

AMSER Case of the Month 2019

71-year-old male with gait instability and nausea

Emily Bulson, OMS IV
Lake Erie College of Osteopathic Medicine

Linda Xu, MD
Stacey Miller, MD
Cody Marshall, DO, PGY-1
Charles Li, MD
Matthew Hartman, MD
Allegheny Health Network
Department of Radiology



Patient Presentation

- HPI: 71 y.o. M completed cycle 15 of sunitinib and noted to have balance issues for the past week along with 2 days of non-bloody vomiting.
- MHx: GERD, HTN, HLD, RCC Fuhrman grade 2 pT3a pNx, Vit D deficiency, drug-induced hypothyroidism
- SHx: cystoscopy w/fulgeration, laparoscopic radical nephrectomy and adrenalectomy, VATS and wedge resection
- Medications: atorvastatin 10mg, omeprazole 20mg, metoprolol 50mg, dexamethasone 4mg, D3, levothyroxine 50mcg, sunitinib 37.5mg

Physical Exam

- **Constitutional:** malaise/fatigue
- **Neuro:** AOX3, normal speech, dizziness, weakness, sensation intact
- **HEENT:** left peripheral field deficit, neg for blurred or double vision, tinnitus, hearing loss, bleeding
- **Cardiovascular:** neg chest pain, palpitations, claudication, LE edema
- **Pulmonary/Chest:** neg for hemoptysis, wheezing, cough, SOB
- **GI:** worsening diarrhea past several days, nausea
- **GU:** no dysuria, hematuria, flank pain

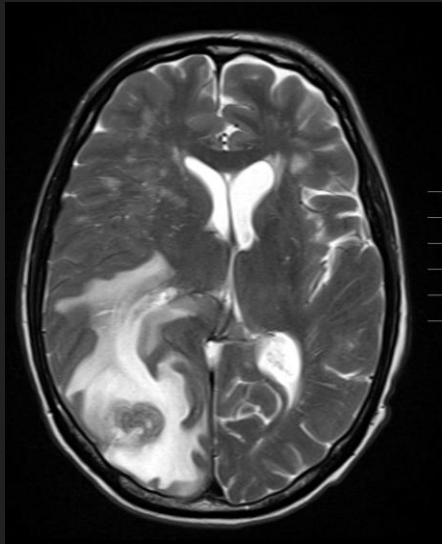
ACR Appropriateness Criteria

Variant 3:

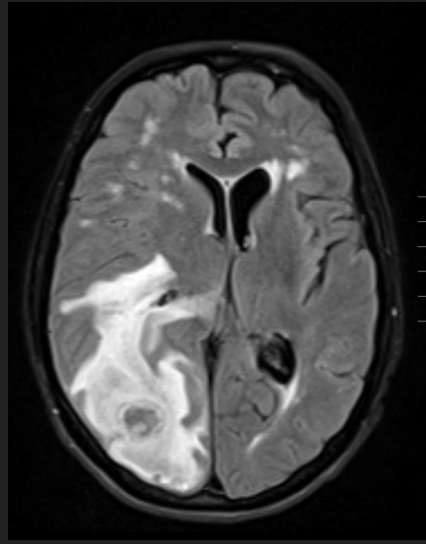
Ataxia. No history of trauma. Suspected intracranial process. Stroke intervention not a consideration. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI head without and with IV contrast	Usually Appropriate	0
MRI head without IV contrast	Usually Appropriate	0
CT head with IV contrast	May Be Appropriate	☼☼☼
CT head without IV contrast	May Be Appropriate	☼☼☼
CT head without and with IV contrast	May Be Appropriate	☼☼☼
CTA head and neck with IV contrast	Usually Not Appropriate	☼☼☼
MRA head and neck without and with IV contrast	Usually Not Appropriate	0
MRA head and neck without IV contrast	Usually Not Appropriate	0
Arteriography cervicocerebral	Usually Not Appropriate	☼☼☼
CTV head with IV contrast	Usually Not Appropriate	☼☼☼
I-123 Ioflupane SPECT/CT brain	Usually Not Appropriate	☼☼☼
MRV head with IV contrast	Usually Not Appropriate	0
MRV head without IV contrast	Usually Not Appropriate	0
In-111 DTPA cisternography	Usually Not Appropriate	☼☼☼

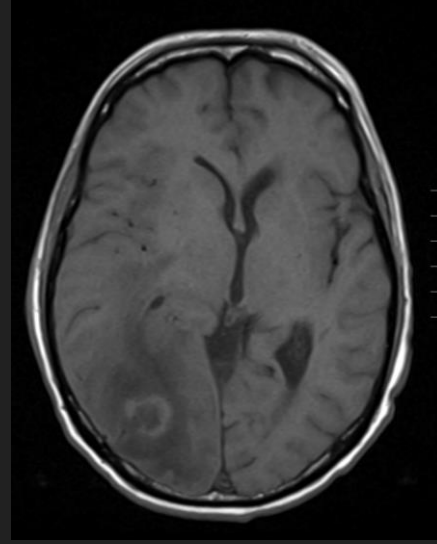
Axial MR



T2



FLAIR

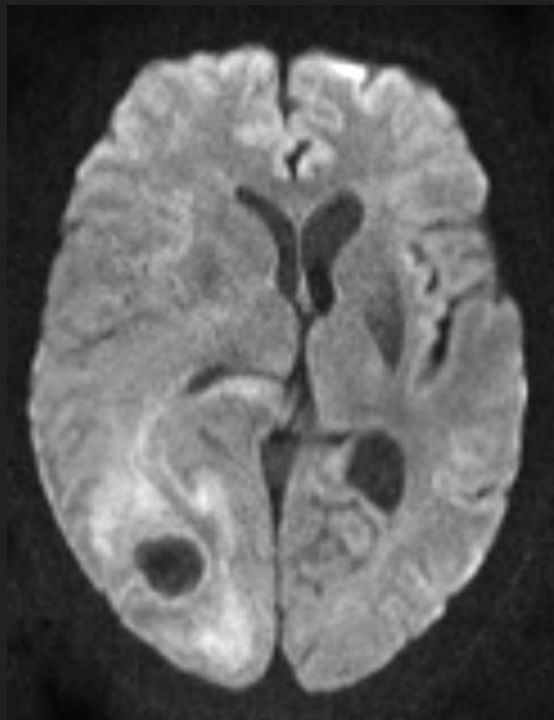


T1 Non-contrast

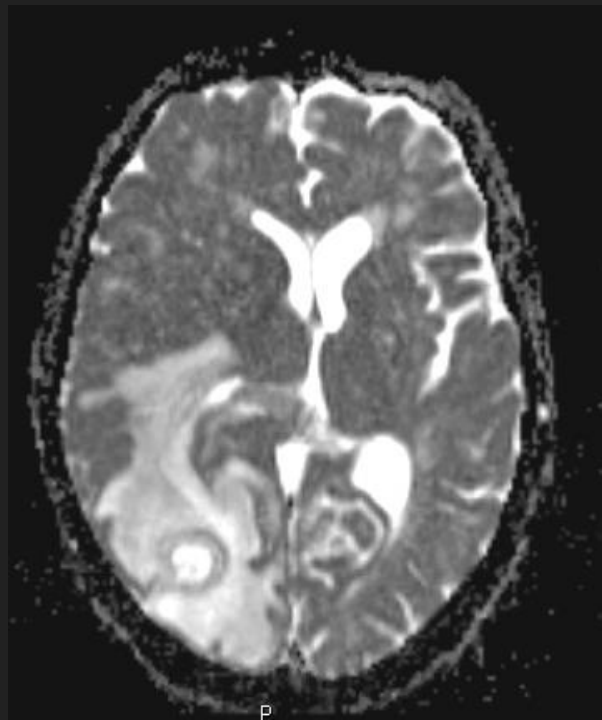


T1 Post-Contrast

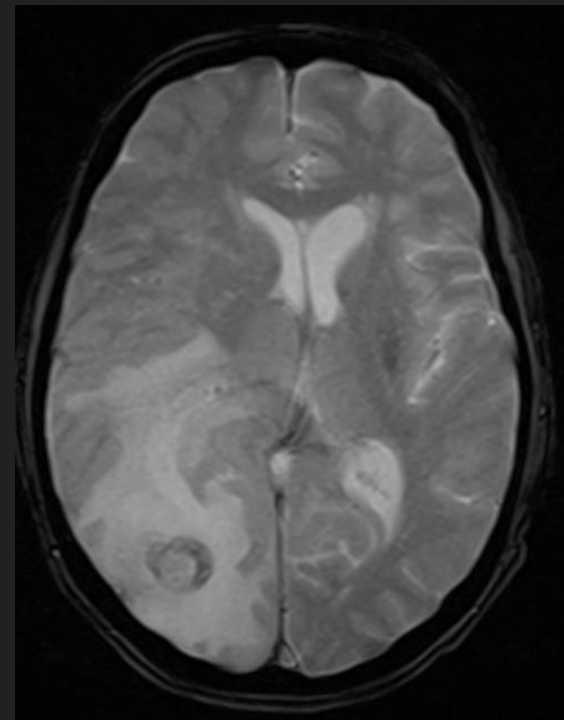
Axial MR



DWI

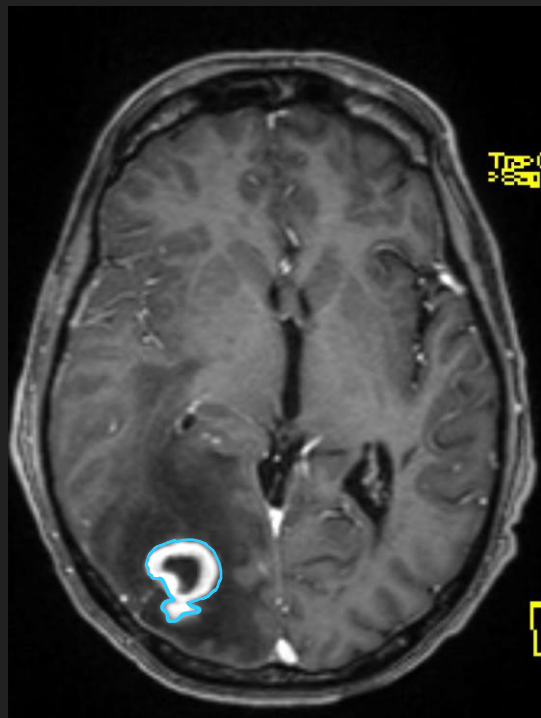


ADC



FLASH

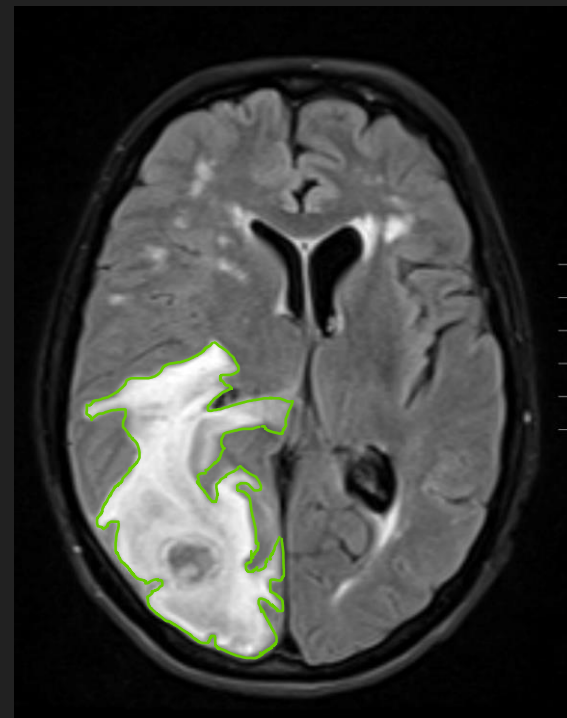
Findings: Labeled MR



Axial T1 post-contrast

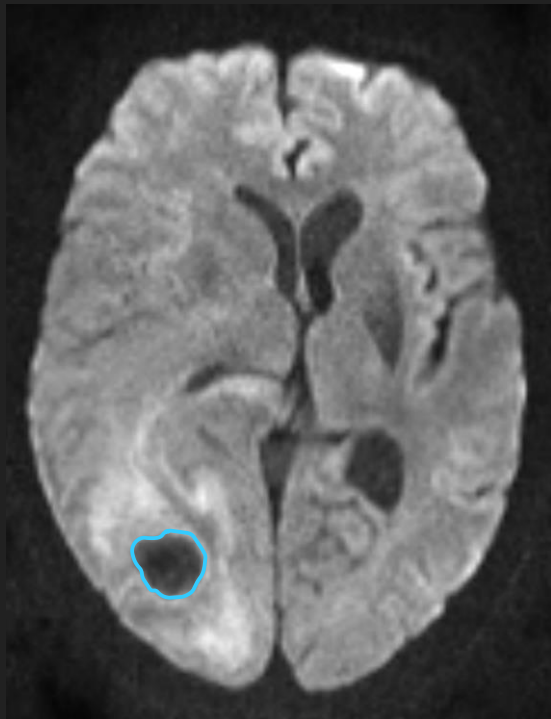
Vasogenic Edema

2.5 cm Intra-axial
ring enhancing subcortical lesion

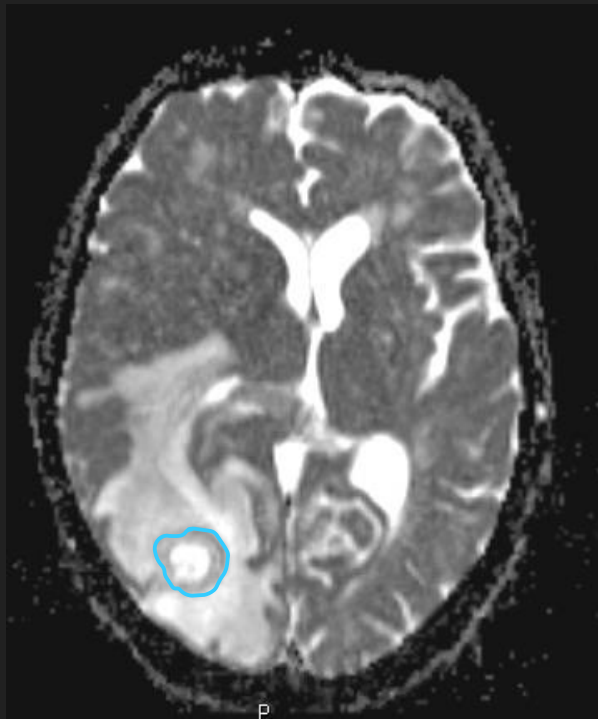


FLAIR

Findings: Labeled MR



DWI



ADC

No diffusion restriction

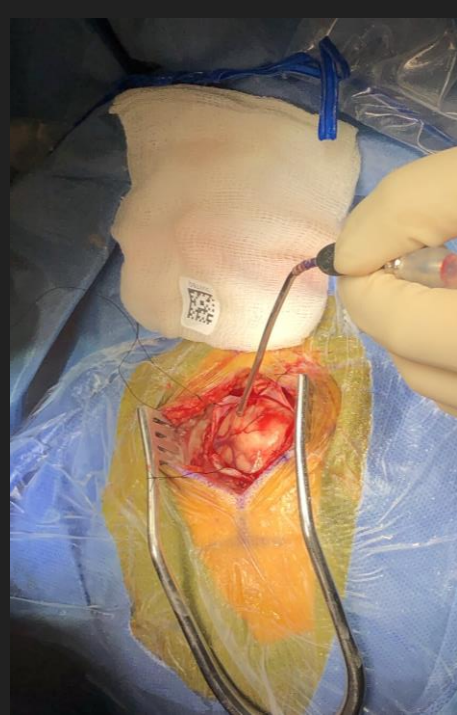
DDx of Ring Enhancing Lesion in the Brain

MAGICAL DR

- Metastasis
- Abscess
- Glioblastoma
- Infarct
- Contusion
- AIDS-related CNS disease
- Lymphoma
- Demyelination
- Radiation necrosis

With a previous large RCC (*), metastasis to the brain is a diagnosis of exclusion





Mass causing protrusion of dura

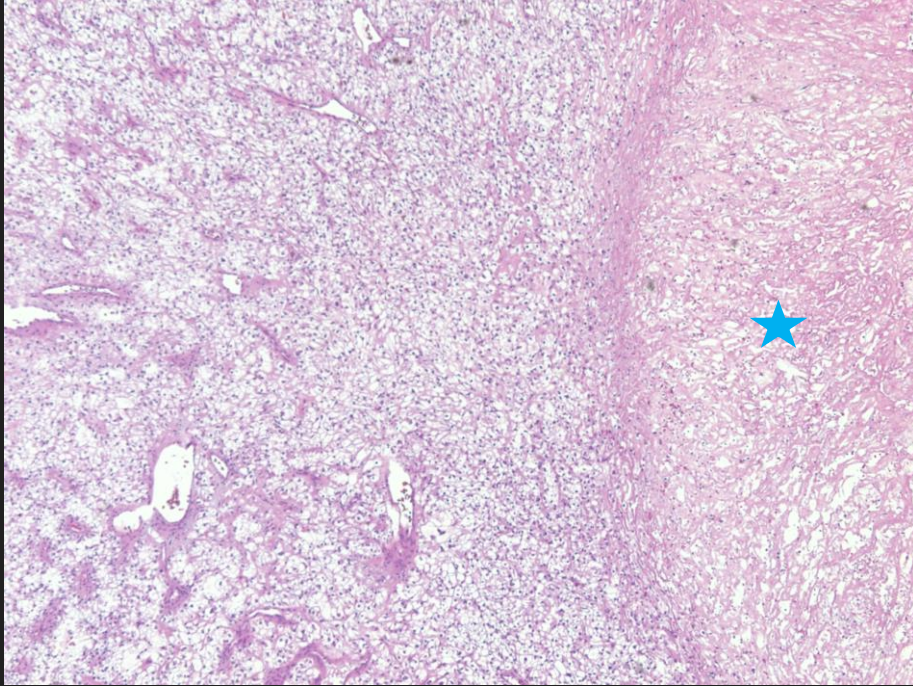


2.1 x 1.4 x 1.3 cm

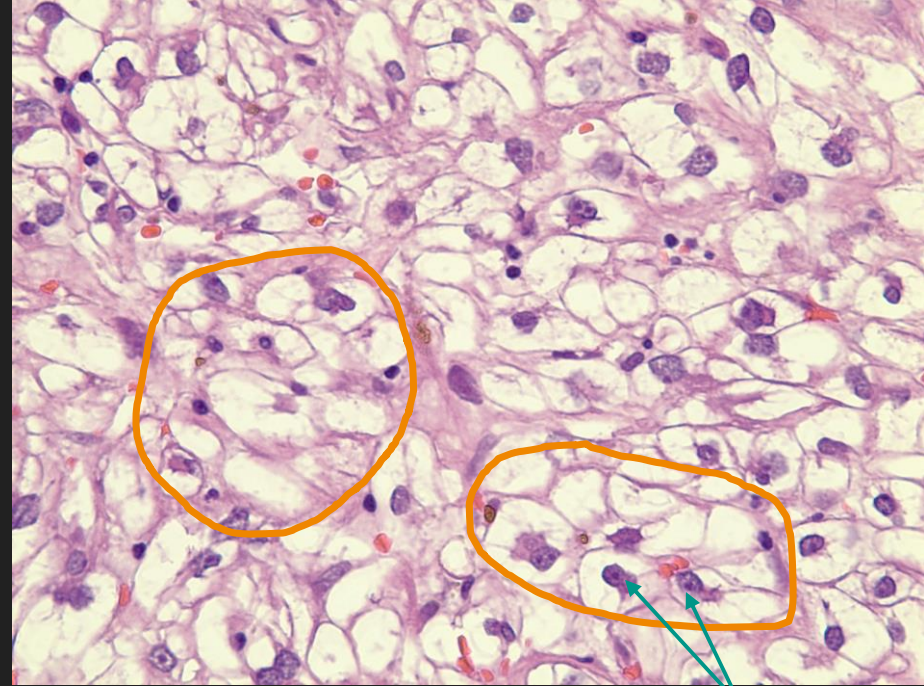


Intra-op

Findings: Histology



Low power H&E: tumor outgrowing its vascular supply as indicated by the **necrotic area***



High power H&E: **nests of cells** with **prominent nucleoli**, irregular nuclei and abundant cytoplasm composed of glycogen and lipids (why hyperintense on T2)

Final Diagnosis:

Metastatic Renal Clear Cell Carcinoma

Patient was discharged two days after his craniotomy and is scheduled to follow up with gamma knife focused radiation within 3-4 weeks

Renal Cell Carcinoma Brain Metastasis (BM)

- Epidemiology: BM occur in 2-10% of patients with recurrent RCC. Greatest risk of recurrence following RCC resection is in the first 2-3 years with an average interval from nephrectomy to brain metastasis of 1–5 years. Median overall survival after diagnosis of RCC BM is 8-10 months, 3 year survival of 28%.
- Pathogenesis: Particular sites of metastatic disease are associated with a greater likelihood of BM: 2% with abdominal metastases vs 16% with thoracic and bone metastases. The size of the lesion and not the number of lesions is found to correlate with symptoms. BM are usually located at the junction of gray and white matter where blood vessels decrease in diameter—acts as a trap for clumps of tumor cells. 80% occur in the cerebral hemispheres and tend to be more common at the terminal "watershed areas" of arterial circulation.

Renal Cell Carcinoma Brain Metastasis

- Clinical Presentation:
 - Asymptomatic in 80% until significant edema develops
 - mean size of asymptomatic lesions was 1.3 cm vs 2.1 cm for symptomatic lesions
 - headache, altered behavior, confusion, or seizure are most commonly reported
- Physical exam:
 - Depends on location of lesion—visual field defects, gait abnormalities
 - Up to 90% have metastatic disease in other locations
- Screening:
 - No clear guidelines, but CNS surveillance after nephrectomy is generally not recommended unless symptoms develop

RCC Brain Metastasis Radiologic Features

- CT:
 - Enhancing nodules with associated vasogenic edema
 - Usually a solitary lesion with a hemispheric location
 - unlike metastasis from other tumors such as melanoma, lung or breast cancer, which usually appear as multiple lesions
- MRI:
 - Contrast enhanced MRI is the **modality of choice** as it is more sensitive than CT for detecting smaller lesions
 - Usually solid but can also show cystic changes or necrosis
 - If predominantly cystic, it can show a marginal enhancing solid component (like this case)
 - Lack of diffusion restriction on DWI-ADC
 - unlike mimickers of metastasis like lymphoma or abscess
 - Hypervascular—can show hemorrhagic changes
 - Hyperintense on T2

RCC Brain Metastasis Management

- Surgery: **standard of care** if in an accessible location and limited volume (1-10)
- Radiotherapy:
 - Overall has low sensitivity to conventional radiation therapy
 - Whole brain radiotherapy used for widespread brain metastasis—typically not effective
 - Repeated **gamma knife (GK)** radiotherapy recommended for *newly developed* brain mets
 - 75,350 lesions treated with GK after surgery demonstrated a 95% actuarial rate of local tumor control, with a median survival of 11.1 months
 - **Stereotactic radiosurgery (SRS)** is the preferred method for *smaller lesions*
 - local control with SRS decreases as the size of the lesion increases
 - 2 cm threshold before the risks for both recurrence and radionecrosis or CNS toxicity increases
 - Overall, >4cm generally considered too large for SRS
- Immunotherapy
 - Adjuvant therapy has controversial beneficial effect, FDA approved 10 therapies in last decade
 - Proven overall survival and progression-free survival benefits:
 - Axitinib + Pembrolizumab, Nivolumab + Opilimumab

References

- Brufau BP, Cerqueda CS, Villalba LB, et al. Metastatic Renal Cell Carcinoma: Radiologic Findings and Assessment of Response to Targeted Antiangiogenic Therapy by Using Multidetector CT. *RSNA*. 2013;33:1691-1716. doi:10.1148/rg.336125110.
- Shuch B, La Rochelle JC, Klatte T, et al. Brain Metastasis From Renal Cell Carcinoma: Presentation, Recurrence, and Survival. *Cancer*. 2008;113:1641-1648. doi:10.1002/cncr.23769.
- Kolsi F, Mechergui H, Kammoun B, Mellouli M, Khrifech M, Zaher Boudawara M. Delayed brain metastasis from renal cell carcinoma. *Urol Case Rep*. 2018;22:54–56. doi:10.1016/j.eucr.2018.10.020
- Suarez-Sarmiento A, Nguyen K, Nolte A, et al. Brain Metastasis from Renal Cell Carcinoma: An institutional Study. *The Journal of Urology*. 2018;199:e867. doi:10.1016/j.juro.2018.02.1873
- Ramalingam S, George DJ, Harrison MR. How We Treat Brain Metastases in Metastatic Renal Cell Carcinoma. *Clinical Advances in Hematology and Oncology*. 2018;16:110-114. <https://www.hematologyandoncology.net/files/2018/02/ho0218Howltreat-1.pdf>. Accessed September 31, 2019.