Analysis of Cancer Pain by the Neurologist

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Introduction

In patients with cancer pain the aim of the neurological diagnosis is the classification of the origin of the pain, with discrimination between structural damage and primary or secondary dysfunction. In cases in which the pain is the first sign of disease, the neurological examination can lead to the detection of the primary lesion. The etiological classification of the pain and its division into individual components allows optimal treatment of the pain and follow-up.

In cancer patients pain can be caused by severe structural damage or, alternatively, it can arise as a combination of several factors. Therefore, it is often not possible to make a diagnosis by the consideration of a single symptom, but only by differential examination of all the body structures in which dysfunction occurs, either from the primary disease or secondarily from the pain syndrome. The cancer pain can be caused by damage of the neuronal structures or can occur as receptor pain.

Pain from Lesions of Neuronal Structures

Lesions of the Peripheral Nerves

Peripheral nerve lesions caused by compression or infiltration of a tumor can lead to an altered afferent pattern, and thus to deafferentation pain through impairment of the integrity of the afferent nerve fibers. Sensory, motor, and vegetative disturbances also occur. The structural lesion can be present in the nerve root, nerve plexus, or peripheral nerve.

Radicular Syndrome

A radicular syndrome arises from primary or secondary blastomatous processes in the region of the vertebrae but can also arise intrathecally from tumors of the nerve roots and their sheaths (Table 1). Paravertebral tumors can also produce root damage. The lesions of the nerve root and the dural sheath lead to violent pain, which usually radiates to the periphery of the relevant dermatome.

Movements which cause stretching or compression of the nerve roots concerned provoke a characteristic radicular pain (Fig. 1). Examination reveals dysfunction of the sensory system in the form of hypoesthesia in the involved dermatome, and in the motor system in

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Table 1. Radicular syndrome

Pain	*Radiation* usually into the periphery of the dermatome
	Provocation by spinal movement, stretching of nerves, pressure on nerves
	Intensity often toothache-like
Sensibility	*Hypoesthesia* in the dermatome
Motoricity	*Paresis* of the corresponding muscle
	Atrophy – reduced or absent tendon reflex
Associated symptoms	*Dysfunction* and *irritation* in typical parts of the spine

Fig. 1. Femoralis Lasègue: stretch movement of the N. femoralis by bending the knee and stretching the hip

the form of partial paralysis and atrophy of the muscles with reduction or absence of tendon reflexes. Neuro-orthopedic examination usually reveals irritation symptom of the spinal egments with monosegmental as well as multisegmental dysfunction (e.g., stiff neck, lumbago).

Lesions of the Nerve Plexus

Irritation or lesion of the nerve plexus or peripheral nerves caused by a tumor leads to projection of pain into the areas served by these nerves. Sometimes pain is delayed or may be absent. The sensibility test shows hypalgesia, but also dysesthesia and hyperalgesia in parts of the involved area. Lesions of motor fibres cause partial paralysis and atrophy of the involved muscles, with reduced or absent tendon reflexes. Changes of the autonomic nervous system can lead to alteration of the vasomotor function and cause trophic dysfunction.

Cauda Equina Syndrome

Bilateral paralysis, hypoesthesia, pain in the lower extremities, and bladder and rectal dysfunction are typical symptoms of a cauda equina syndrome, which can be caused by a tumor in the region of the lumbosacral canal.

Paraneoplastic Syndrome

A peripheral neuron lesion does not only occur as a direct result of tumor growth, infiltration, or compression, but also as a consequence of the carcinomatous disease in the form of a paraneoplastic neuropathy, somtimes accompanied by a paraneoplastic myopathy. Because of the poor general condition of the patient, a herpes zoster with severe pain in the affected dermatome may result, usually with involvement of the nerve roots, which exhibit a mechanical lesion from metastases of the spine. This may often be the first sign of a carcinomatous lesion.

Side Effects of Therapy

Peripheral nerve damage can also occur secondarily as a result of cancer therapy. Nerve lesions due to radiation are most frequently found in the region of the plexus brachialis in mammary tumors, in the plexus lumbosacralis, and in the nervus femoralis (Stöhr 1980). Radiogenic vascular damage, in the form of a proliferative radiation vasculopathy or a radiation-induced fibrosis, leads to nerve damage. Moreover, operative therapy, especially radical operations, can lead to lesions of the peripheral nerves. Lymphatic edema can cause lesions of the plexus and peripheral nerves. Phantom stump pain is sometimes experienced following amputation of the limbs. A further iatrogenic impairment of the peripheral nerves is possible following treatment with cytostatic drugs leading to neuropathy with pain, and can be associated also with a myelopathy and encephalopathy. Likewise, polyneuropathy, accompanied by pain, can result from malabsorption and malnutrition.

Spinal Cord Lesions

A carcinomatous process can cause partial paralysis as a result of compression or infiltration of the spine, as well as secondary myelopathy following radiotherapy. At the same time, pain in the affected spastic musculature as well as shooting pains and phantom sensations in the paralyzed limbs can occur (Berger and Gerstenbrand 1981).

Cerebral Lesions

Primary or secondary brain tumors can cause central pain in the form of thalamic pain when the posterior thalamic structures are involved. This can manifest itself as an intolerable pain in one side of the body, accompanied by various dysesthesiae. Headache associated with intracranial tumor can be caused by deposits in the meninges or by increased volume of the brain. According to Weber (1970), headache occurs in 60%–80% of patients with cerebral tumors and in 80%–100% with tumors in the posterior cranial fossa, whereas 40% of brain tumor patients do not complain of headache. Headache and facial pain caused by an intracranial tumor usually start paroxysmally in a projection zone and later become persistent and diffuse.

Pain Caused by Stimulation of Pain Receptors

Whereas it is usually easy to clarify the origin of pain in a carcinomatous lesion of the peripheral or central nervous system, cancer pain as a result of irritation of the pain receptors presents many differential diagnostic problems. Pain receptors, which react to pressure, traction, endogenous or foreign chemicals, temperature, are present in all body structures with the exception of the brain and spinal cord. Provocation of these pain receptors can occur primarily as pressure or traction from the tumors, or secondarily as muscle or joint pain caused by the dysfunction of the motor system. Chemosensitive pain receptors can be stimulated by the liberation of endogenous pain substances, but also by the side effects of chemotherapeutic drugs (Swerdlow 1978). The various causes of receptor pain will not be dealt with in greater detail here.

Lesions of Visceral Structures

Stimulation of pain in the visceral structures can give rise to local pain, as well as referred pain, caused by irritation of larger parts of organs. Moreover, the facilitation and convergence phenomena of the spinal cord can cause a referred visceral pain syndrome, with radiation of organ-specific pain to various parts of the body. As well as this radiating pain, several other objective disturbances in the various body structures can occur, which are not given enough priority in the examination of patients with cancer pain.

The symptoms of the referred visceral pain syndrome (Table 2) are radiation of pain to the organ-specific projection areas of the skin (Head's zone) and the musculature (McKenzie's zone). Pain provocation is partly organ-specific, and complaints of a nocturnal maximum are frequent. Diagnosis of dysesthesic or hyperalgesic zones can help in the etiologic classification of the referred visceral pain syndrome: dysesthesia and hyperalgesia can occur in dermis, epidermis, musculature, or deep structures in a dissociated fashion (Fig. 2).

In the pain region, not only the sensitivity, but also the mechanical quality of the dermis and epidermis is often altered. Impairment can occur in muscles which are functionally or segmentally associated with the diseased organ and can manifest as muscle spasm, tendinopathy, or altered muscle tone. Functional lesions can occur in organ-specific segments of the spine as alteration of active and passive motility and as segmental irritation symptoms.

Lesions of the Locomotor System

Damage to structures of the locomotor system caused by primary or secondary carcinomatous processes can lead to muscular or articular disturbances due to reflex mechanisms, resulting in a pseudoradicular syndrome (Table 3). These symptoms consist of dysesthesia and radiating pain to one or more dermatomes, muscular impairment such as muscle spasm, tendinopathy, or myotendinosis, as well as altered muscle tone in segmentally and functionally associated muscles (Brügger 1980). Disturbances of autonomous nerve function occur in the dermis and epidermis in the form of altered local sweat secretion, skin edema, etc. (Lewit 1977). Involvement of the spinal column or neighboring structures by carcinomatous lesions can lead to a local spinal syndrome or, in severe cases, to a stiff-neck or lumbago syndrome (Brocher and Willert 1980).

Table 2. Referred visceral pain

Pain	*Radiation* in organ-specific projection zones (dermatome. Head's zone: myotome. McKensie's zone) *Provocation* partly organ-specific *Intensity* partly severe. often nocturnal maximum
Sensibility	*Hyperalgesia* and *dysesthesia* in projection zones (dermis. epidermis. musculature)
Motoricity	*Secondary muscle dysfunction* in projection zones (muscle spasm. myogelosis. tendinopathy)
Associated symptoms	Dysfunction of the affected *visceral* organs *Secondary lesions* in typical parts of the spine *Dysfunction* of the autonomous nervous system in the projection zones of the dermis and epidermis (Kibler's zone. etc.)

Table 3. Pseudoradicular syndrome

Pain	*Local pain* in the region of damaged structures *Radiation* often into the dermatome *Provocation* by pressure and movement of the involved joint and muscles *Intensity* usually not severe
Sensibility	*Dysesthesia* and *hyperalgesia* over the damaged structures or in the dermatome
Motoricity	Muscular *hyper-* or *hypotonus*. muscle spasm. myogelosis. tendinopathy
Associated symptoms	*Dysfunction* of the autonomous nervous system in typical zones of the dermis and epidermis (Kibler's zone. etc.)

Fig. 2. 53-year-old patient with hypernephroma on left side: referred visceral pain with projection into the dermatome (D.12) and pain caused by pressure on the tip of the 11th rib and on the iliacus muscle

Summary

Pain intensity and the importance of pain for the cancer patient depend on a variety of individual factors and show considerable divergence (Bonica and Ventafridda 1979). They are greatly influenced by the enigma of the cancer disease as well as the consequential psychiatric problems (Frey 1980). An effective neurological analysis of the cancer pain, although demanding for the physician, is important for further specific diagnostic procedures and for the indication of appropriate therapy. Sometimes thorough neurological examination can lead to the first diagnosis of the carcinoma; when there is already evidence of metastases, the unfavorable prognosis can be made at the same time.

References

Berger M, Gerstenbrand F (1981) Phantom illusions in spinal cord lesions. In: Siegfried S, Zimmermann M (eds) Phantom and stump pain. Springer, Berlin Heidelberg New York, pp 66–73

Bonica JJ, Ventafridda V (eds) (1979) Advances in pain research and therapy, vol 2. Raven, New York

Brocher IEW, Willert HG (1980) Differentialdiagnose der Wirbelsäulenerkrankungen. Thieme, Stuttgart

Brügger A (1980) Die Erkrankungen des Bewegungsapparats und seines Nervensystems. Fischer, Stuttgart

Frey M (1980) Diagnose und Therapie des Tumorschmerzes. In: Frey R (ed) Schmerz. Aesopus, Basel, pp 235–242

Lewit K (1977) Manuelle Medizin im Rahmen der medizinischen Rehabilitation. Urban und Schwarzenberg, München

Stöhr M (1980) Iatrogene Nervenläsionen. Thieme, Stuttgart

Swerdlow M (1978) Relief of intractable pain. Excerpta Medica, Amsterdam

Weber G (1970) Kopfschmerzen bei raumfordernden intracraniellen Prozessen. In: Cephalea, Bücherreihe Hommel, Adliswil, pp 185–199