Breast Cancer Metastases in the Brain

Breast Cancer Care Virtual teaching session
1-2pm Friday 10th February 2017

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Topics

• Brain metastases: a changing field
• Presentation and diagnosis
• Which patients should be referred to a neuro-oncology MDT?
• Treatment options: surgery, SRS, WBRT
• Case history
• Supportive care – steroids, epilepsy, rehabilitation, driving
Natural History of Brain metastases: The traditional view

- Occurred near the end of illness, when systemic disease was progressing
- Without treatment, average survival 2-4 months
- With palliative cranial radiotherapy up to 6 mths
  - QUARTZ trial in lung cancer patients questions that
Brain metastases: a changing field

- Occurring in fitter patients with good performance status
- May be diagnosed when asymptomatic
- Occurring when extra-cranial disease is controlled (or synchronously prior to any treatment)
- Occurring in patients with higher expectations of treatment
- All mets are *not* the same
  - Her 2+ve breast
  - ALK-mutated lung
  - BRAF mutant melanoma
- Much less nihilism and more treatment options from all disciplines
- Many patients embark on a ‘brain mets journey’
Presenting symptoms

- Functional deficits relating to location
  - Motor weakness
  - Cranial nerve palsies
  - Dysphasia – expressive / receptive
  - Visual changes
  - Personality changes

- New onset seizures

- Raised intracranial pressure
  - Headaches, vomiting, confusion, drowsiness

*Symptoms may be vague or minimal; ‘just mentioned in passing’*
Episode of collapse, and some unsteadiness mentioned at a routine chemo clinic appointment

Tiny, solitary brain metastasis

Immediate loss of driving licence
Focal, localising symptoms from a tumour arising in the motor strip
Non-specific symptoms – unsteadiness, slurred speech, headache

Multiple, widespread brain metastases
Symptoms of raised intracranial pressure

Morning headaches / headaches worse on leaning forward, coughing or sneezing, nausea / vomiting / visual disturbance / photophobia

2 large cystic mets
Diagnosing Brain Metastases

• Brain scan
• If present acutely with symptoms, most patients have a CT brain scan first
• If scan arranged for clinical suspicion, go straight to MR brain scan *WITH CONTRAST*
• Imaging appearances are rarely in doubt
  • main differential is infection – TB or abscess
**Diagnosing Brain metastases:**

*MR + Contrast is vital*

- **MR Pre-contrast**
- **MR Post-contrast**

CT scan
Treatment options

- Whole Brain radiotherapy
- Stereotactic Radiosurgery
- Surgery
- A combination of the above during a ‘brain mets journey’

But who gets what, and why?
Treatment decisions are based on an interplay between:

- Extra-cranial disease
  - Controlled / controllable / progressing
  - Prognosis \(\Leftrightarrow\) number of lines of treatment
- Performance status
- Intra-cranial disease:
  - Number / volume / location of metastases
  - Mass effect
  - Certainty of diagnosis
- Patient-related factors
  - Preference
  - Intercurrent medical problems eg COPD
Treatment decisions are based on an interplay between:

- **Extra-cranial disease**
  - Controlled / controllable / progressing
  - Prognosis $\Leftrightarrow$ number of lines of treatment

- **Performance status $\geq 70$**

- **Intra-cranial disease:**
  - Number / volume / location of metastases
  - Mass effect
  - Certainty of diagnosis

- **Patient-related factors**
  - Preference
  - Intercurrent medical problems eg COPD
Decision-making in a neuro-oncology MDT: Choice of treatment modality
Stereotactic Radiosurgery (SRS) is accurate, conformal, highly targeted radiotherapy

- High dose, small volume, single fraction
- Sub-millimetre accuracy
- Spares normal brain
- **When we talk about SRS, it is *platform independent***
  - Gamma knife
  - Cyberknife
  - Linacc-based / Novalis
Methods of SRS delivery: Gamma Knife
Methods of SRS delivery: Cyberknife

Compact, 6MV linacc head  ‘Car-building robot’ body
Methods of SRS delivery:
Linear accelerator – Novalis TX
Surgery: Mass effect
Surgery: Hydrocephalus
SRS: Multiple lesions / inoperable locations

Metastasis in brain stem
So......SRS or surgery?
Surgery vs SRS: Pros and cons

**Surgery**
- Confirms histology
- Larger lesion
- Complications usually immediate (6%)
- Faster tapering of dex
- Faster resolution of symptoms
- Risk of neurological decline
- Relies on fitness for GA

**SRS**
- Known histology
- Smaller lesion <3cm, no mass effect
- Possible in eloquent regions
- Complications usually delayed
- Longer use of steroids
- Risk of radiation necrosis
- Out-patient treatment; possible in older, less fit patients
2 or more lesions: 1 best treated with surgery, others for SRS
Controversies in patient selection:

- NHS eligibility:
  - Controlled / controllable systemic disease
  - KP ≥ 70
  - Total mets vol ≤ 20cc
- Volume is more important than number
- **Number of metastases treatable with SRS?**
What about whole brain radiotherapy?

- Meningeal metastases
- Patients not suitable for SRS
  - Intra-cranial disease too extensive
    - (Can use WBRT initially, then SRS later)
  - Extra-cranial disease progressing / uncontrolled
- Adjuvant, after neuro-surgical resection
  - Post-op WBRT improves control within the brain, but not overall survival

  Intracranial control
  vs

  Risk of neurocognitive decline
  (and other late effects)

- Variations in local practice
Toxicity of SRS vs WBRT:
Relates to treatment volume, RT dose and fraction size

- **SRS:** Small volume, high dose, single #
  - Increased risk of acute oedema
    - Prolongation of dexamethasone use
  - Increased risk of later changes - radio necrosis
    - Increase in symptoms; imaging uncertainty

- **WBRT:** Large volume, lower dose, smaller daily #
  - Increased risk of neurocognitive effects

- Both can cause fatigue, hair loss, nausea, headache
Clinical History

- Sept 2011: Previously fit 61 year old lady noticed a mass left breast
- Nov 2011: Left mastectomy and ANC – 18/27 nodes +ve,
  - ER+ve PR-ve HER2-ve
- Staging CT scan: equivocal lung nodules and bilateral hilar lymphadenopathy; subsequently unchanged and presumed benign
- Jan 12- March 12: Adjuvant chemo - FEC-T
- June12: Adjuvant XRT to chest wall
- July 12: Commenced arimidex
Clinical History

- April 2013: Developed increasing headaches and falls, but not systemically unwell; KP 80 / WHO PS 1
- Contacted her breast consultant
- MR Brain scan 21/5/13
What would you do next?
What would you do next?

- Commence dexamethasone
  - Patient has headaches and falls
  - MR scan shows oedema

- Restaging CT Thorax Abdo Pelvis

- Refer neuro-oncology MDT
  - WHO PS 1 / KP 80 (KP 100 on dex)
  - Controlled / controllable extracranial disease (small volume; many treatment options)
  - Life expectancy > 6/12
Is she eligible for SRS?

• That may depend on who you ask….
• Pros:
  • Fit lady
  • Controlled / controllable extracranial disease
• Cons:
  • Extensive intracranial disease
  • SRS does not treat micro-metastatic disease
Treated with WBRT

Treated with WBRT, 30Gy in 10# 21/6/13 – 1/7/13
21 May 13 vs 6 September 13: Excellent response
Routine follow-up MR 6 May 14
Increase in size of L cerebellar lesion
New lesion R cerebellum
Minimal residual intracranial disease elsewhere
Occasional word-finding difficulties, occasional dizziness

WHO PS 1 / KP 70
CT TAP: minimal progression eg 0.8cm -> 0.9cm
What next?

- Intracranial progression; still of good PS
- CT 23/7/14: Minor increase in lung disease, no metastases elsewhere
- Systemic treatment changed to oral capecitabine
Clinical History

- Discussed at neuroMDT: offered SRS
- At planning, additional lesion seen in left superior temporo-parietal lobe
SRS to 3 isocentres July 15 (treated volumes 1.7cc, 1.1cc, 0.6cc)

Dizzy for a few days post SRS, resolved spontaneously. Nil else.
Continued 3 monthly follow-up scans
12 Sept 14: Routine follow-up scan:
Reduction in left and right cerebellar treated areas; new lesion
right putamen
What would you do now?
Clinical History

- CT TAP 16/9/14 and 9/12/14:
- Further PD in lungs
- Changed to weekly paclitaxel
- Observe brain
26 Jan 15:
Stable appearances in the cerebellum
Resolution of right putamen lesion

CT TAP:
Responding to systemic chemo; commenced maintenance tamoxifen
29 May 15:
New lesions seen
Restaging CT: Lung-only disease, minimal PD

Discussed at neuroMDT: decision made to offer further SRS to 4 mets
Subsequent events: July 2015
(Brain mets diagnosed April 2013)

- 6 week telephone FU:
  - Increased dizziness
- Extended steroid regime (re-treatment & cerebellum)
- Symptoms ongoing
  - Increased unsteadiness – series of falls
  - Struggling
- MRI scan:
  - Increase in left cerebellar lesion (0.7x0.7cm → 1.1x0.9cm)
  - Other lesions shown response
- NeuroMDT: Post-treatment effect, no evidence of disease progression
- GP referral to ensure home support
- Clinical, continued deterioration
  - ? Meningeal disease (ocular symptoms, headaches)
  - Dex titrated downwards, but not discontinued
Supportive care in brain mets patients

- Steroid management
- Epilepsy
- Physical disability
- Neuro-cognitive decline
Dexamethasone: A Double-edged sword

- Initial often complete or near-complete resolution of symptoms

- **Acute effects:**
  - Agitation
  - Sleeplessness
  - Weight gain
  - Hyperglycaemia

- **Longer term:**
  - Proximal myopathy
  - Skin thinning
  - Oral thrush
Managing Steroids

• There are no guidelines or protocols to dictate what steroid dose a patient should be on.
• Everyone is different; very individualised
• Dose will depend on:
  • Stage of brain mets journey: acute diagnosis vs post-treatment vs end of life
  • Treatment: Surgery vs SRS vs WBRT
  • Personal sensitivity to dex

• The correct dose for any individual is *the lowest dose which keeps them symptomatically stable*
Steroids are reduced step-wise
- Acutely eg post-op, may be able to reduce and stop quickly
- Patients who have been on steroids for longer need to reduce more gradually
- Many patients need to stay on a low dose of steroids

**In general:**
- Reduce every 7 days in steps of 2mg, until you get to 2mg od
- Then reduce by 0.5mg every 7 days, to stop if possible.

There are no ‘right answers’ – just the lowest dose which keeps them well – anywhere between 0 - 16mg!
Epilepsy
Seizures in brain metastases patients

- Common, but seizures can take many forms
- The vast majority of patients achieve seizure control with appropriate anti-epileptics
  - Prescribe as per BNF

In patients with known seizures, care should focus on empowering people to cope at home
- Education
- Reducing anxiety
- Lifestyle factors – stress, tiredness, hunger, regularity of meds
- An ambulance is not needed every time
- If paramedics attend, they may decide not to bring patients to A&E – calling paramedics was still legitimate
The Christie NHS Foundation Trust

www.epilepsy.org.uk

Advice and information
The basics
Diagnosis
Treatment
Living with epilepsy
Help and support
Health matters
People with epilepsy
Education and work
The law
Syndromes
Advice and information references
A to Z

Advice and information

The basics

Introduction to epilepsy, seizures, first aid

Diagnosis

How it happens

Treatment

Living with epilepsy

Call or get in touch

Epilepsy Action Helpline
0808 800 5050

If you would like to talk to someone about epilepsy, our trained advisers are here to help

• Confidential, personal advice
• UK calls free – won’t show up on your landline bill
• Tell us as much or little as you want
• No question is a silly question
• Phone, email or text

Support us by visiting our shop
Rehabilitation
‘Rehabilitation’ in brain metastases

- Restoring function eg post-op
- Maintaining function
  - Long-term steroid use
- Optimising function
  - Mobility ‘techniques’
  - Aids
- Living with disability
  - Maintaining safety
Neurocognitive changes following WBRT

• WBRT can cause neurocognitive decline
  • Short term memory loss
  • Reduced ability to initiate and sequence

• But uncontrolled intracranial disease causes more neuro-cognitive decline and disability

• Occupational therapy referral can be very helpful
Driving

- DVLA website
  - [www.gov.uk/dvla](http://www.gov.uk/dvla) - health and medical conditions
- Very specific guidance
- Mandatory loss of licence, usually 2 years
- Huge impact on lifestyle and well-being
Conclusions

• Brain metastases are no longer necessarily an end-stage event
• A proportion of our patients now embark on a ‘brain mets journey’ with different treatments appropriate for different configurations of intracranial disease
• Prognosis depends on the underlying disease – more aggressive treatment is only beneficial in good PS patients with controlled or controllable extracranial disease
• Neuro-oncology MDT advice is worth seeking, esp in HER2+ve patients
Conclusions

• Dexmathasone dose needs to be individualised
  • review the dose at every contact
  • wean down gradually
  • is this person on the lowest dose which keeps them symptomatically stable?
• Epilepsy related to brain mets is not ‘special’
  • Don’t be afraid to encourage management as per BNF
• ‘Rehab’ is about much more than restoring function
Thankyou

Any questions?