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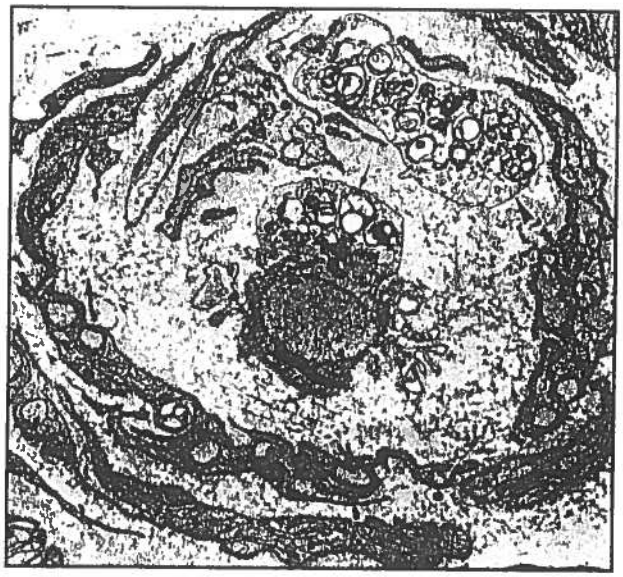

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CASE REPORT

Intraneural nerve metastasis with multiple mononeuropathies

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Abstract Although cancer is a frequent condition, neoplastic involvement of the peripheral nervous system is rare. The mechanisms are heterogeneous and include lesions within the cerebrospinal fluid (CSF) space, local invasion (e.g. brachial plexus), compression, rarely direct infiltration, perineurial spread and even rarer intranerval metastasis. A 47-year-old woman had been treated for a carcinoid 10 years earlier and had received axillar irradiation. At presentation she suffered from weakness of the biceps brachii and was experiencing pain radiating from the axilla into the forearm and thumb. MR scans of the brachial plexus were negative and her symptoms were primarily considered to stem from a postradiation brachial plexopathy. Because of increasing pain, the brachial plexus was explored and a metastasis in the left musculocutaneous nerve was resected. Several months later, numbness and pain appeared in the ulnar nerve and another intrafascicular metastasis in the ulnar nerve was discovered. Resection with preservation of remaining fascicles was performed. This rare case report demonstrates that multiple mononeuropathies, resembling multiplex neuropathy, may be caused by intranerval metastasis.

Key words: cancer, neoplastic peripheral nerve involvement, peripheral nerve metastasis, brachial plexus, ulnar nerve metastasis, mononeuropathy

Introduction

The peripheral nervous system can be involved in various settings in cancer patients *(Clouston et al., 1992; Stübgen, 1995; Hovestadt et al., 1990; Wondrusch et al., 1996).* Direct neoplastic involvement of peripheral nerve structures or nerve plexus is rare except for local involvement of brachial plexus in breast carcinoma, local spread in the sacral plexus in regional pelvic tumors and hematologic malignancies. Solitary metastasis in peripheral nerves is extremely rare and may cause a painful mononeuropathy *(Rosenberg et al., 1991).*

Other causes of peripheral nerve injury include radicular involvement by compression of infiltration, compressive or entrapment, or toxic but rarely paraneoplastic causes. In locally pre-irradiated patients, clinical symptoms of nerve injury may be hard to distinguish from tumor recurrence or radiation injury, although clinical criteria have been described *(Thomas and Holdorff, 1993).*

Case Report

A 47-year-old woman underwent surgery for a carcinoid (mediastinal site) 10 years earlier; lymph nodes in the left axilla were also removed. Postoperatively she had received local and axillar irradiation but no chemotherapy. Eight years later she noted weakness of her left biceps brachii muscle and sensory disturbances in the left cutaneous antebrachii medial nerve. Upon neurologic presentation, she described severe radiating and neuralgic pain in the left arm in an area resembling the C6 dermatome. Attacks either occurred spontaneously several times a day or mechanically, triggered by carrying loads. The duration of the neuralgic and excruciating pain episodes was 2–3 minutes. During the at-

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tacks, painful muscle twitches were described by the patient in the painful sites of the arm.

Neurologic examination

Skin changes due to local radiation were noted at the dorsal circumference of the left axilla with typical hyperpigmentation (diameter: approximately 3 × 4 cm). The palpation of the axilla and supraclavicular fossa was normal. There was severe atrophy of the left biceps brachii with inability to lift lower arm against gravity (2–3). Left BSR was absent; left RPR was diminished. Upon sensory examination there was a small hyperpathic area in the left cutaneous antebrachii medial and radial superficial nerve.

MRI scan of the cervical vertebral column and brachial plexus was negative. Electromyography (EMG) revealed denervation in the biceps brachii and an absent sensory conduction of the superficial radial nerve (Table 1). Postradiation fibrosis was suspected.

Three months later a general tumor recurrence was noted and palpation revealed a small nodule in the axilla at the caudal border of the pectoral minor muscle. Local pressure induced pain that radiated into the arm. The musculocutaneous nerve was explored and revealed a local tumor with a diameter of approximately 2.5 cm (Fig. 1). Microsurgically, no intact fascicles were found and the tumor was resected *in toto*. Intraoperative pathologic examination revealed metastasis of a carcinoid; a reconstruction of the musculocutaneous nerve was not pursued.

Postoperatively the patient was treated with hormonal therapy and interferon therapy. Three months later she noted sensory loss in left ulnar distribution, weakness and wasting of intrinsic hand muscles of her left hand. A local tumor could be palpated in the proximal bicipital ulnar sulcus. The resection showed that the tumor included some, but not all, fascicles. The tumor was microsurgically removed and the remaining fascicles provided sufficient function for ulnar nerve function (Fig. 2).

Two years after the first tumor resection, the patient's oncologic situation has stabilized and she is continuing her professional work; apart from the biceps brachii atrophy and some wasting in the intrinsic hand muscles of her left hand, she has no neurologic deficit.

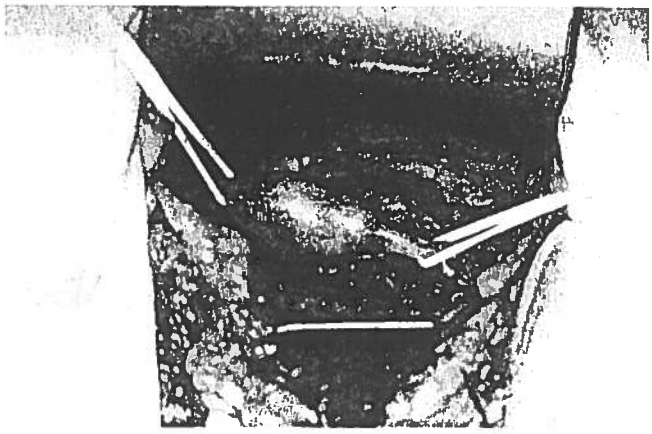

Figure 1. Intranerval metastasis, intraoperative site. Local tumor bulge caused by metastasis into musculocutaneous nerve (intraoperative photograph).

Table 1. Electrodiagnostic findings

	Distal Latency (ms)	CMAP	NCV (m/sec)
Motor NCV			
Lt median	3.21	12	47
Lt ulnar	2.6	9	58
Lt Musculocutaneous latency*	5, 8		
Sensory-NCV			
Lt median	2.9	10	66
Lt ulnar	2.9	10	48
Lt radial superficial: absent			
EMG			
Muscle	Spontaneous activity (fib., positive sharp waves)	motor unit potentials	maximum innervation
Lt deltoid	–	normal	interference pattern
Lt biceps brachii	Spontaneous activity +++	prolonged AP, markedly	reduced interference pattern
Lt EDC	-	normal	interference pattern
Lt Abductor digiti quinti	-	normal	interference pattern
Lt abductor poll. brevis	-	normal	interference pattern

CMAP, compound action potential; NCV, nerve conduction velocity.
*At first examination, approximately 3 months prior to surgery for metastasis in the musculocutaneous nerve.
Spontaneous activity is graded from absent (0) to maximum (+++).

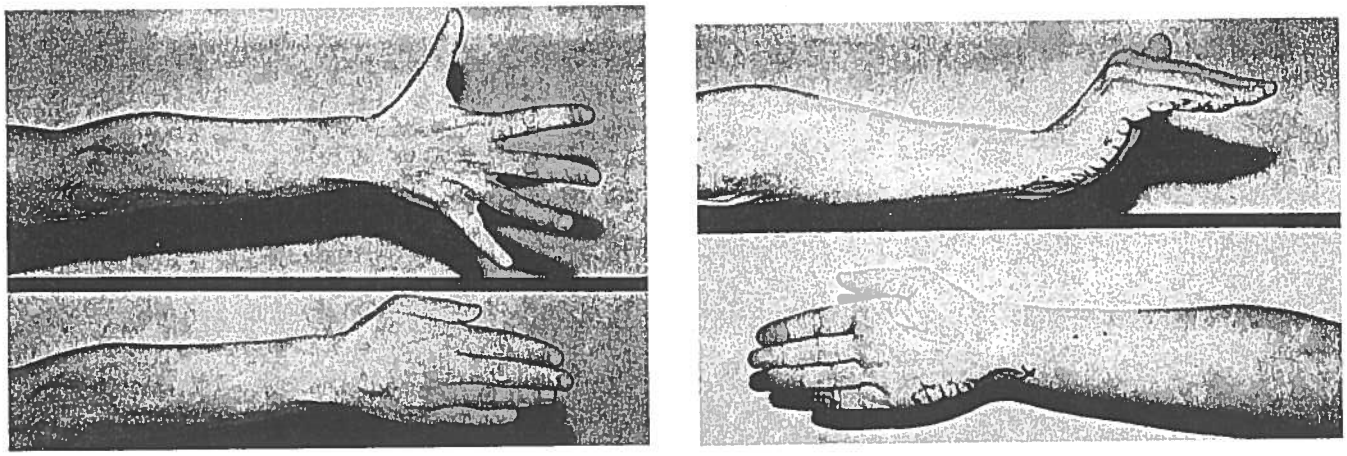

Figure 2. Intranerval metastasis. Functional recovery after ulnar nerve metastasis resection.

Histologically, metastasis of a carcinoid tumor with solid and trabecular aggregates of tumor cells were found in both peripheral nerve metastases (Fig. 3).

Immunohistochemistry of the metastasis stained positive with NSE, synaptophysin and chromogranin A and CK. Weakly positive staining was noted for anticalcitonin and antiserotonin. The staining pattern confirmed a carcinoid tumor.

Peripheral nerve structures were either compressed by tumor mass (Figs. 3-A and 3-B) or diffusely infiltrated (Figs. 3-C and 3–D). Remaining fascicles were either well myelinated or diffusely demyelinated with scarcely remaining myelinated fibers.

Discussion

The peripheral nervous system can be affected by several types of tumors *(Mumenthaler and Schliack, 1993)*. Neurofibromas usually cause pain and sensory loss. Schwannomas can remain without symptoms and may be revealed by palpation only.

In cancer patients, several types of neoplastic peripheral nerve damage have to be considered *(Hughes et al., 1996)* (Table 2). Meningeal carcinomatosis occurs in hematologic malignancies and some types of solid tumors (most frequently, breast cancer, lung cancer and melanoma) and causes cranial nerve lesion, mono- or poly-radicular *(Mackinnon and Dellon, 1988)*, or cauda equina involvement *(Grisold et al., 1998)*. Brachial plexus involvement is observed most frequently in breast or lung cancer *(Kline and Judice, 1983; Lusk et al., 1987)*, although in both malignancies plexus lesions occur at different stages of the malignancy and involve different mechanisms (lymph node involvement, direct infiltration). In pre-irradiated patients, despite the use of imaging methods and clinical criteria *(Thomas and Holdorff, 1993)*, it may be difficult to distinguish between late sequela of radiation therapy or tumor infiltration and explorative surgery may be necessary *(Van Daal and Van der Kogel, 1993)*.

Local pelvic tumors, such as intestinal, genital or urogenital, may affect the lumbosacral plexus by local spread; postirradiation sequela has also been described. Local peripheral nerve damage affects the recurrent laryngeal nerve, the phrenic nerve, and the cervical sympathetic chain predominantly in lung cancer patients *(Son, 1967)*. Other sites where adjacent tumors or metastasis cause peripheral nerve damage are the base of the skull *(Greenberg et al., 1981)*, the parotid gland, intercostal nerves, deposits at the rostral humerus (axillar nerve lesion), and the obturator nerve. A rare affection of cranial nerves described as perineurial spread has been described in melanoma patients *(Hughes and McQueen, 1995)*.

Intranerval metastasis is very rare and is usually not considered in the differential diagnostic consideration in cancer patients *(Barron et al, 1960; McLeod, 1993; Wondrusch et al., 1996)*. Leukemias and lymphomas affect peripheral nerves either by invasion, infiltration or local growths, or may have a particular growth in the peripheral nerves as in neurolymphomatosis *(van den Bent et al., 1999; Diaz-Arrastia, et al., 1992; Grisold et al., 1990)*, angioendotheliomatosis *(Glass et al., 1993; Levin and Lutz, 1996)*, or local tumorous nerve growth causing mononeuropathies as described by *Vital et al. (1989)* and *van den Bent et al. (1995)*. Also local plasmocytoma can cause peripheral nerve damage *(Hitzenberger et al., 1996)*.

Asymmetric multiplex neuropathy can occur in association with inflammatory neuropathies or vasculitis. Vasculitis has been reported to occur in association with cancer; however, there are few case reports and the presentation is not always homogenous *(Grisold and Drlicek, 1999; Oh et al., 1991)*. The occurrence of mono-

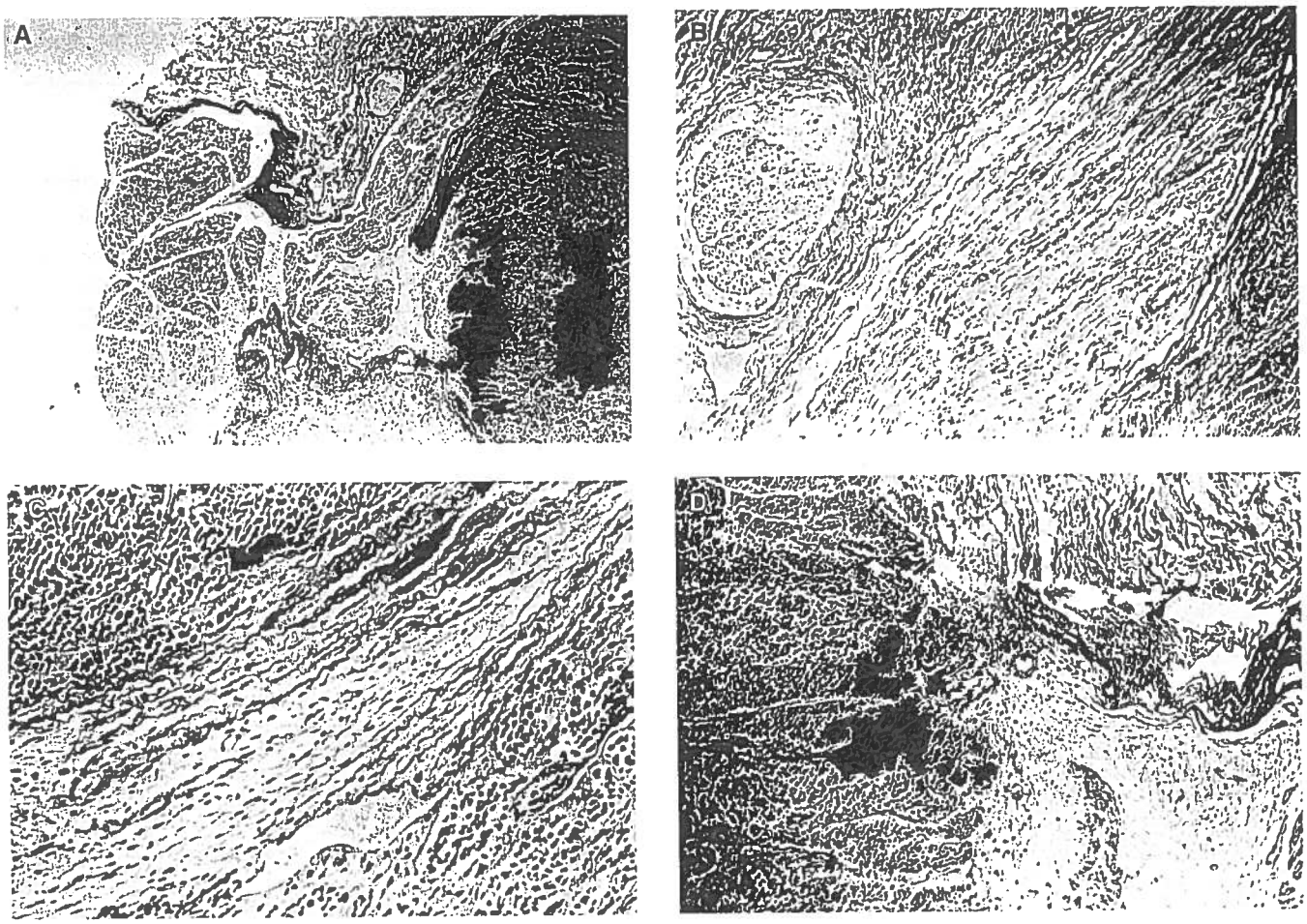

Figure 3. (A) Lower power view of local tumor adjacent to peripheral nerve structure; (B) tumor in vicinity of nerve fascicle; (C) diffusely infiltrating tumor; (D) infiltrating tumor, invading nerve tissue.

neuropathies in cancer patients other than compression is restricted to peroneal neuropathies *(Rubin et al., 1998)* and focal damage in the carpal tunnel in paraproteinemias.

Mononeuropathies and cranial nerve lesions occurring in patients treated with chemotherapy can be directly induced (e.g. vincristine), or a possible influence of toxic neuropathies can be speculated upon. Most frequently, symmetric polyneuropathies of different types can be expected *(Windebank, 1999)*. Cranial nerve lesions are most frequently caused by tumour compression (e.g. base of the skull) or infiltration (as in meningeal carcinomatosis).

This case demonstrates that the peripheral nerves may be the site of intranerval metastasis. The presentation was a painful mononeuropathy that was first attributed to a radiation fibrosis. This view was supported by the negative MRI scan of the brachial plexus. General tumor spread and repeated careful palpitation of the axilliary fossa indicated exploratory surgery, revealing the local metastasis in the musculocutaneous nerve. Microsurgically, the whole diameter of the musculocutaneous nerve was affected by tumor and complete resection was necessary.

The ulnar nerve metastasis occurred several months later, indicated by sensory symptoms. In this case the metastasis was successfully removed, preserving sufficient fascicles for the ulnar nerve function to remain.

Some uncertainty prevailed at the time of diagnosis of the primary tumor 10 years earlier, but reevaluation of tumor metastasis with modern immunohistochemistry techniques confirmed a carcinoid tumor. Metastasis of carcinoid tumors primarily affect the lung. Neurologic complications of carcinoids have been subject to investigation *(Patchell and Posner, 1986)*. The reason this tumor affected peripheral nerves on 2 occasions and 2 different sites remains unclear.

Acknowledgements

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Table 2. Sites of peripheral nerve damage in cancer patients

Structure	CSF	Local infiltration	Diffuse invasion	Compression	Perineurial spread	Fascicular metastasis
Cranial nerve	+	+	+ leukemia and lymphoma	+	+	
Radicular lesion	+	+	+	+		
Cauda equina	+	+ leptomeningeal carcinomatosis	+ leukemia and lymphoma	+		
Brachial plexus		+	+	+		
Lumbar and sacral plexus		+	+	+		
Peripheral nerves			leukemia and lymphoma			
Mononeuropathies				+		
Autonomic nervous system		+ e.g.,cervical sympathetic chain		+		

+ = involvement

References

Barron KD, Rowland LS, Zimmerman HM (1960). Neuropathy with malignant tumour metastases. J Nerv Ment Dis 131:10–31.

Clouston PA, DeAngelis LM, Posner JB (1992). The spectrum of neurological disease in patients with systemic cancer. Ann Neurol 31:268–273.

Diaz-Arrastia R, Younger DS, Hair L, Inghirami G, Hays AP, Knowles DM, Odel JG, Fetell MR, Lovelace RE, Rowland LP (1992). Neurolymphomatosis: A clinicopathological syndrome reemerges. Neurology 42:1136–1141.

Glass J, Hochberg FH, Miller DC (1993). Intravascular lymphomatosis. A systemic disease with neurologic manifestations. Cancer 71:3156–3164.

Greenberg HS, Deck MD, Vikram B, Chu FC, Posner JB (1981). Metastasis to the base of the skull: Clinical findings in 43 patients. Neurology 31:530–537.

Grisold W, Marcus D, Ulrike S (1998). LC: Clinical syndrome in different primaries. J Neurooncology 38:103–110.

Grisold W, Jellinger K, Lutz D (1990). Human neurolymphomatosis in a patient with chronic lymphatic leukemia. Clin Neuropathol 9:224–230.

Grisold W, Drlicek M (1999). Paraneoplastic neuropathy. Curr Opin Neurol 12:617–625.

Hitzenberger P, Balogh C, Grisold W, Piza H, Zifko U (1996). Radial nerve compression by an amyloid tumor [abstract]. Eur J Neurol 3(Suppl 5):214.

Hovestadt A, Van Woerbom CM, Vecht CJ (1990). Frequency of neurological disease in a cancer hospital. Eur J Cancer 26: 766–767.

Hughes R, Sharrack B, Rubens R (1996). Carcinoma and the peripheral nervous system. J Neurol 243:371–376.

Hughes TAT, McQueen INF (1995). Neurotropic malignant melanoma presenting as a trigeminal sensory neuropathy. J Neurol Neurosurg Psychiatry 58:381–382.

Kline DG, Judice DJ (1983). Operative management of selected brachial plexus lesions. Neurosurgery 58:631–649.

Levin KH, Lutz G (1996). Angiotrophic large cell lymphoma with peripheral nerve and skeletal muscle involvement. Early diagnosis and treatment. Neurology 47:1009–1011.

Lusk MD, Kline DG, Garcia CA (1987). Tumors of the brachial plexus. Neurosurgery 21:439–453.

Mackinnon SE and Dellon AL (1988). Tumors of the peripheral nerve. In: Surgery of the Peripheral Nerve, 6. Aufl Thieme, Stuttgart, pp. 535-548.

McLeod JG (1993). Paraneoplastic neuropathies. In: Peripheral Neuropathy (Third Edition). Dyck PJ, Thomas PK, Griffin JW, Low PA, Poduslo JF (Eds). WB Saunders, Philadelphia, pp 1583–1590.

Mumenthaler M, Schliack H (1993). Läsionen peripherer Nerven. Georg Thieme Stuttgart, New York, p 21.

Oh SJ, Slaughter R, Harrell L (1991). Paraneoplastic neuropathy: A treatable neuropathy. Muscle Nerve 14:152–156.

Patchell RA, Posner JB (1986). Neurologic complications of carcinoid. Neurology 36:745–749.

Rosenberg AE, Dick HM, Botte MJ (1991). Benign and malignant tumors of peripheral nerve. In: Operative Nerve Repair and Reconstruction. Gelbermann RH (Ed). J.B. Lippincott Company, Philadelphia, pp 1587–1625.

Rubin DI, Kimmel DW, Cascino TL (1998). Outcome of peroneal neuropathies in patients with systemic malignant disease. Cancer 83:1602–1606.

Son YH (1967). Effectiveness of irradiation in peripheral neuropathy caused by malignant disease. Cancer 20:1447–1450.

Stübgen JP (1995). Neuromuscular disorders in systemic malignancy and its treatment. Muscle Nerve 18:636–648.

Thomas PK and Holdorff B (1993). Neuropathy due to physical agents. In: Peripheral neuropathy (Third Edition). Dyck PJ, Thomas PK, Griffin JW, Low PA, Poduslo JF (Eds). WB Saunders, Philadelphia, pp 990–1013.

Van Daal WAJ, Van der Kogel (1993). Non metastatic complications. 14.1. Side effects of radiation on the nervous system. In: Neuro-oncology. Twijnstra A, Keyser BW, Ongerboer der Visser (Hrsg), Elsevier, pp 357–365.

van den Bent MJ, de Bruin HG, Beun GD, Vecht CJ (1995). Neurolymphomatosis of the median nerve. Neurology 45:1403–1405.

van den Bent MJ, de Bruin HG, Bos GM, Brutel de la Riviere G, Sillevis Smitt PA (1999). Negative sural nerve biopsy in neurolymphomatosis. J Neurol 246:1159–1163.

Vital C, Heraud A, Vital A, Coquet M, Julien M, Maupetit J (1989). Acute mononeuropathy with angiotrophic lymphoma. Acta Neuropathol (Berl) 78:105–107.

Windebank AJ (1999). Chemotherapeutic neuropathy. Curr Opin Neurol 12:565–571.

Wondrusch E, Zifko U, Grisold W, Drlicek M, Setinek U (1996). Neuromuscular disorders in systemic malignancy and its treatment [letter]. Muscle Nerve 19:1362–1363.