

Case-based learning: neuro-oncology



Soon-Tae Lee, MD, PhD

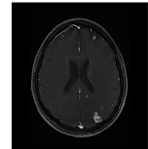
Department of Neurology, Integrated Cancer Care Center, Center for Neuro-Oncology, Seoul National University Hospital, Seoul, Korea

Contents

1. AED in cancer patients
2. Cognitive protection in radiation
3. Cancer stroke
4. Chemotherapy-induced peripheral neuropathy
5. CNS infection in cancer patients
6. DDX in encephalitis-like lesion
7. CSF tapping in low platelet counts

Case: AED in cancer patient

- 27세 여자 환자 A가 seizure로 응급실에 내원하였다. 3년 전 Lung cancer (non-small cell lung cancer)로 진단받은 뒤 1년전부터 표적항암제인 Crizotinib을 복용하고 있었으며, 약물 부작용으로 skin rash와 간헐적인 neutropenia를 겪고 있었다. 이번 seizure는 right head version 및 right arm tonic posture를 취하던 중 이후 generalized tonic clonic seizure가 1분여 있었고, 이후 confusion이 서서히 회복되는 상태로 응급실에 내원하였다. 내원하여 촬영한 brain MRI는 우측과 같다.
- 적절한 항경련제는?

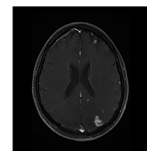


Considerations in AED for cancer patients

	Considerations in cancer	Implications
Drug interaction	Hepatic enzyme inducers reduce blood levels of chemo drugs and steroid (by ~70% AUC reduction)	Avoid EIAEDs *Enzyme-inducing AED (EIAED): DPH, PB, CBM, OXC *Enzyme-inhibiting AED: VPA
Rash	Chemo drugs causes rashes	Choose rash-innocent drugs
Cytopenia	Cytopenia delays the next chemo cycle.	Choose cytopenia-innocent drug
Edema	Edema may be the cause of seizure	Dexamethasone is anti-epileptic
Cognitive function	Underlying cognitive dysfunction by Tumor, RT, and chemo	Choose AED with low cognitive side effects
Weight loss	Cachexia	Consider weight change by AED (topiramate, zonisamide, valproic acid)
Cancer progression	Seizure may be the sign of tumor progression	Check recurrence or progression by MRI

Case: Cognitive side effect by radiation

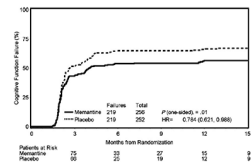
- Seizure로 내원하였던 환자 A(27세/여자)가 seizure는 잘 조절 되었고, multiple brain metastasis에 대해 whole brain radiation 치료를 받게 되었다.
- 환자는 전뇌 방사선 치료로 인해 인지기능이 저하될 것을 매우 우려하고 있고, 신경과로 예방 방법이 없는지 문의되었다.
- 방법은?



Prophylactic memantine in WBRT

- RTOG0614 trial
- Indication: Brain metastases + WBRT (37.5Gy/15Fx)
- Treatment arm: Placebo vs. memantine
 - 5mg qd → 5mg bid → 10mg-5mg → 10-10mg
 - within 3 days of initiating RT, for 24 weeks

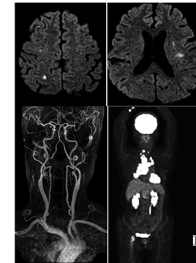
	Memantine	Placebo	P*
Week 24			
HVLT-R Total Recall	-0.23	-0.415	.2093
HVLT-R Delayed Recall	0	-0.895	.0587
HVLT-R Delayed Recognition	0	-0.715	.0115
TMT-A	0.075	-0.365	.0237
TMT-B	-0.45	-0.49	.2966
COWA	-0.1	-0.16	.3080
CTB Composite	-0.03	-0.41	.0212



Brown et al., Neuro-Oncol, 2013

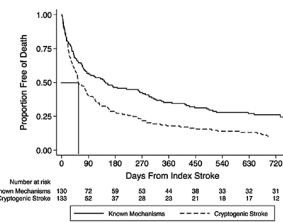
Case: Management of cryptogenic infarction in cancer

- 환자 A는 이후 항암제를 바꾸어 항암치료를 진행하던 중 갑자기 발생한 구멍창으로 응급실에 내원하였다. 1주일전 마지막 항암치료를 받았고 (gemcitabine-cisplatin), 고열악, 당뇨, 고지혈증, 심방세동은 없었다. 혈중 D-dimer는 15.7 ug/ml로 상승되어 있었고 혈소판 수치가 67k로 저하되어 있었다. MRI diffusion 과 MR angiography, 전신 양전자 단층촬영은 우측과 같다.
- 환자의 기대 여명은? 적절한 2차 예방약제의 선택은?



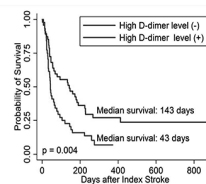
Cancer-stroke: poor survival

Memorial Sloan Kettering Cancer Center



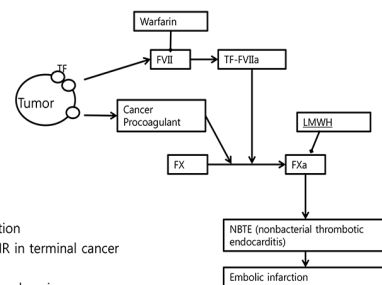
Median survival: 55 days,
In-hospital death: 10%

Seoul National University Hospital



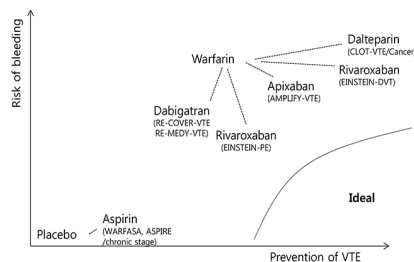
Median survival: 62 days,
In-hospital death: 29%
High D-dimer >5.5 µg/ml

Stroke mechanism in cancer patients

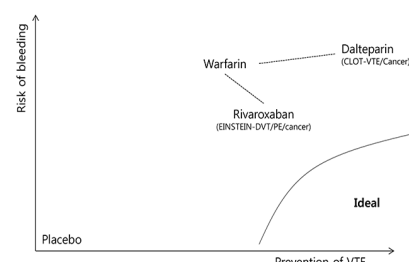


- Limitation of warfarin:
 - Targets TF-FVIIa function
 - Spontaneous High INR in terminal cancer
 - Drug interactions
 - Poor monitoring during hospice care
- Dalteparin protocol: 200 IU/kg/day sc → 150 IU/kg/day sc after 3 weeks → continue more than 3 months and until NED

LMWH/NOAC for venous thromboembolism



LMWH/NOAC of venous thromboembolism in Cancer

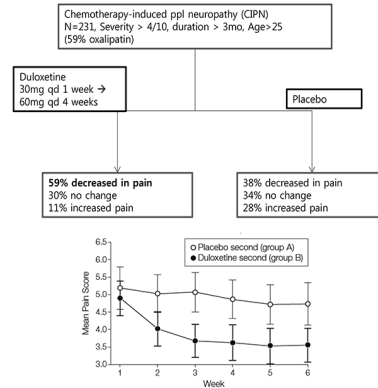


	General	Injection pain	Low plt	Bleeding	Renal failure
Dalteparin	O	X	△	△	△
Enoxaparin	O	X	△	△	△
Warfarin	X	X	X	X	△
Heparin	O	X	X	△	O
Rivaroxaban	O	O	O	△	△
Dabigatran	△	△	△	X	X

Case: CIPN (chemotherapy-induced peripheral neuropathy)

- 환자 A는 뇌졸중에 대해 입원치료하는 동안 양손발의 저린 증상을 호소하였다. 병력상 3개월전 cisplatin 항암치료를 시작한 뒤로 서서히 저리기 시작하여 1주전 마지막 항암치료 이후로 stocking-glove pattern의 저린증상이 심하여, 일상생활에 불편을 호소하고 있다.
- 증상 개선에 도움이 되는 약물은?

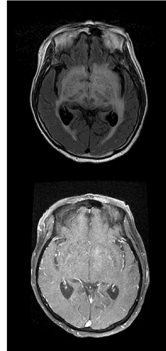
Duloxetine (Cymbalta) in chemo-induced peripheral neuropathy a double-blind, randomized, placebo-controlled Phase III study



Smith et al., JAMA, 2013

Case: CNS infection in cancer patients

- 환자 A는 다행이 뇌졸중 재발없이 예정된 항암치료 (gemcitabine-cisplatin 6 cycle)를 마칠 수 있었다. 그러나 항암치료 종료후 1달 되는 시점에, 40도의 발열과 함께 진행되는 stupor mentality로 의식저하가 있어서 응급실에 내원하였다.
- CSF 검사에서 pressure는 18cm, protein 93 mg/dL, glucose 75 (serum 180), WBC 54 (lympho 40, poly 5, other 9)였다. MRI는 우측과 같다.
- 원인은?

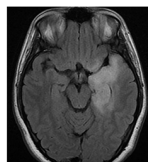


Neuroinfection in cancer: DDx by host defense abnormality

Host defense abnormality	Risk factor	Infections	Bacteria	Fungi	Parasite	Viruses
T-lymphocyte / phagocytic defect	Lymphoma Steroid Alkylating agents	Meningitis Encephalitis, abscess	Listeria Listeria, Norcadia	Cryptococcus Coccidioides Histoplasma	Toxoplasma	Varicella zoster (VZV), Cytomegalovirus (CMV), PML, CMV, HSV
Neutrophil defect	Chemo	Meningitis Abscess or encephalitis	G (-) Enteric bacilli: Pseudomonas, E. coli, Klebsiella, Listeria, S. pneumoniae, S. aureus	Candida Aspergillus, Mucor, Candida	Rare	Rare
CSF device	VP shunt, Ommaya reservoir	Meningitis, Abscess	S. aureus, Coagulase-negative staphylococcus, Propionibacterium, acnes, Enteric bacilli	Candida	Trichomonadida	Rare

Case: Differential diagnosis of encephalitis-like lesion

- 69세 남자 환자가 처음 발생한 generalized tonic clonic seizure로 응급실에 내원하여 촬영한 MRI 영상이 우측과 같다. 조영증강되는 부위는 없었으며, diffusion restriction 도 없었다. 환자는 발열, 최근의 인지기능 저하도 호소하지 않았고, virus PCR을 포함한 CSF tapping, 전신 CT 검사 및 자가면역뇌염 항체검사 에서도 이상이 없었다.
- 의심 질환 및 감별점은?



MRI Tips in differential diagnosis

	NMDAR	LGII	GABAbR	Hu/Ma	Herpes	Glioma	AE-noDAB
Initial MRI	Normal or subtle	Multiple subcortical	Hippocampus	Hippocampus+brainstem	Hemorrhage, swelling	Homogenous, infiltrative (gray+white)	None specific
F/U MRI	Atrophy (-)	Atrophy (-)	Atrophy (-)	Atrophy (++)	Atrophy (++++)	No atrophy ~progression	Atrophy (-~++)
Mode of onset	Progressing over weeks	Seizure or months	Seizure	Limbic, brainstem, cerebellum	Short history of progression (<2 weeks), Fever >3 days	Mild Sx with large lesion	Progressing without treatment
Dx	Antibody	Antibody	Antibody	Antibody, systemic cancer	Viral PCR	Resection	Immune response, other auto-Abs

AE-noDAB= autoimmune encephalitis with no detectable antibody

Case: CSF tapping in low platelet counts

- 69세 남자 환자가 두통과 발열이 있다. 3년 전 진단된 AML (acute myeloid leukemia)이 있는 환자로 금번에 항암치료 중으로 neutropenia와 platelet count 저하 (37,000/uL)가 있다. 발열의 병소가 명확하지 않은 상태로, CSF tapping을 시행해야 할지에 대해 신경과로 의뢰해왔다.
- 혈소판 수치가 lumbar puncture 하기에 안전한가?

CSF tapping in low platelet counts

Major surgery: 10만이상	}	5만이상: CSF tapping 가능
Invasive procedure: 5만이상		
Spontaneous bleeding: 2만이하	}	2만~ 5만: 가급적 혈소판 수혈 후
	}	<2만: 반드시 혈소판 수혈 후.

Suggested reading

Continuum: Neuro-Oncology. 2012 & 2015