GE Healthcare

Case studies with Lawrence N. Tanenbaum, MD FACR using macrocyclic CLARISCAN™ (gadoterate meglumine) injection for intravenous use

Lawrence N. Tanenbaum, MD FACR is Vice President/Chief Technology Officer Director of CT, MR, and Advanced Imaging for RadNet with 37+ years experience in the medical field. He is a member of editorial boards of several journals/educational organizations and reviewer for scientific journals. He has authored 100+ scholarly and peer-reviewed articles, chairs educational/academic meetings, and has delivered 2000+ invited global lectures.*

PRODUCT INDICATIONS AND USE:
CLARISCAN™ (gadoterate meglumine) is a gadolinium-based contrast agent indicated for intravenous use with magnetic resonance imaging (MRI) in brain (intracranial), spine, and associated tissues in adult and pediatric patients to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

Additional pediatric use information is approved for Guerbet LLC's Dotarem (gadoterate meglumine injection). However, due to Guerbet LLC's marketing exclusivity, this drug product is not labeled with that pediatric information.

IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™
Contraindications
History of clinically important hypersensitivity reactions to Clariscan

Please see the Boxed Warning to the right and additional Important Safety Information on the following pages. Click here for full Prescribing Information, including patient Medication Guide.

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)
See full Prescribing Information for complete Boxed Warning.
Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle, and internal organs.

- **The risk for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR <30 mL/min/1.73 m^2), or**
  - **Acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended Clariscan dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

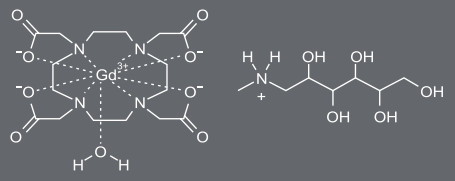
Clariscan™
(gadoterate meglumine)
injection for intravenous use

Macrocyclic, ionic GBCA

Cagelike structure encloses the Gd^{3+} ion[1]

Highest chelate stability among GBCAs[2]

Strong chemical bond[3]



Gadoterate meglumine

Case Study #1

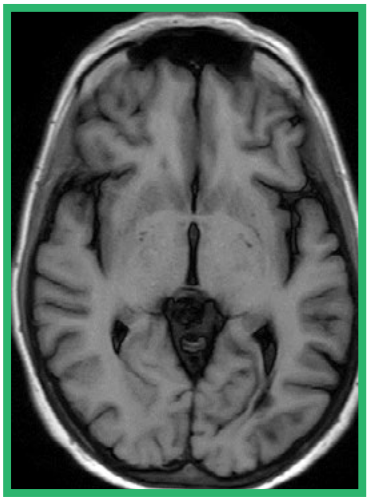
Clinical Presentation

47-year-old female weighing 170 lbs, presented with headache

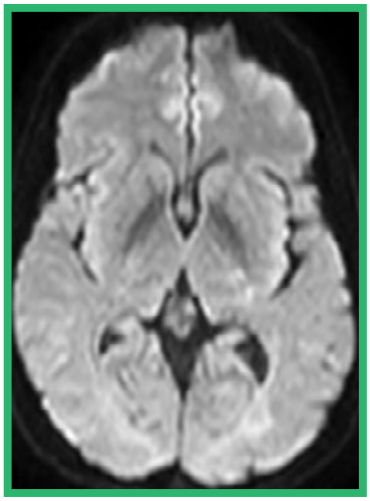
Imaging

MR of the brain and pituitary with and without 17 mL of Clariscan™ (gadoterate meglumine)

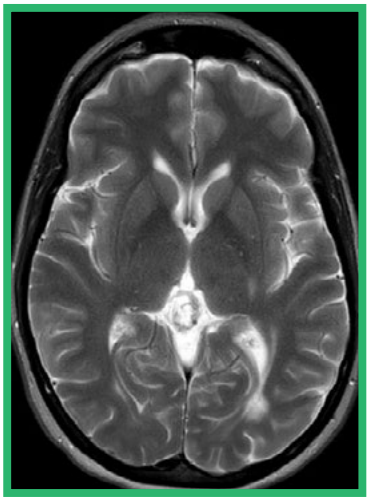
Precontrast T1 axial



Precontrast DWI axial



Precontrast T2 axial



- **Complex, predominantly cystic pineal lesion noted**

(Continued)

IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™

Warnings and precautions

- Nephrogenic Systemic Fibrosis has occurred in patients with impaired elimination of GBCAs. Higher than recommended dosing or repeat dosing appear to increase the risk.
- Hypersensitivity: Anaphylactoid/anaphylactic reactions with cardiovascular, respiratory or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred. Monitor patients closely for need of emergency cardiorespiratory support.
- Gadolinium is retained for months or years in brain, bone, and other organs.

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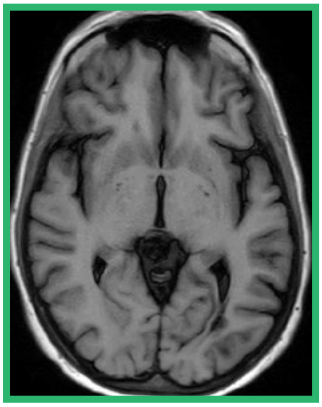
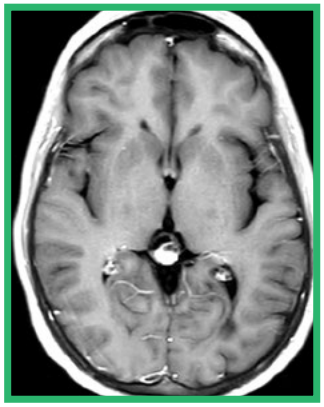
Clariscan™
(gadoterate meglumine)
injection for intravenous use

Case Study #1 (cont'd)

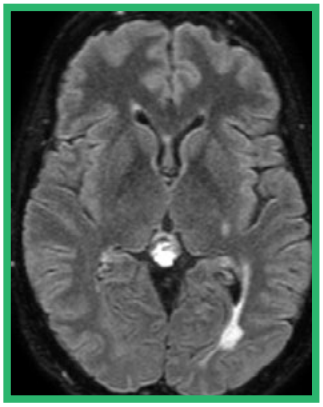
Precontrast T1 axial



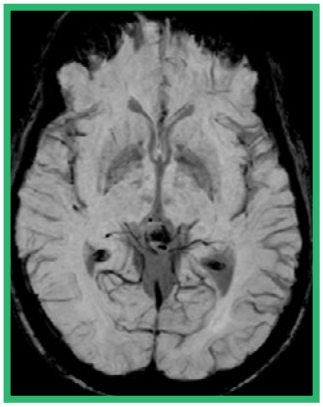
Postcontrast T1 axial



Postcontrast FLAIR



SWI axial



- **Complex, partially cystic pineal lesion with enhancing, solid components**
- **Note the prominent susceptibility effects associated with likely calcified lesion components**

Imaging Findings

Complex, partially cystic pineal lesion with enhancing solid components

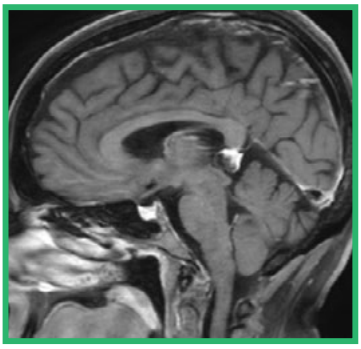
Diagnosis

Complex pineal lesion

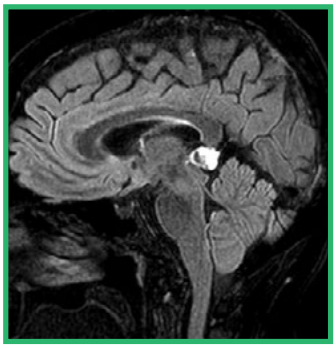
Treatment

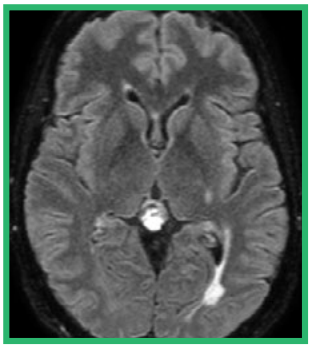
Surveillance

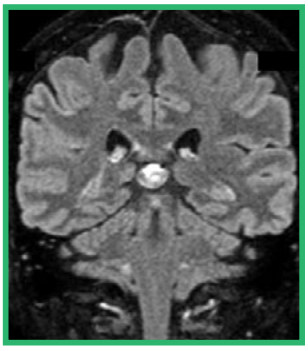
Postcontrast T1 sagittal



Postcontrast FLAIR







IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™ (Cont'd)

Warnings and precautions (cont'd)

- **Acute kidney injury**: In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent; administer the lowest dose necessary for adequate imaging.

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Clariscan™
(gadoterate meglumine)
injection for intravenous use

Case Study #2

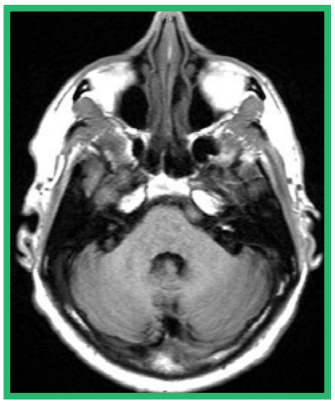
Clinical Presentation

55-year-old male weighing 170 lbs, presented with headache and tinnitus

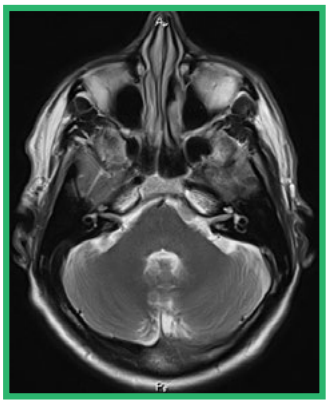
Imaging

MRI of the brain with internal auditory canals/temporal bones with and without 17 mL of Clariscan™ (gadoterate meglumine) intravenous administration

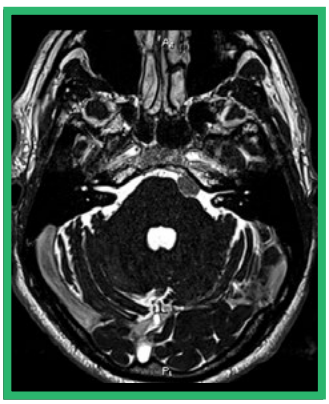
Precontrast T1 axial



Precontrast T2 axial

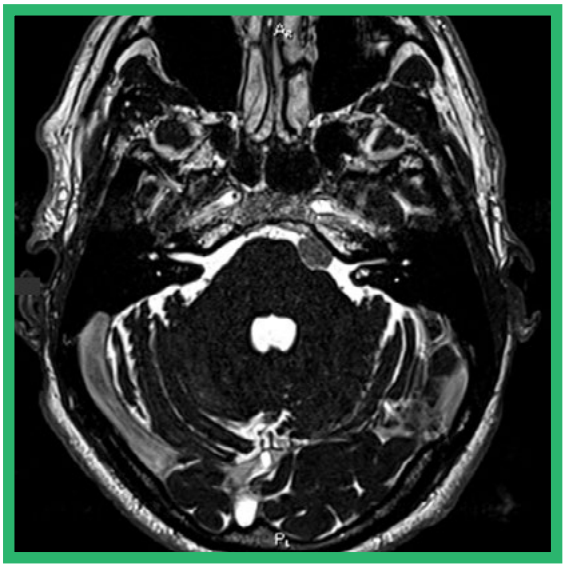


Balanced SSFP (C- cisternographic) imaging

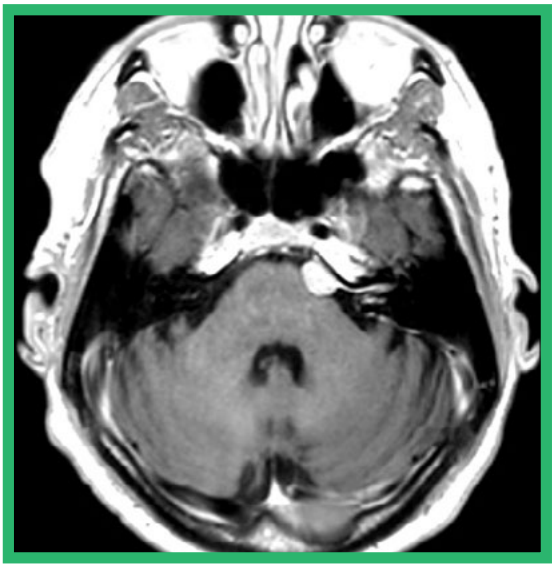


- **Possible extra-axial lesion at the left lateral aspect of the pons**

Balanced SSFP (C- cisternographic) imaging



Postcontrast T1



- **Balanced SSFP (left) and postcontrast T1 axial demonstrate a small left lateral pontine extra-axial mass with a tail of enhancing dura extending into the left internal auditory canal most consistent with a meningioma**

IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™ (Cont'd)

(Continued)

Adverse reactions

- **Extravasation and injection site reactions:** Ensure catheter and venous patency before the injection of Clariscan. Extravasation into tissues during Clariscan administration may result in tissue irritation.
- The most common adverse reactions (≥ 0.2%) associated with gadoterate meglumine in clinical trials were nausea, headache, injection site pain, injection site coldness and rash.
- Serious adverse reactions in the postmarketing experience have been reported with gadoterate meglumine. These serious adverse reactions include but are not limited to: arrhythmia, cardiac arrest, respiratory arrest, pharyngeal edema, laryngospasm, bronchospasm, coma and convulsion.

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Clariscan™
(gadoterate meglumine)
injection for intravenous use

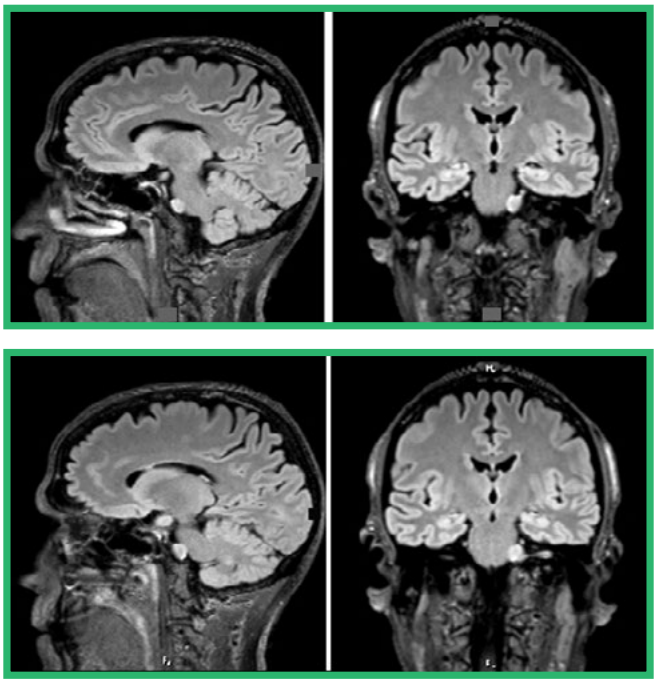
Case Study #2 (cont'd)

Imaging Findings
Small extra-axial lesion at the left lateral aspect of the pons, which shows significant enhancement on postcontrast images.

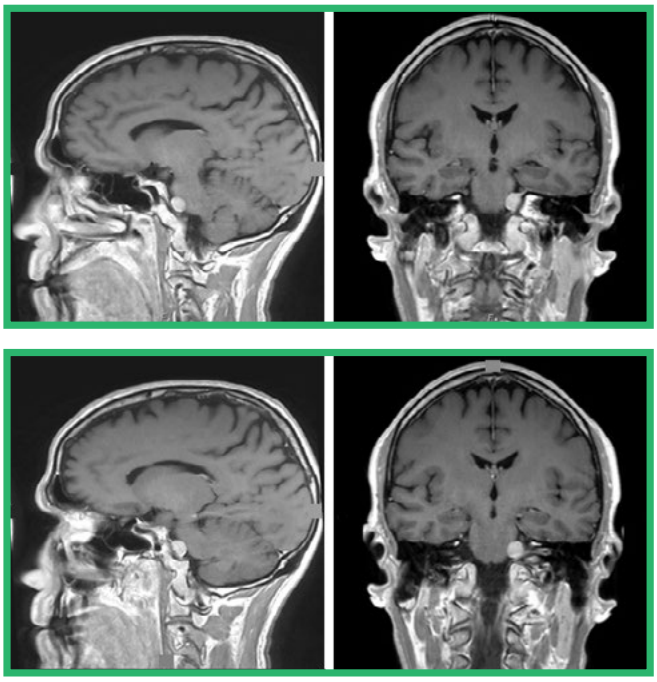
Diagnosis
Meningioma

Treatment Plan
Stereotactic radiosurgery

Postcontrast FLAIR sagittal and coronal



Postcontrast T1 sagittal and coronal



IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™ (Cont'd)

Use in specific populations

- **Pregnancy:** GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. The human data on the association between GBCAs and adverse fetal outcomes are limited and inconclusive. Because of the potential risks of gadolinium to the fetus, use Clariscan only if imaging is essential during pregnancy and cannot be delayed. Advise pregnant women of the potential risk of fetal exposure to GBCAs.
- **Lactation:** There are no data on the presence of gadoterate in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.

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Clariscan™
(gadoterate meglumine)
injection for intravenous use

Case Study #3

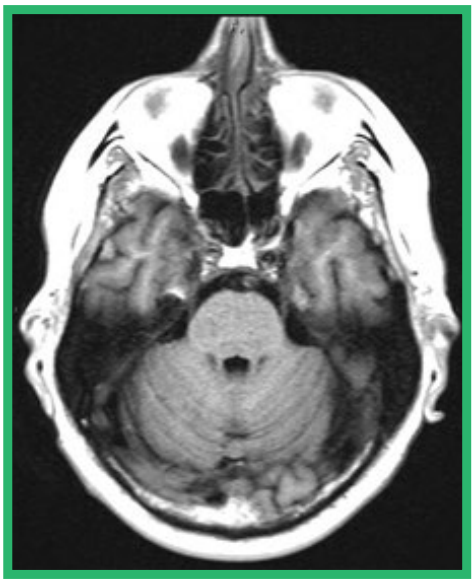
Clinical Presentation

A 60-year-old male weighing 200 lbs, presented with new onset of seizures

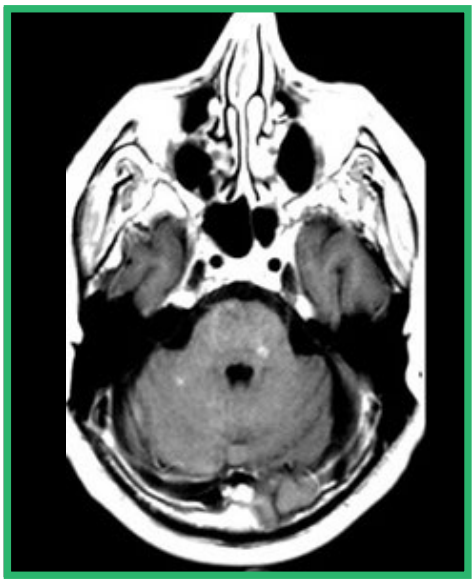
Imaging

MR of the brain was performed with and without 20 mL of Clariscan™ (gadoterate meglumine)

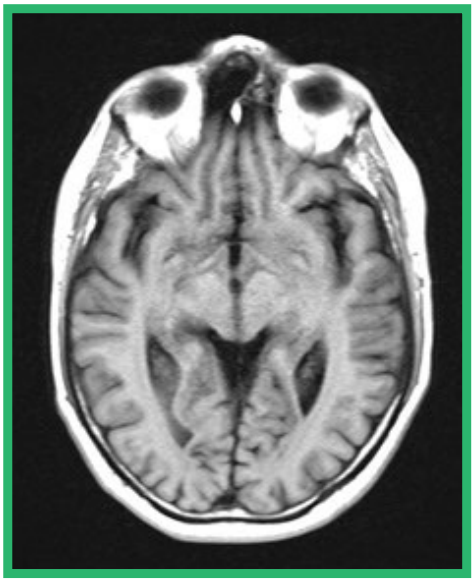
Precontrast T1 axial



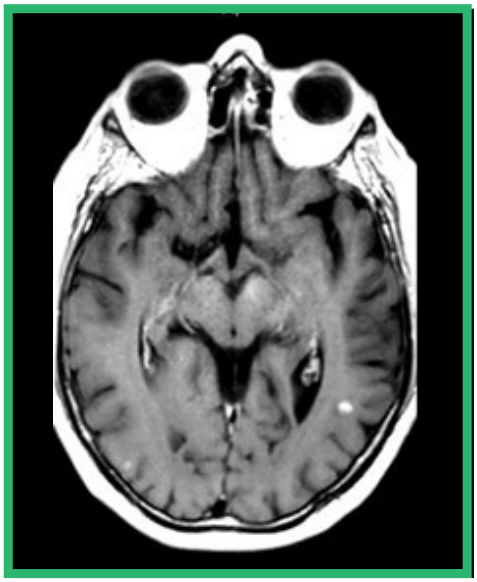
Postcontrast T1 axial



Precontrast T1 axial



Postcontrast T1 axial



- **Multiple additional enhancing lesions appeared after administration of Clariscan (not apparent on precontrast T1)**

(Continued)

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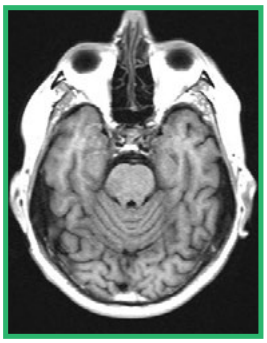
Clariscan™
(gadoterate meglumine)
injection for intravenous use

Case Study #3 (cont'd)

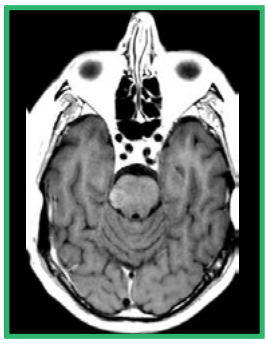
Imaging Findings
Numerous nodular enhancing lesions consistent with metastatic disease

Diagnosis
Brain metastasis

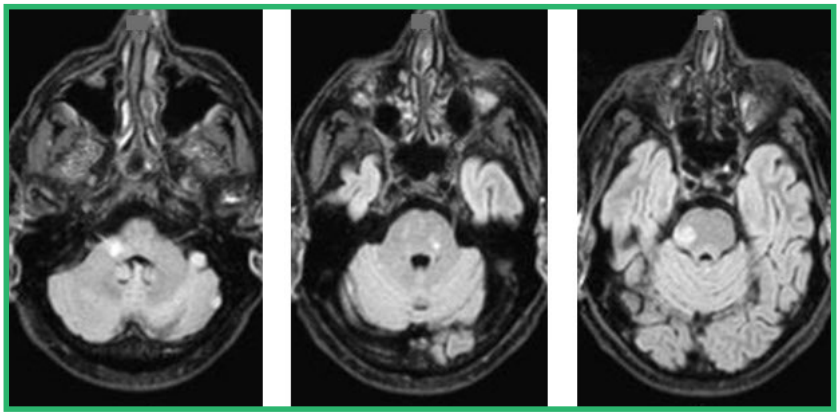
Precontrast T1 axial



Postcontrast T1 axial

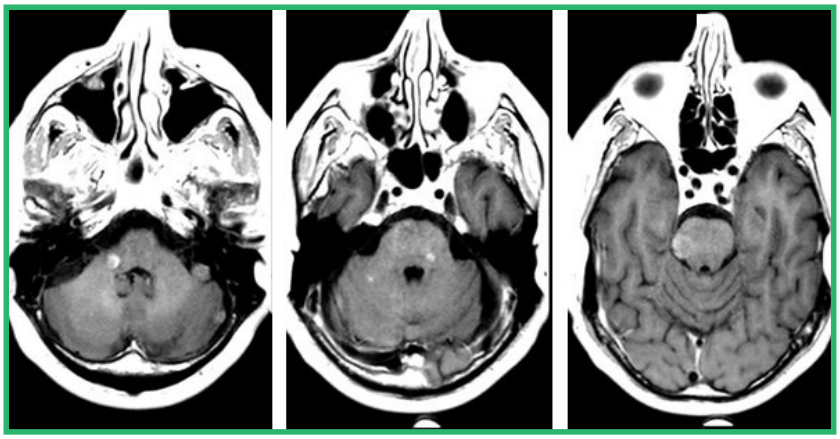


Postcontrast axial FLAIR



- Probable right pontine solitary lesion that is much more clearly defined on Clariscan-enhanced T1 weighted image (right)

Postcontrast T1 axial



- Postcontrast FLAIR axial and T1 reveal multiple nodular enhancing lesions consistent with metastatic disease

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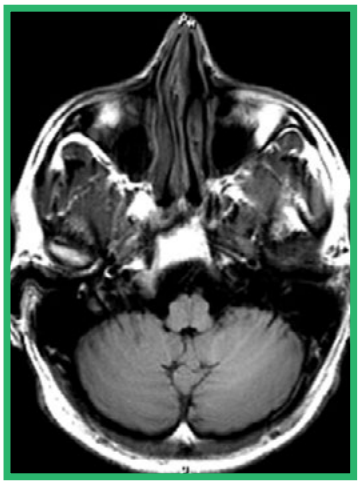
Clariscan™
(gadoterate meglumine)
injection for intravenous use

Case Study #4

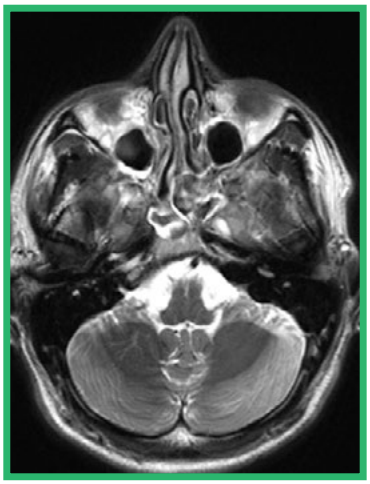
Clinical Presentation
A 32-year-old male weighing 180 lbs, presented with left facial paresthesias

Imaging
MR of the brain with and without 18 mL of Clariscan™ (gadoterate meglumine)

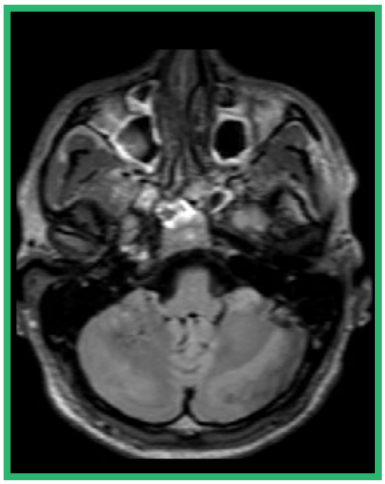
T1 axial



T2 axial

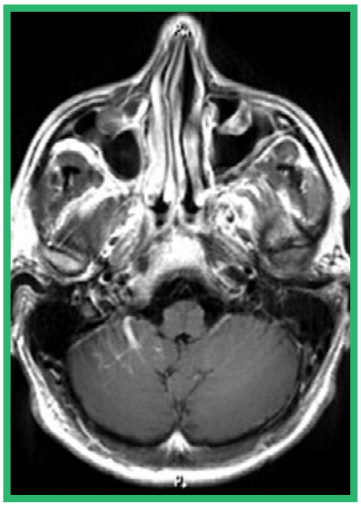


Postcontrast FLAIR axial

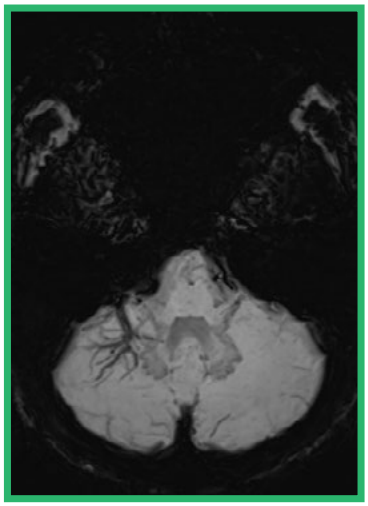


- **Precontrast images show no obvious abnormality**

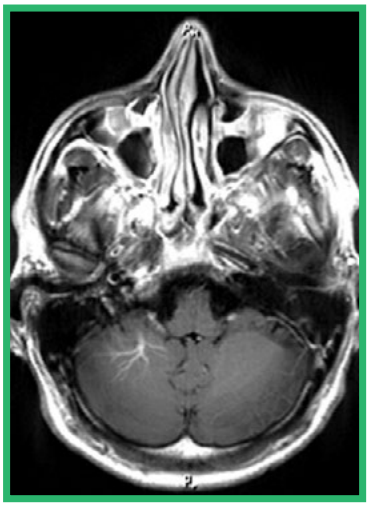
Postcontrast T1 axial



Postcontrast SWI



Postcontrast T1 axial



Imaging Findings
Multiple dendritic enhancing vascular structures coalescing on a single draining vein consistent with a developmental venous anomaly

Diagnosis
Developmental venous anomaly

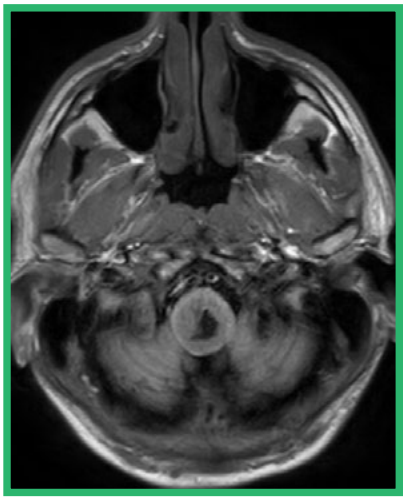
Treatment
None

Case Study #5

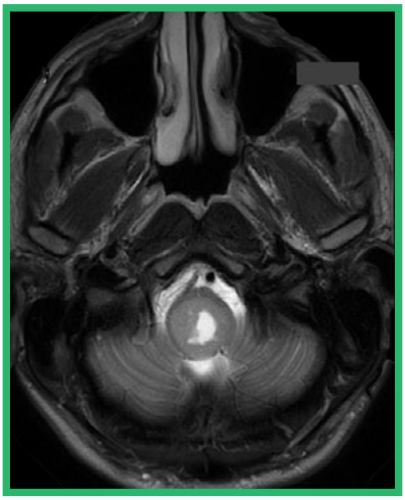
Patient Presentation
A 28-year-old female weighing 150 lbs, presented with headache and weakness

Imaging Plan
MR of the brain with and without 15 mL of Clariscan™ (gadoterate meglumine)

Precontrast T1

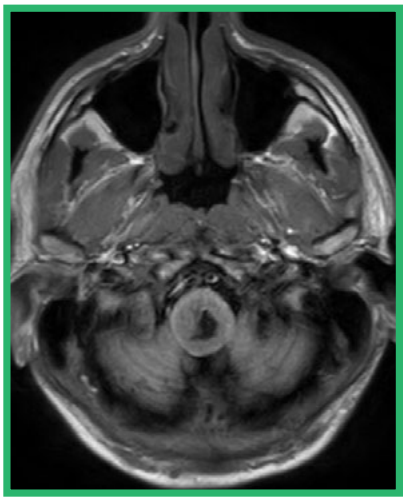


T2

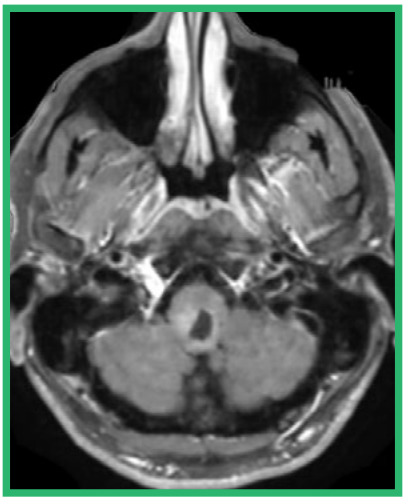


- **Imaging reveals a complex, exophytic lower brainstem lesion**

Precontrast T1



Postcontrast



- **Complex, exophytic lower brain stem lesion with enhancing and non-enhancing components**

Imaging Findings
Complex, dorsally exophytic lower brainstem lesion

Diagnosis
Diffuse midline-brainstem glioma

Treatment
Radiation and chemotherapy

(Continued)

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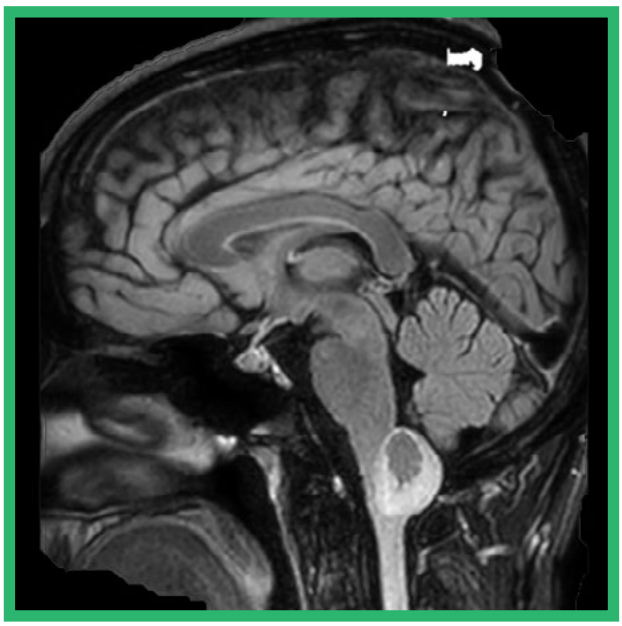
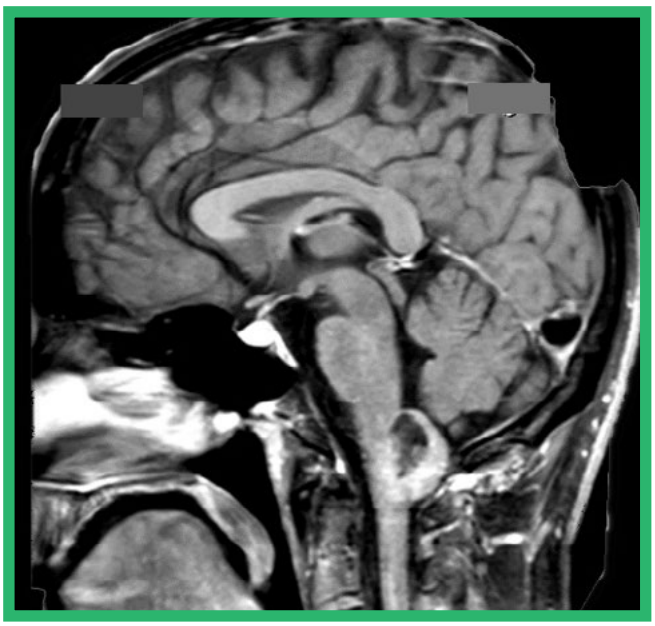
Clariscan™
(gadoterate meglumine)
injection for intravenous use

Case Study #5 (cont'd)

Postcontrast sagittal FLAIR



Postcontrast T1 FSE



- **Partially enhancing, complex dorsally exophytic lower brainstem lesion**

All case study images courtesy of Lawrence N. Tanenbaum, MD FACR and RadNet.

Support for Clariscan

GE Healthcare Reimbursement Support Line

GE Healthcare is pleased to offer toll-free customer support and documentation for coding and reimbursement related to our products. Please contact us at 800 767 6664.

Customer Service

To place an order, call 800 292 8514.

Medical Affairs

For technical or product-related questions and/or to reach a Clinical Applications Specialist, call 800 654 0118 (option 2, then option 3) or email medical.affairs@ge.com.

*Dr. Tanenbaum is a consultant of GE Healthcare.

References:
1. Tweedle MF et al. *App Radiol.* 2014;(suppl):1-11.
2. Port M et al. *Biometals.* 2008;21:469-490.
3. Morcos SK. *Eur J Radiol.* 2008;66:175-179.

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Clariscan™
(gadoterate meglumine)
injection for intravenous use

PRODUCT INDICATIONS AND USE:
CLARISCAN™ (gadoterate meglumine) is a gadolinium-based contrast agent indicated for intravenous use with magnetic resonance imaging (MRI) in brain (intracranial), spine, and associated tissues in adult and pediatric patients to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

Additional pediatric use information is approved for Guerbet LLC's Dotarem (gadoterate meglumine injection). However, due to Guerbet LLC's marketing exclusivity, this drug product is not labeled with that pediatric information.

IMPORTANT SAFETY INFORMATION ABOUT CLARISCAN™

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)
See full Prescribing Information for complete Boxed Warning.

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle, and internal organs.

- **The risk for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR <30 mL/min/1.73 m^2), or**
  - **Acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended Clariscan dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Contraindications
History of clinically important hypersensitivity reactions to Clariscan.

Warnings and precautions
- **Hypersensitivity reactions:** Anaphylactic and anaphylactoid reactions have been reported with gadoterate meglumine, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of gadoterate meglumine administration and resolved with prompt emergency treatment.
  - Before Clariscan administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to Clariscan.
  - Administer Clariscan only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.
- **Gadolinium retention:** Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by brain, skin, kidney, liver and spleen. The duration of retention also varies by tissue and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs.
  - Consequences of gadolinium retention in the brain have not been established. Adverse events involving multiple organ systems have been reported in patients with normal renal function without an established causal link to gadolinium retention.
- **Acute kidney injury**: In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent; administer the lowest dose necessary for adequate imaging.
- **Extravasation and injection site reactions:** Ensure catheter and venous patency before the injection of Clariscan. Extravasation into tissues during Clariscan administration may result in tissue irritation.

Adverse reactions
- The most common adverse reactions (≥ 0.2%) associated with gadoterate meglumine in clinical trials were nausea, headache, injection site pain, injection site coldness and rash.
- Serious adverse reactions in the postmarketing experience have been reported with gadoterate meglumine. These serious adverse reactions include but are not limited to: arrhythmia, cardiac arrest, respiratory arrest, pharyngeal edema, laryngospasm, bronchospasm, coma and convulsion.

Use in specific populations
- **Pregnancy:** GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. The human data on the association between GBCAs and adverse fetal outcomes are limited and inconclusive. Because of the potential risks of gadolinium to the fetus, use Clariscan only if imaging is essential during pregnancy and cannot be delayed. Advise pregnant women of the potential risk of fetal exposure to GBCAs.
- **Lactation:** There are no data on the presence of gadoterate in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.
- **Pediatric use:** The safety and efficacy of gadoterate meglumine at a single dose of 0.1 mmol/kg has been established in pediatric patients from 2 to 17 years of age based on clinical data in 133 pediatric patients 2 years of age and older. Adverse reactions in pediatric patients were similar to those reported in adults. No dosage adjustment according to age is necessary in pediatric patients. No cases of NSF associated with gadoterate meglumine or any other GBCA have been identified in pediatric patients age 6 years and younger. The safety of gadoterate meglumine has not been established in preterm neonates.

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Prior to Clariscan administration please read the full Prescribing Information, including the Boxed Warning and patient Medication Guide, for additional important safety information.

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 800-654-0118 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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