Difficult climbing: treatment of gliomas and a tribute to Prof. G.P. Biti

Best Supportive Care

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Best supportive care

- Supportive care is an ‘umbrella’ term for all services, both generalist and specialist, that may be required to support people with cancers and their carers.
- Supportive care is required throughout the diagnostic, treatment and follow-up phases of care

Best supportive care

- Supportive care needs include:
  - Social needs
  - Information needs
  - Psychological needs
  - Physical needs

All members of the multidisciplinary team have a role in the provision of supportive care.

Best supportive care social/practical needs

- Practical supports
- Physiotherapy

Best supportive care information needs

- Cognitive impairment may affect the ability to retain information
- Carers require information about cognitive impairments and advice about what to do

Best supportive care psychological needs

- Distress
- Depression: the incidence of depression ranges from 5 per cent to 95 per cent in this group and can be a result of increased dependency
- Self-esteem

Taillibert et al., Current Opinion in Oncology, 16: 587-592

Best supportive care
Information and psychological needs

Table 2. Rates of symptoms in patients with primary brain tumor at end of life

Symptom	Sizoo et al. 2010[56]	Pace et al. 2009[54]	Faithfull et al. 2005[55]	Oberndorfer et al. 2008 (final 2 weeks of life)[57]
Neurological				
Drowsiness, loss of consciousness	87%	85%		90%
Weakness/hemiparesis			62%	
Seizures/epilepsy	45%	30%	56%	48%
Focal neurological deficits e.g. motor/ dysphasia	51%			
Poor mobility			77%	
Poor communication			64%	
Visual disturbance			21%	
Cognitive/Psychological				
Cognitive deficits/memory loss	33%		39%	
Confusion	29%			
Anxiety/depression	9%			
Agitation/delirium/confusion		15%	31%/na/51%	

Best supportive care

- Supportive care needs include:
  - Social needs
  - Information needs
  - Psychological needs
  - ***Physical needs***

Best supportive care physical needs

- Seizures
  - Up to 30% of malignant glioma patients have seizures (more common in low-grade gliomas)
    - 10-40% of pts with brain tumors have seizeures as a presenting feature
    - 20-62% will experience a seizure during the course of thier illness
  - Antiepileptic monotherapy is associated with higher compliance and less adverse effects

Glantz et al., Neurology 2000, 54: 1886-1893

Best supportive care physical needs

- Seizures
  - Which antiepileptic drug (AED) to choose?
    - Older AEDS induce cytocrome P450-mediated metabolism of most antineoplastic drugs (except temozolomide)
    - Non –enzyme inducing AEDs are now increasingly used

23.8% of brain tumor pts on AED experience side effects severe enough to warrant a change in or discontinuation of AED therapy

(Glants MJ et al., Neurology, 2000, 54:1886-1893)

Best supportive care physical needs

TABLE 3: Overview of Antiepileptic Drugs Commonly Used in Glioblastoma Patients

EIAED/Non-EIAED	Drug	Common Adverse Effects
EIAED	Phenobarbital	Sedation, rash, impaired cognitive function
	Phenytoin	Gingival hypertrophy, hirsutism, hepatotoxicity, rash, lymphadenopathy
	Carbamazepine	Drowsiness, dizziness, diplopia, rash, leukopenia, hyponatremia, hepatotoxicity, nausea/vomiting, cardiac arrhythmia
	Oxacarbazepine	Drowsiness, dizziness, diplopia, rash, hyponatremia, hepatotoxicity, nausea/vomiting
Non-EIAED	Valproic acid	Weight gain, nausea/vomiting, hair loss, thrombocytopenia, hepatotoxicity
	Gabapentin	Somnolence, dizziness, agitation/anxiety, ataxia
	Lamotrigine	Somnolence, dizziness, rash, hepatotoxicity
	Levetiracetam	Drowsiness, fatigue, agitation/anxiety, headache
	Pregabalin	Somnolence, dizziness, weight gain, ataxia

EIAED = enzyme-inducing antiepileptic drug.

Preusser et al., Annal Neurology 2011, 70: 9-21

Best supportive care physical needs

- Seizures
  - One reason that many brain tumor pts receive prophylactic AEDs is because they have undergone craniotomy.

A DEFINITIVE RANDOMIZEDE STUDY IS NECESSARY TO DETERMINE THE VALUE OF AED PROPHYLAXIS FOLLOWING CRANIOTOMY FOR BRAIN TUMORS, BUT THE CURRENTLY AVAILABLE DATA SUGGEST THAT IT IS OF LITTLE OR NO BENEFIT

(De Santis et al., Epilepsia, 2002, 43 (2):175-182)

- Prophilactic AED therapy in patients without a history of seizures is not reccomended

(Sirven et al., Mayo Clin Proc,2004, 79:1489-1494)
(Glants MJ et al., Neurology, 2000, 54:1886-1893)

- REFRACTORY SEIZURES:
  - Associations of more AEDs
  - Association with radiant therapy
  - Surgery

Best supportive care physical needs

- Brain edema
  - it is associated with increased intracranial pressure with:
    - Headache
    - Vertigo
    - Nausea/vomiting

  And can lead to brainstem compression and herniation

  VASOGENIC EDEMA SURROUNDING BRAIN TUMORS CONTRIBUTES SIGNIFICANTLY TO THE MORBIDITY EXPERIENCED BY PATIENTS

Best supportive care physical needs

- Brain edema treatment
  - Dexamethasone (orally or intravenously) is usually the drug of choice (12-16 mg per day)

    (Kaal et al., Curr Opin Oncol, 2004, 16 (6):593-600)
  - Occasionally other measures may be required: fluid restriction, mannitol, diuretics and hyperventilation

Best supportive care physical needs

- Brain edema treatment
  - Dexamethasone is generally used as it has relatively little mineralcorticoid activity, and possibly a lower risk of infection and cognitive impairment, compared to other corticosteroides.

    (Batchelor et al., Neurosur Clin,1996, 7:435-446)
  - Dexamethasone can be used:
    - At time of presentation of glioma to alleviate symptoms and improve neurological deficits
    - To reduce oedema during radiotherapy

Best supportive care physical needs

- Brain edema treatment
  - Steroid dosage should be rapidly reduced and tapered to individual needs
  - In emergency situation, intravenous dexamethasone may be combined with osmotic agents such as mannitol or glicerol
  - Despite their usefulness corticosteroids are associated with a lareg number of side effects.

A: Systemic complications of corticosteroids

General
- Increased appetite
- Weight gain
- Cushingnoid features (moon face, centripetal obesity, buffalo hump)
- Increased susceptibility to infections
- Candidiasis

Bone
- Osteoporosis
- Avascular necrosis

Cardiac/Vascular
- Hypertension
- Increased cardiovascular and cerebrovascular disease

Eye
- Cataracts
- Glaucoma
- Central serous chorioretinopathy

Gastrointestinal
- Peptic ulceration
- GI bleeding

Genitourinary and Reproductive
- Menstrual irregularities
- Infertility

Hematologic
- Neutrophilia
- Lymphopenia

Metabolic
- Hyperglycemia
- Hypokalemia
- Hyperlipidemia
- Fluid retention

Skin
- Hirsuitism
- Fragile skin
- Purpura
- Acne
- Striae

- Brain edema treatment (dexamethasone)

SIDE EFFECTS

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EDITOR'S INVITED MANUSCRIPT

Medical management of patients with brain tumors

Patrick Y. Wen · David Schiff · Santosh Kesari · Jan Drappatz · Debra C. Gigas · Lisa Doherty

B: Neurologic complications of corticosteroids

Common
- Myopathy
- Behavioral changes
- Visual blurring
- Tremor
- Insomnia
- Reduced taste and olfaction
- Cerebral atrophy

Uncommon
- Psychosis
- Hallucinations
- Hiccups
- Dementia
- Seizures
- Dependence
- Epidural lipomatosis

Best supportive care physical needs

- Brain edema treatment side effect:
  - These complications and their severity correspond to the hight of the dose and the duration of therapy
  - Most of complications of steroid administration resolve after withdrawal of therapy, with the exception of osteoporosis and cataracts.

Best supportive care physical needs

Several complications of corticosteroid therapy are of particular concern to brain tumor pts:

- Gastrointestinal complications:
  - use of histamine blockers or proton pump inhibitors.
  - attention especially in association with NSAIDs
- Steroid myopathy:
  - Occurs in 2-21% of pts, generally in the elderly and after prolonged use of high dose of corticosteroids
  - Treatment is difficult and generally limited to physical therapy and recovery of strenght may occur over several months after discontinuation of steroid therapy

Best supportive care physical needs

Several complications of corticosteroid therapy are of particular concern to brain tumor pts:

- Pneumocystis pneumonitis (PP):
  - Use of moderate to high doses of steroids can result in clinically significant suppression of the immune system and vulnerability to opportunistic infections
  - Pneumocystis is a fungus capable of causing life-threatening pneumonitis in immunocompromised pts
  - PP may also be increased in pts receiving prolonged dose of temozolomide
  - Because of the risk of PP, it may be prudent to consider prophylactic therapy against PP for brain tumor patients receiving prolonged corticosteroid therapy

Best supportive care physical needs

- Deep vein thrombosis (DVT) and pulmonary emboly (PE)
  - Incidence of symptomatic DVT or PE in pts with HGG outside the perioperative periods: 20 to 30%
  - Risk increased in pts in the post-operative period or those with hemiplegia
  - The exact mechanism leading hypercoagulability is unclear:
    - Released of procoagulants (e.g.: tissue factor) or fibrinolytic inhibitors
    - Reduced mobility
    - High dose corticosteroids therapy

Best supportive care physical needs

- Deep vein thrombosis (DVTE) and pulmonary embolism
  - Because of high risk of developing DVT, brain tumor pts undergoing surgery require adequate prophylaxis. The optimal method of prophylaxis is unclear
  - In case of estabilished DVTE, treatment and secondary prophylaxis is usually done with low-molecular weight heparin with or without consequent anticoagulation
  - Due to bleeding risk, anticoagulation has long been considered controidicated for brain tumor patients

Journal of Thrombosis and Haemostasis, **8**: 1959–1965 DOI: 10.1111/j.1538-7836.2010.03973.x

ORIGINAL ARTICLE

PRODIGE: a randomized placebo-controlled trial of dalteparin low-molecular-weight heparin thromboprophylaxis in patients with newly diagnosed malignant glioma

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Conclusions: Trends suggesting reduced VTE and increased intracranial bleeding were seen in the LMWH thromboprophylaxis group. The role of long-term anticoagulant thromboprophylaxis in patients with brain tumors remains uncertain.

Best supportive care - physical needs

- DVT and PE – Algorithm for the treatment

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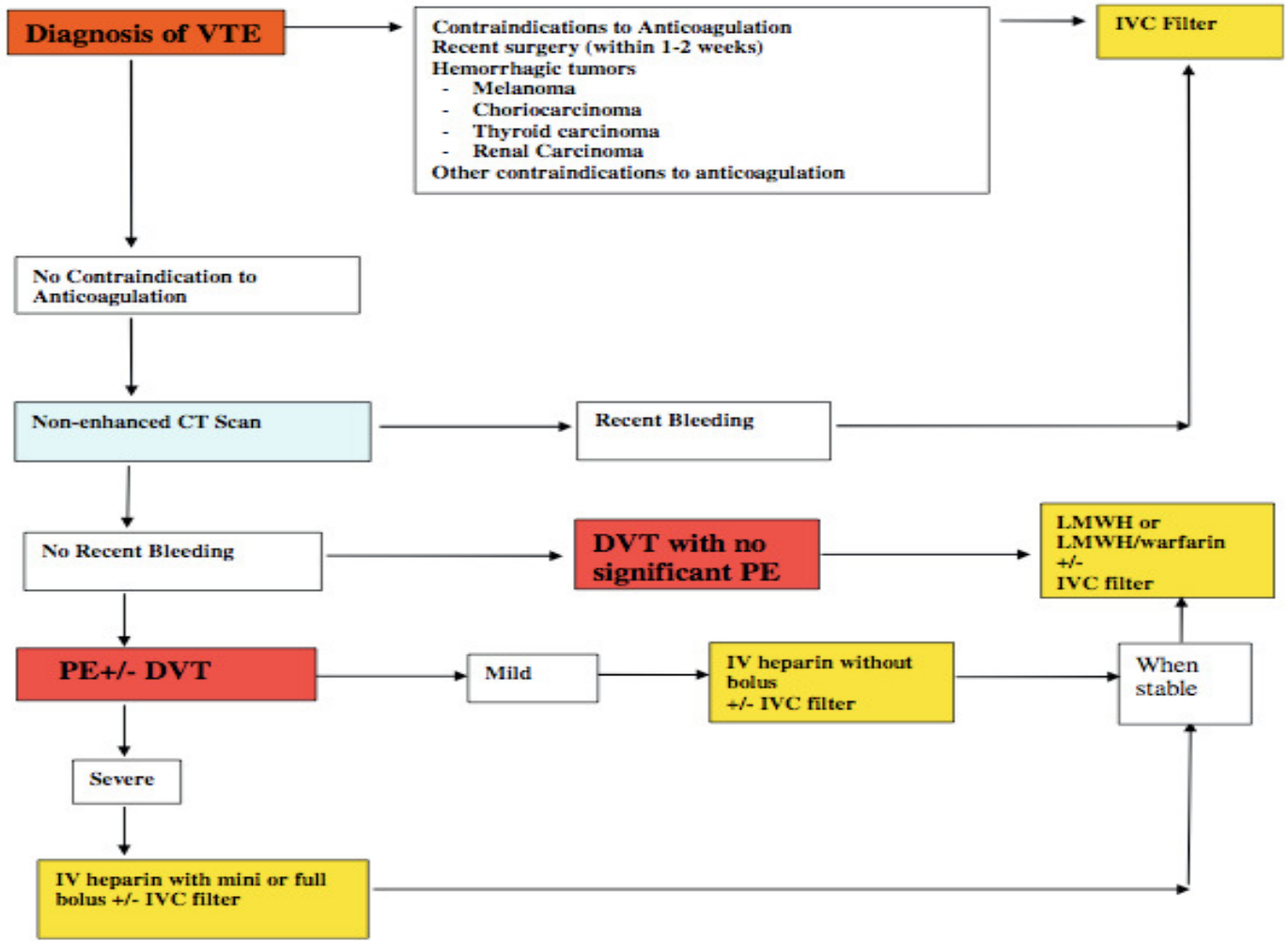
Fig. 4 Algorithm for the treatment of venous thromboembolic disease in brain tumor patients. LMWH: low molecular weight heparin; IVC: inferior vena cava; PE: pulmonary embolism; DVT: Deep-vein thrombosis



Conclusion

- Best supportive care is required in all phases of management of brain tumor patients
- Supportive care could be considered alone or in association with other treatments
- There are no specific criteria about timing of introduction and/or discontinuation of best supportive care and about what kind of patients could benefit of it.

Thanks for your attention