25.

BRAIN METASTASES AS FIRST MANIFESTATION OF NON-SMALL CELL LUNG CANCER: DIAGNOSTIC AND THERAPEUTIC PROBLEMS.

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While brain metastases in patients with solid tumors are a familiar problem, their incidence and significance as first tumor manifestation in non-small cell lung cancer has been underestimated. At the University Hospital Basle, over one year, 7 of 102 patients with newly diagnosed non-small cell lung cancer had brain metastases as first manifestation of systemic cancer. Three of the seven patients were women with a mean age of 48 years. Initial symptoms were headaches, vertigo and vomiting, which prompted the diagnosis of brain metastases. In only 3 patients was the primary lung cancer diagnosed immediately after diagnosis of the brain metastases, while in the remaining 4 a period of up to 6 months elapsed. Therapeutically corticosteroids are often used as initial symptomatic treatment. Radiotherapy is usually the treatment of choice achieving good palliative response as well as prolongation of survival in a high percentage of patients. Surgical excision may be indicated in selected patients with solitary peripheral metastases, if the primary tumor can be controlled too. Only recently it has been shown that chemotherapy can also be effective applied systemically or by local intraarterial infusion.
As bronchogenic cancer is the most frequent primary in patients presenting with brain metastases of unknown origin, diagnostic tests should be aimed in that direction. Immediate diagnosis and treatment of brain metastases is important as this may result in good palliation as well as in prolonged survival.

26.

THE VALUE OF ROUTINELY REPEATED BONE SCANS FOR DETECTION OF BONE METASTASES IN EARLY BREAST CANCER.

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Data on 1601 patients (pts) with node-positive operable breast cancer who were randomized in four different prospective adjuvant therapy trials were analyzed to evaluate the role of routine bone scan in screening for bone involvement. Bone scan was a prerequisite for randomization and was routinely repeated within the first 12 months in 90% (1441) of the pts. Positive or doubtful scans had to be verified by x-ray examination. The repeated scan was negative in 1263 (87.8%) pts, doubtful but with no radiological evidence of bone metastasis in 161 (11%), and positive (radiologically confirmed) in 17 (1.2%). After a median follow-up of 4 years 210/1263 (16.6%) of the pts whose repeated scan within a year was negative developed bone metastasis: 87 (6.9%) as first, 55 (4.4%) as a subsequent recurrence and 68 (5.4%) at autopsy. Of the 161 pts with doubtful repeated scan 41 (25.5%) developed bone metastasis [18 (11.2%), 13 (8.1%) and 10 (6.2%), respectively]. The difference in the incidence of bone metastasis between the two groups is 8.9% (p=0.008). In only 11% of a selected high-risk group (doubtful scan) do routinely repeated scans provide information about first recurrence in bone. In addition, early detection of bone metastasis, especially if isolated, rarely has therapeutic consequences. For most of the pts an appropriate policy is to start palliative therapy only when metastasis-related symptoms appear. Routine bone scan in the follow-up of pts with operated breast cancer serves no useful purpose.

27.

CANCER METASTASES IN CHILDREN.

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Experimental data indicate that tumor evolution generates tumor cell heterogeneity within the parent tumor and within and among metastases. This is well illustrated by the spread of neuroblastic tumors in children. We focus on neuroblastoma (NB), a malignant tumor arising from postganglionic neurons of the peripheral sympathetic nervous system, because NB account for 10-15% of all malignant solid tumors in childhood and because over two thirds of NB initially present with metastases. One third of all NB occur in infancy. Infants with liver, skin and bone marrow involvement survive and are cured with a minimum of therapy, while older children with lymph node invasion and osteolytic lesions die despite of aggressive therapy. Cluster analysis data suggest,that besides the classical Pepper (NB with liver metastases) and Hutchinson (NB with osteolytic lesions) syndromes, other patterns of spread exist. In the CNS, NB, similar to other central neuroblastic tumors such as retino-, pinealo- and medulloblastoma, metastasize to both the leptomeninges (neural crest-derived) and the dura mater (mesoderm-derived) but do not or only per continuitatem spread to the parenchyma. Recently cytogenetic studies revealed, that NB cells of children with osteolytic lesions, but not NB cells of infants with liver metastases, have characteristic alterations on the short arm of chromosome 1. Cytogenetic expressions of amplified DNA, non-specific for metastasizing NB, correspond to v-myc. In the light of Knudson's hypothesis, metastasizing NB of infants might correspond to a 1-hit, metastasizing NB of older children to a 2-hit tumor.

28.

PATTERN OF METASTATIC OR LOCAL FAILURE AFTER CISPLATIN + ETOPOSIDE + DOXORUBICIN (AVP) IN SMALL CELL LUNG CANCER (SCLC).

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One hundred and three evaluable patients (pts) with limited(55) or extensive(48) SCLC received cisplatin 20 mg/sqm on days 1,2,3, etoposide 80 mg/sqm IV on days 1,2,3 - 15,16,17 and doxorubicin 40 mg/sqm on day 1 q4W. After 1-4 cycles complete-partial(CR-PR) response/performance status(PS) were(%):

	limited(L)			extensive(E)			total		
	CR	PR	Tot	CR	PR	Tot	CR	PR	Tot
PS 0	87	0	87	33	44	78	67	17	83
PS 1	46	46	92	17	58	75	36	50	84
PS 2	36	57	93	18	59	76	26	55	84
PS 3	(2/3)	(1/3)	(3/3)	0	89	89	17	75	92
Total	55	36	91	17	62	79	38	48	85

Post-induction treatments were selected by participant institutions for CR+PR's. 24 pts relapsed early, 11 had 1-4 maintenance AVP, 32 had another maintenance chemotherapy(MT) and 21 had no MT. Median survival was 402(conf.lim.95%:336-429) days for L and 254(217-318) days for E and correlated with PS but not with MT. 2 pts survived 3+ years without relapse. The site of first failure with/without radiotherapy on mediastinum(RTMED)(24/64) or CNS(RTCNS)(13/75) were(%):

site	RTMED	NO RTMED	RTCNS	NO RTCNS
local	42	45	38	45
liver	8	8	15	7
bone	0	2	0	1
CNS	25	16	8	20
other	21	20	31	19
no fail.(liv+dead)	4	9	8	8