Advances in Treatment of Metastatic Brain and Spine Tumors

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Metastatic Brain Tumors

- In the U.S. in 2016 according to American Cancer Society
  - Approximately 1.7 million new cancer cases
  - Almost 1 in 4 cases will have metastases to the brain
    - ~ 400,000 cases
Solitary or Oligo Metastatic Brain Tumors (<3 )

Diagnosis

- Known cancer history

- Unresectable, <2cm, deep, - edema, radiosensitive

- Resectable, >2cm, superficial, + edema, radioresistant

Surgery followed by WBRT, SRS, SRS + WBRT

Whole Brain Radiation Therapy and/or Stereotactic Radiosurgery
Solitary or Oligo Metastatic Brain Tumors (<3 )

Diagnosis

Unknown cancer history

Systemic work-up negative

Biopsy/resect

WBRT, SRS, SRS +WBRT

Surgery followed by WBRT, SRS, SRS +WBRT

Systemic work-up positive

Biopsy non-CNS site

WBRT, SRS, SRS +WBRT
Multiple Metastatic Brain Tumors (>3)

- Known cancer history
  - WBRT or SRS
- Unknown cancer history
  - Systemic work-up negative
    - Biopsy
    - Systemic work-up positive
      - Biopsy non-CNS site
      - WBRT or SRS
Surgical Resection of Solitary Metastatic Brain Tumors

- Patchell et al. 1990, Vecht et al. 1993, Mintz et al. 1996.\(^1\)\(^-\)\(^3\) - compared Surgery+WBRT vs. WBRT alone

  - **Median survival** (Patchell - 40 wks vs. 15 wks, Vecht - 10 mos vs. 6 mos, Mintz - 5.6 mos vs. 6.3 mos)

  - **Rate of local recurrence** (Patchell - 20% vs. 52%)

  - **Maintained QOL** KPS $\geq$ 70 (Patchell - 38 wks vs. 8 wks). Better functional independent survival with combined treatment (Vecht)

- Patchell et al. 1998 - compared Surgery vs. Surgery +WBRT \(^4\)

  - **Rate of local recurrence** - 46% vs. 10%

  - **Overall recurrence** - 70% vs. 18.18%

  - **Median survival** - 43 wks vs. 46 wks

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Whole Brain Radiation Therapy versus Stereotactic Radiosurgery

- **WBRT Toxicity**

  - Brown et al. for oligo-metastatic disease randomized SRS (111 pts) vs. SRS+WBRT (102 pts)

    - **Cognitive deterioration** at 3 mos (63.5% vs. 91.7%)
    - **QOL change from baseline** at 3 mos (-0.1 pts vs. -12.0 pts)
    - 3 & 12 mos intracranial tumor control rate (75.3%/50.5% vs. 93.7%/84.6%)
    - 3 & 12 mos local tumor control rate (89.0%/72.8% vs. 96.8%/90.1%)
    - Medial overall survival (10.4 dos vs. 7.4 mos)

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Surgery, WBRT, SRS - Maximizing benefit, minimizing harm

- Surgery - Part of combined therapy for local disease control and maintaining functional capacity
- WBRT - Primary/adjuvant therapy for CNS disease control. Negative neurocognitive effects
- SRS - Primary/adjuvant therapy for local disease control. Avoids neurocognitive effects of WBRT
What to do?

58 year old female with metastatic Breast Ca, 30-40 brain mets, large left cerebellar lesion with obstructive hydrocephalus
Endoscopic intraventricular surgery

- Endoscope adapted from cystoscope
- Endoscopic treatment of hydrocephalus. L’Espinasse and Kanavel first performed in 1910
- Mixter performed first endoscopic ventriculocisternostomy in 1923
- 1960s significant improvement of endoscope by Hopkins reinvigorated technique
58 year old female with metastatic Breast Ca, 30-40 brain mets, large left cerebellar lesion with obstructive hydrocephalus

- Endoscopic third ventriculostomy
- Whole Brain Radiation therapy POD#1
- Dc’ed to home POD#2
Laser Interstitial Thermal Therapy

- Stereotactic image-guided technique using laser fiber to ablate lesion soft tissue
- Originally introduced in 1983
- Laser interstitial irradiation to produce thermal damage
  - Greatest degree of penetration in the near-infrared spectrum
  - Selective thermal injury of pathologic tissue
    - Sharp ablation zone border
- Early efforts confounded by ability to control thermal damage

Laser Interstitial Thermal Therapy

- Development of real-time MR thermography to monitor treatment
- Coupled cooling mechanism over probe with feedback control mechanism and temperature limits
- Preliminary studies into malignant gliomas, cranial and spinal metastases, radiation necrosis, and epilepsy

Post-ablation Images

Damage model
Tumor Treating Fields

- Trial TTF + maintenance temozolomide vs TMZ alone ⁶
  - Terminated early at interim analysis
  - PFS 7.1 mos vs 4.0 mos
  - Overall survival 20.5 mos vs 15.6 mos

- Application of Tumor-Treating Fields to other cancers
  - Ongoing Trials

Targeted Systemic Therapy

- Targeted inhibitors and immunotherapy may improve control of CNS metastatic disease
  - Melanoma
  - Breast Ca
  - NSCLC

CPMC experience

- 79 patients with metastatic melanoma to the brain treated with CTLA-4Ab, PD-1Ab or BRAF (+/- MEK) inhibitors
  - Historically, melanoma with brain mets OS ~ 5mos
  - Median OS from brain met dx 12.8 mos
  - Median OS from stage IV dx 18.2 mos
Metastatic Spine Tumors

- Bone is the 3rd most common site of cancer metastasis after lungs and liver
- Majority of bony metastasis are in the spine
- Up to 40% of patients with metastatic cancer will have spinal metastasis during the course of their disease
Surgical intervention for metastatic spine tumors

- Patchell et al. landmark 2005 study evaluating the role of surgery for metastatic spine tumors
  
- Demonstrated benefit of surgery+RT over RT alone
  
  - Ambulating after Tx (84% vs 57%); Maintained ambulation (122 days vs 13 days); Regained ability to ambulate (62% vs 19%)

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Surgical intervention for metastatic spine tumors

Laufer et al. 2013

- Laufer et al. study evaluated the outcomes of “Separation Surgery” approach using NOMS (Neurologic, Oncologic, Mechanical stability, Systemic disease) criteria.

- Resection of epidural tumor, creating “separation” of 2-3mm plus stabilization followed by single fraction or hypo fractionated SRS.

- 1 yr local progression 16.4%
  - Low dose hypo-fractionated (30Gy in 5-6 fractions) 22.6% progression
  - High dose hypo-fractionated (27Gy in 3 fractions) 4.1% progression
  - Single-fraction (24Gy) 9% progression

- “Minimally Invasive” Approach

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Metastatic Spine Tumors

Diagnosis → Known cancer history → NOMS criteria: Neurologic Oncologic Mechanical Systemic → Fractionated Radiation Therapy or Stereotactic Radiosurgery → Separation Surgery followed by SRS
Metastatic Spine Tumors

Diagnosis → Unknown cancer history → Systemic work-up

Biopsy spine lesion

NOMS criteria: Neurologic Oncologic Mechanical Systemic

Biopsy non-spine site

Separation Surgery followed by SRS

Fractionated Radiation Therapy or Stereotactic Radiosurgery
Minimally invasive surgery for metastatic spine tumors

- Retrospective comparison between MIS (23 patients) vs traditional open surgery (19 patients)\(^{10}\)

  - Pathology included Lung, Breast, Myeloma, Renal, Melanoma, Prostate, Ovarian, Thyroid

  - MIS vs Open: OR time (2.2 hrs vs 3.2 hrs), EBL (240ml vs. 900ml), Postop transfusions (0 pts vs 12 pts), Postop bedres (2 d vs 4 d), LOS (7.2 d vs 9.25 d), EORTC QOL-C30 improvement (13.6 vs. 9.8), QLQ-BM22 improvement (14.07 vs. 4.65)

Minimally Invasive Spine Surgery for Malignant Spine Tumors

• 87 yo male who developed new LBP x 4 mos. L4 lesion concerning for malignancy. IR biopsy returned as Leiomyosarcoma. Represented with progressive low back pain, weakness, and left radicular leg pain.

• MIS decompression of left L4 nerve root and Percutaneous pedicle stabilization from L3-L5
  • Discharged to rehab POD3
  • Discharged to home POD14
• Stereotactic radiation therapy 2 weeks postop
Evolving Technologies and Therapeutics

• Surgery
  • Minimally invasive cranial surgical techniques (Endoscopic, Laser Interstitial Thermal Therapy)
  • Minimally invasive spine surgery (Minimally invasive decompression, Percutaneous stabilization, Vertebral augmentation)

• Radiation therapy
  • Stereotactic radiosurgery

• Tumor Treating Fields

• Targeted systemic therapy

• Maximizing Benefit, Minimizing Harm
Thank You