secondary to the invasion of the spinal extra-dural space by high-grade B cell lymphomas with aggressive behaviour (Simiele *et al*., 2003) from other sites and rarely are the presenting manifestations of this condition. The patient reported did not manifest evidence of advanced disease including SCC until shortly before his death. This is in consonance with previous finding. Aarbo and Walborm (1986) has opined that the duration of symptoms before the development of spinal cord compression by lymphomas can be quite long, often lasting months to years and that this distinguishes them from cases involving carcinomas of the epidural space. The survival of patients with spinal cord compression resulting from NHL varies with cytological subtype and therapy. A unique international study of 1175 patients from USA and Italy (NL PCP, 1982) confirmed that patients with a diffuse architectural tumour pattern like the case reported carry a poorer prognosis within the same cytological subtype than those with nodular or follicular architecture; (Rosenbery, 1985) the cytological subtype being useful in predicting clinical characteristics and outcome (Rosenbery, 1985). In addition, the large size (approximately 1 kg weight) of the excised lumbosasal mass also predicted a worse prognosis, the bulk of the lymphoma mass at presentation, especially for the high-grade lymphomas, being a vital prognostic factor (Gospodarowicz *et al*., 1980).

The treatment option for a patient with spinal NHL depends on the grade of the lymphoma (low, intermediate, or high), the stage of the disease, areas of the body affected and the general health of the patient. This ranges from watchful waiting in the earliest stage of the disease to high-dose chemotherapy and radiotherapy and stem cell transplantation for patients with aggressive NHL who fail to respond to standard treatment. More so than any other group of patients with a neoplasm, patients with high grade NHL like ours are highly responsive to therapy and a substantial proportion can be cured of their tumours, or would benefit from therapy with very good palliation and probable prolongation of life (Rosenberg, 1985). This benefit was discarded as the patient discharged against medical advise. A belated diagnosis made two years after recognizable clinical onset when the disease was already advanced and spinal cord compression had occurred also contributed to a poor outcome.

CONCLUSION

This case illustrates the grave consequence that accompanies a belated diagnosis of a treatable condition and that cord compression is not always due to NF1 related lesions in patients with NF-1. The significance of histological verification of mass lesions of NF-1 in avoiding missed diagnosis cannot be overemphasized.

REFERENCES

Acquaviva, A., S. Marconcini, G. Municchi, I. Vallone and L. Palma, 2003. Non-Hodgkin Lymphoma in a child presenting with acute paraplegia: A case report. Pediatr Haematol Oncol, 20: 245-251.

Aabo, K. and S. Walborm-Jorgensen, 1986. Central nervous system complication by malignant lymphoma. Int. J. Radiol Oncol Biol Phys., 12: 197-202.

Braam, P., C.J. Sanders and M.R. Canninya-van Dijk, 2002. Neurofibromatosis type 1 and mycosis fungoides. Int. J. Dermatol., 41: 236-238.

Bruce, R.K., 2000. Malignancy in Neurofibromatosis Type-1. The oncologist, 5: 477-485.

Costi, R., P. Caruna and L. Sarli *et al*., 2001. Ampullary adenocarcinoma in neurofibromatosis type-1. Case report and literature review. Mod. Pathol., 14: 1169-1174.

Gospodarowicz, M.K., R.S. Bush, D.E. Bergsagel and T.C. Brown, 1980. Bulk of Tumour as an important prognostic factor in Non-Hodgkin's lymphomas. Proc. Am. Soc. Clin. Oncol., pp: 21-463.

Kim, S.J., J.H. Seo, S.W. Lee, E. Han, *et al*., 2003. A case of Non-Hodgkin's lymphoma in a patient with neurofibromatosis type-1 Korean J. Intern. Med., 18: 202-205.

Luo, C.C., 2005. Spinal cord compression secondary to metastatic non-Hodgkins lymphoma: A case report. Arch. Phys. Med. Rehabil, 86: 332-334.

Odebode, T.O., E.A.O. Afolayan, I.A. Adigun and O.O.M. Daramola, 2005. Clinicopathological study of Neurofibromatosis Type-1: An experience in Nigeria. Int. J. Dermatol., 44: 116-120.

Rosenberg, S.A., 1985. Non-Hodgkin's Lymphoma. In: Calabresi, P., P.S. Schien, S.A. Rosenberg, (Eds.), Chapt. 16. Medical Oncology: Basic Principles and Clinical Management of Cancer, New York: Macmillan Publishing Company, pp: 476-495.

Simiele, N.A., R.N. Gomez and S.F. Novoa, 2003. Spinal epidural involvement as presentation form of Non-Hodgkin's lymphoma: Report of 6 cases. An Med. Int., 20: 466-469.

Schneither, N. and B. Dawson, 1994. Genetic Disorders. In: R.S. Cotran, V. Kumar, S.L. Robbins, (Eds.), Rubbins Pathologic Basis of disease, (5th Edn.) Philadelphia: WB. Saunders Co., pp:1352-1353.

Wei, S.H., J.M. Sheen, C.B. Huang and C.C. Hsiao, 2005. Primary spinal epidural non-Hodgkin's lymphoma in a child. Chang Gung Med. J., 24: 820-825.