



BRAIN



Case studies from Lawrence N Tanenbaum, MD FACR using macrocyclic CLARISCAN™ (gadoteric acid)

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

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

macrocyclic
Clariscan™
gadoteric acid

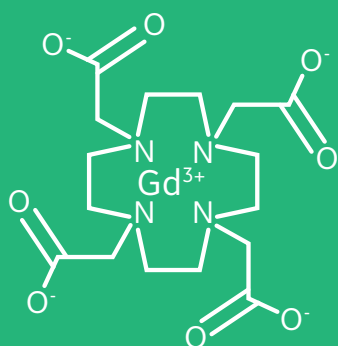
Clariscan™

Macrocyclic, ionic GBCA

Cage-like structure encloses and tightly binds the Gd^{3+} ion¹

Highly stable²

Rapid biodistribution and elimination³



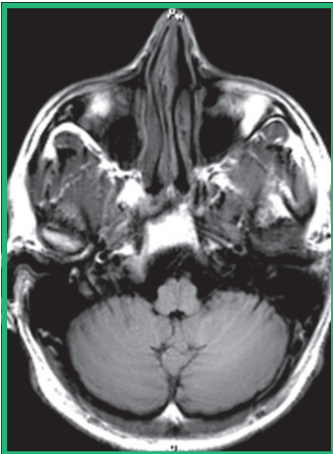
Clinical presentation

A 32-year-old male weighing 85 kg, presented with left facial paresthesias

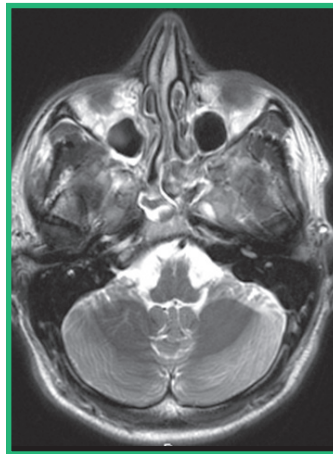
Imaging

MRI of the brain without contrast and with 18 mL of Clariscan

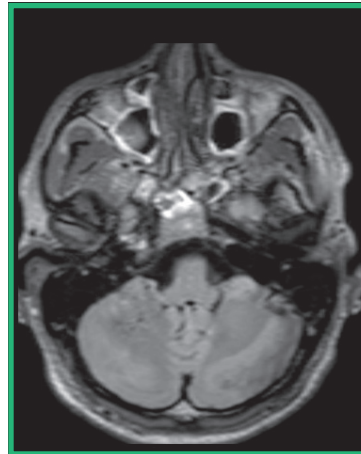
T1 axial



T2 axial



Post-contrast FLAIR axial



- Pre-contrast images show no obvious abnormality

Imaging findings

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

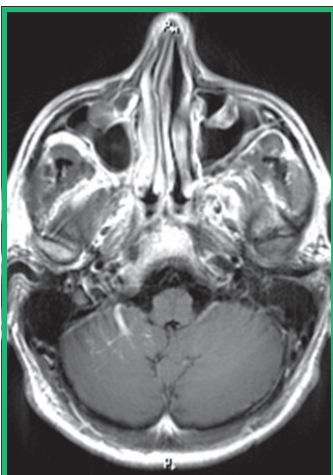
Diagnosis

Developmental venous anomaly

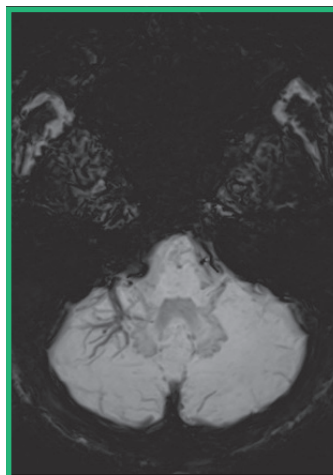
Treatment plan

None

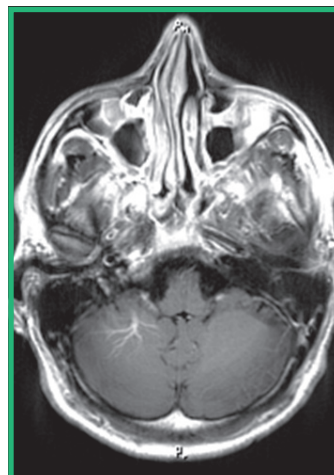
Post-contrast T1 axial



Post-contrast SWI



Post-contrast T1 axial



Case study 2

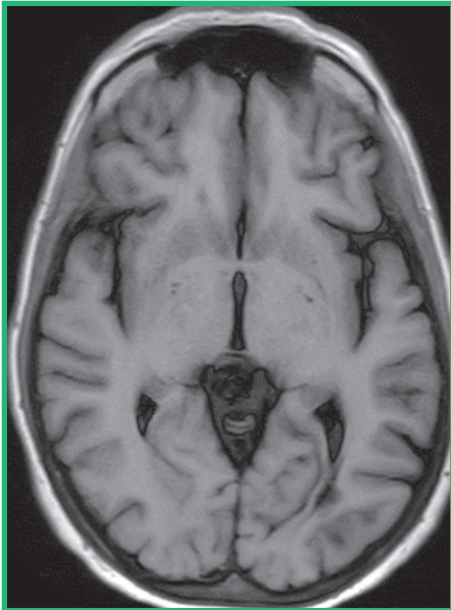
Clinical presentation

47-year-old female weighing 80 kg, presented with headache

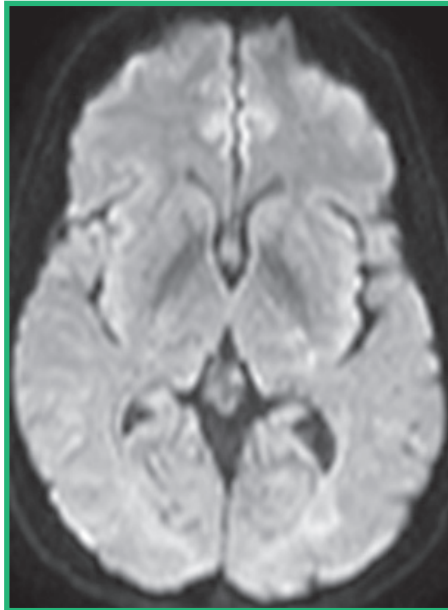
Imaging

MRI of the brain and pituitary without contrast and with 17 mL of Clariscan

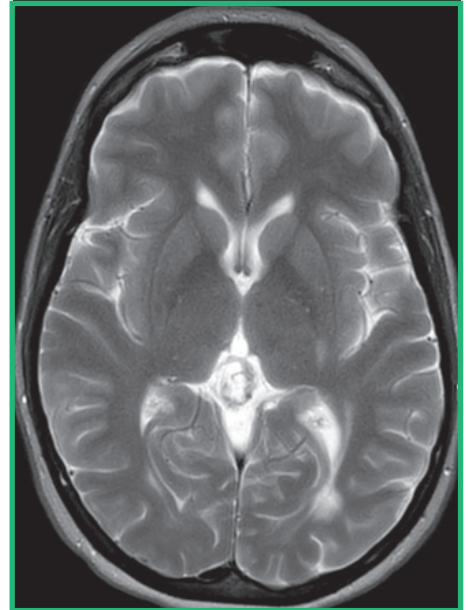
Pre-contrast T1 axial



Pre-contrast DWI axial

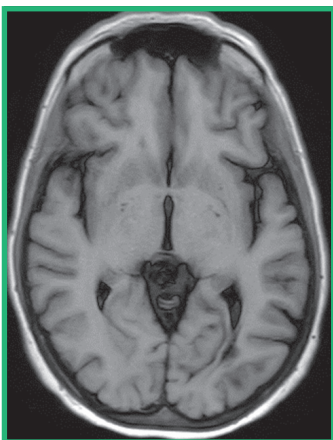


Pre-contrast T2 axial

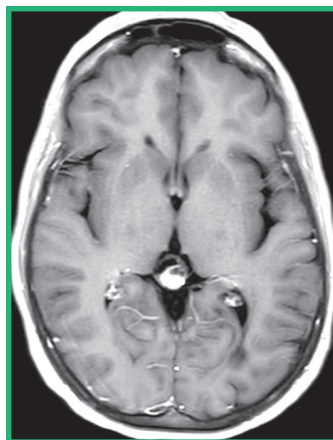


- Complex, predominantly cystic pineal lesion noted

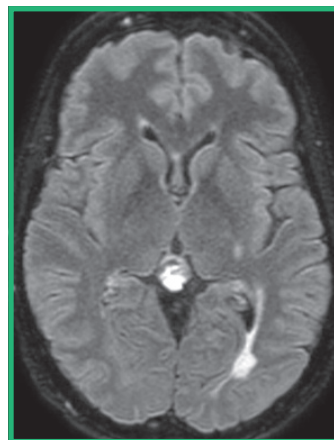
Pre-contrast T1 axial



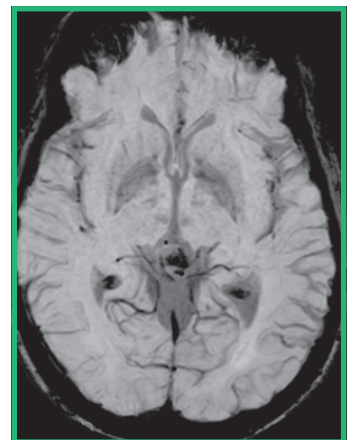
Post-contrast T1 axial



Post-contrast 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

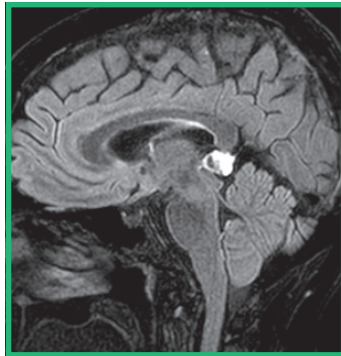
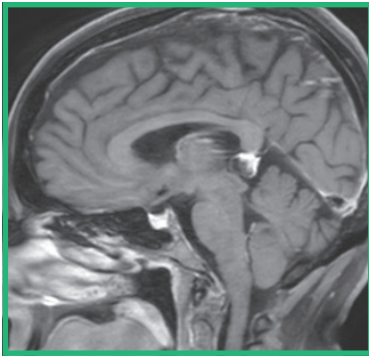
Diagnosis

Complex pineal lesion

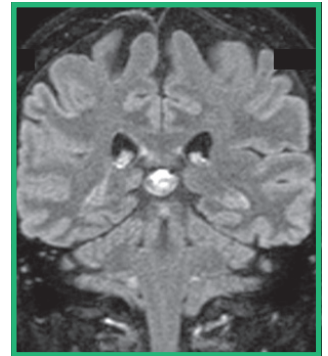
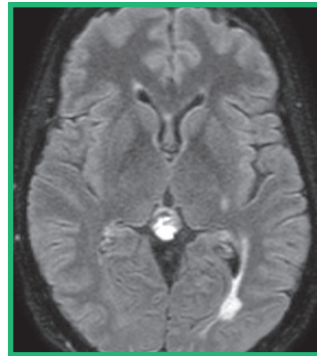
Treatment plan

Surveillance

Post-contrast T1 sagittal



Post-contrast FLAIR



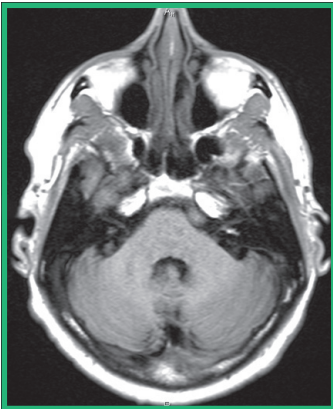
Clinical presentation

55-year-old male weighing 80 kg, presented with headache and tinnitus

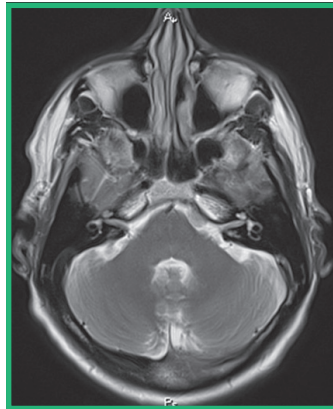
Imaging

MRI of the brain with internal auditory canals/temporary bones without contrast and with 17 mL of Clariscan

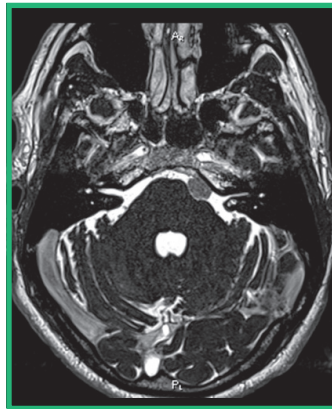
Pre-contrast T1 axial



Pre-contrast T2 axial

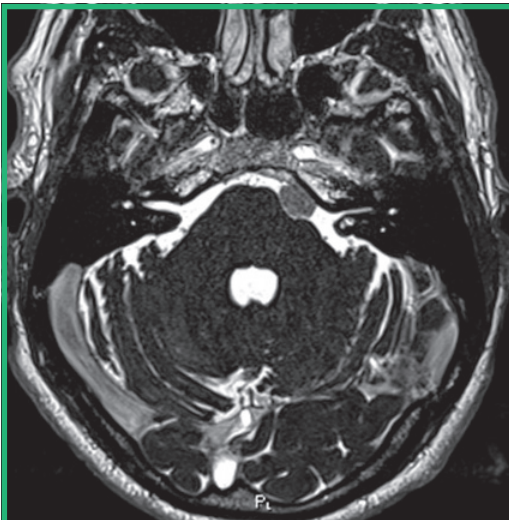


Balanced SSFP (C- cisternographic) imaging

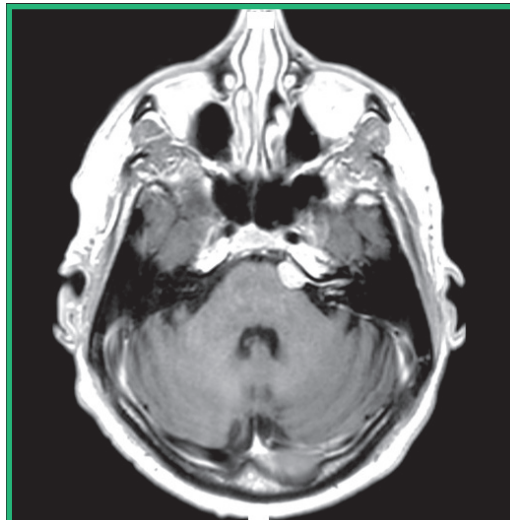


- Possible extra-axial lesion at the left lateral aspect of the pons

Balanced SSFP (C- cisternographic) imaging



Post-contrast T1



- Balanced SSFP (left) and post-contrast 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

Imaging findings

Small extra-axial lesion at the left lateral aspect of the pons, which shows significant enhancement on post-contrast images

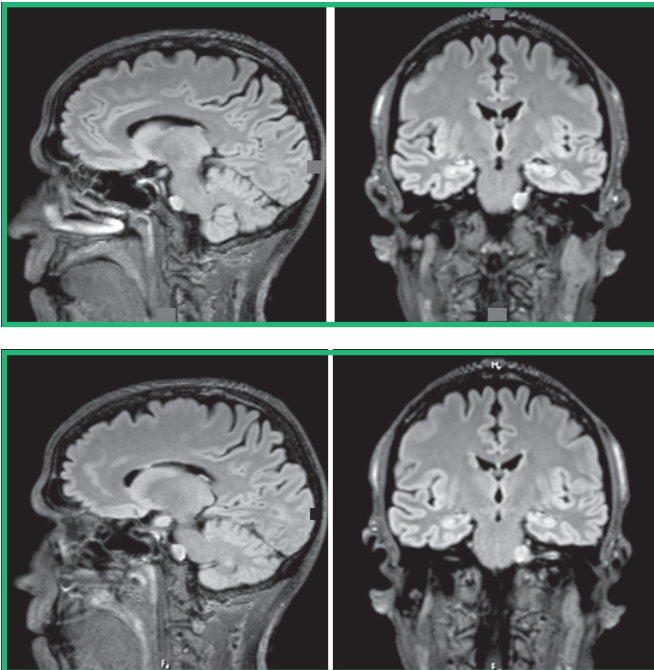
Diagnosis

Meningioma

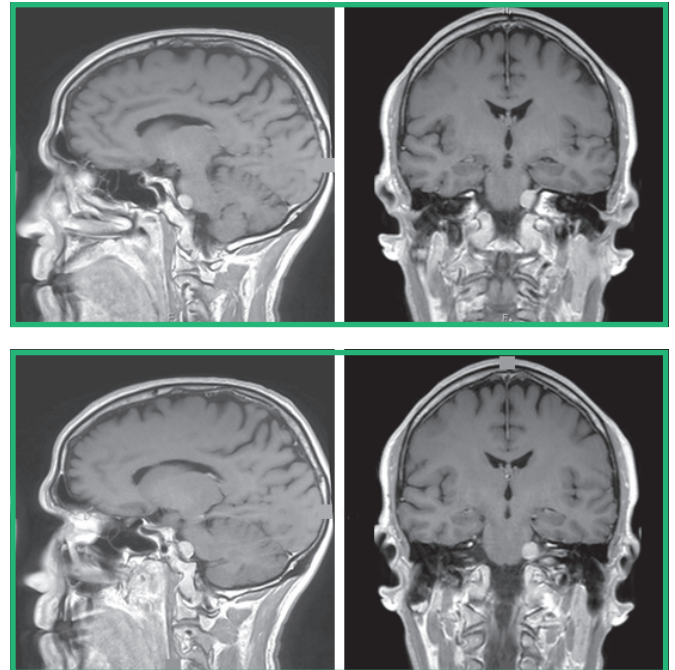
Treatment plan

Stereotactic radiosurgery

Post-contrast FLAIR sagittal and coronal



Post-contrast T1 sagittal and coronal



Case study 4

macrocyclic
Clariscan™
gadoteric acid

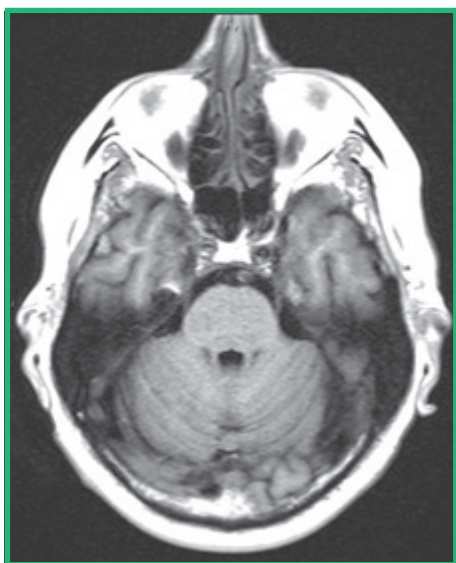
Clinical presentation

A 60-year-old male weighing 90 kg, presented with new onset of seizures

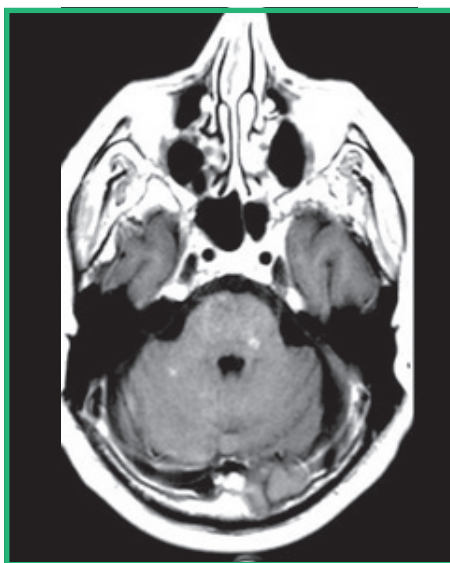
Imaging

MRI of the brain was performed without contrast and with 20 mL of Clariscan

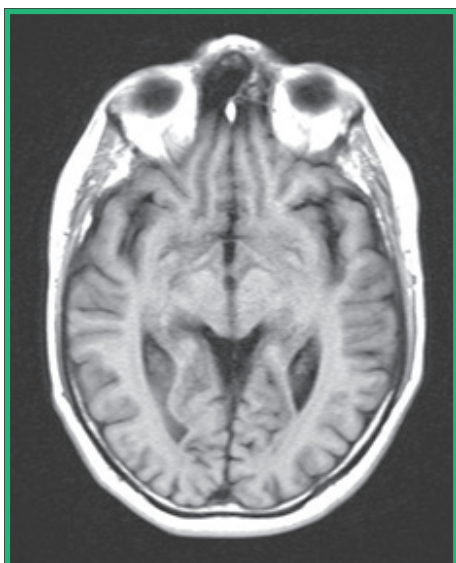
Pre-contrast T1 axial



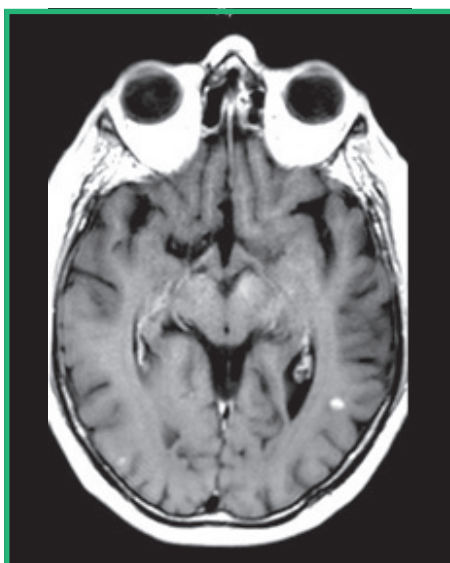
Post-contrast T1 axial



Pre-contrast T1 axial



Post-contrast T1 axial



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

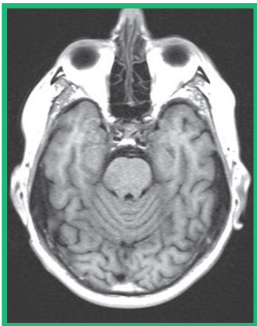
Imaging findings

Numerous nodular enhancing lesions consistent with metastatic disease

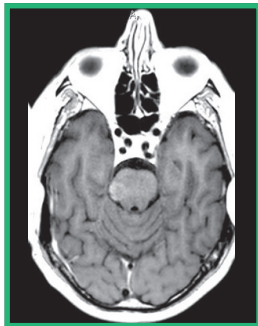
Diagnosis

Brain metastasis

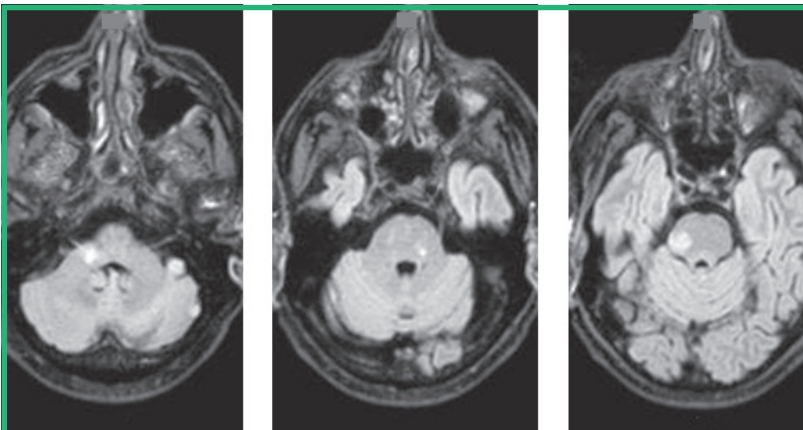
Pre-contrast T1 axial



Post-contrast T1 axial

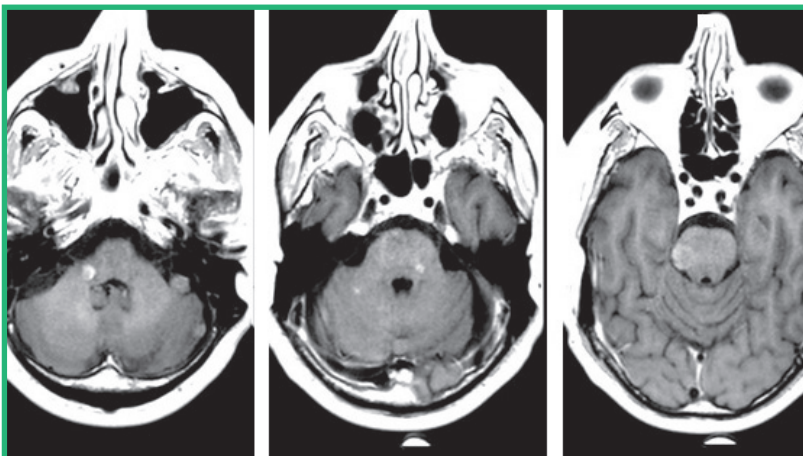


Post-contrast axial FLAIR



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

Post-contrast T1 axial



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

Case study 5

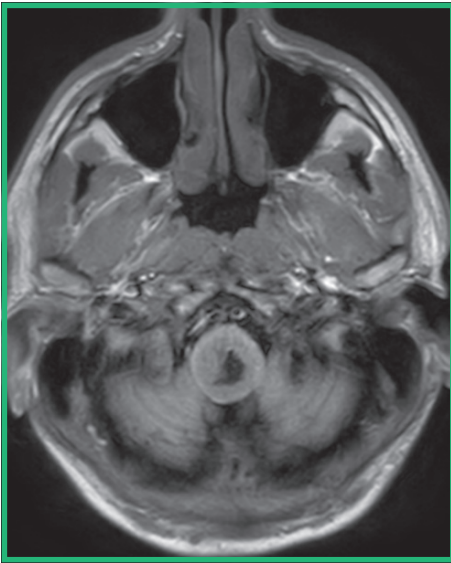
Clinical presentation

A 28-year-old female weighing 70 kg, presented with headache and weakness

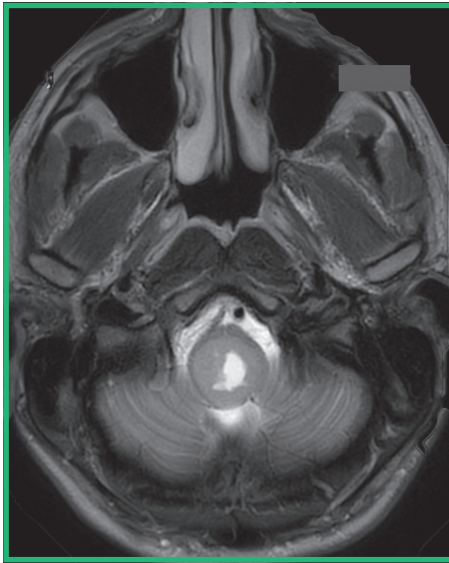
Imaging

MRI of the brain without contrast and with 15 mL of Clariscan

Pre-contrast T1

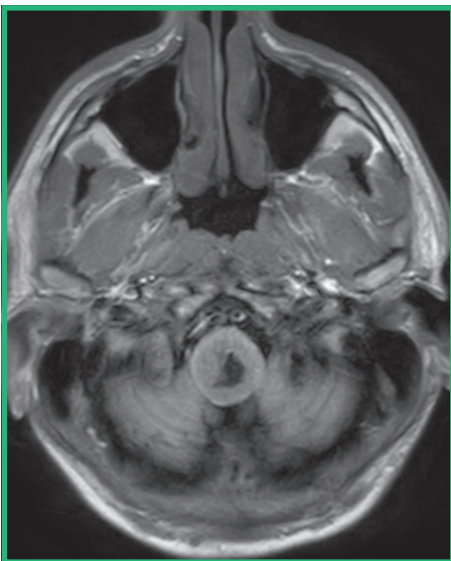


T2

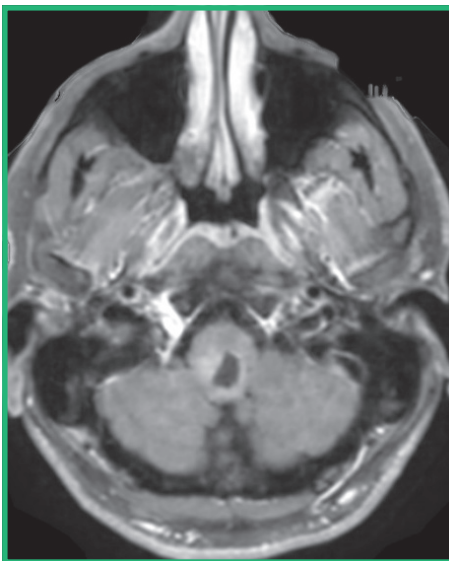


- Imaging reveals a complex, exophytic lower brainstem lesion

Pre-contrast T1



Post-contrast



- 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

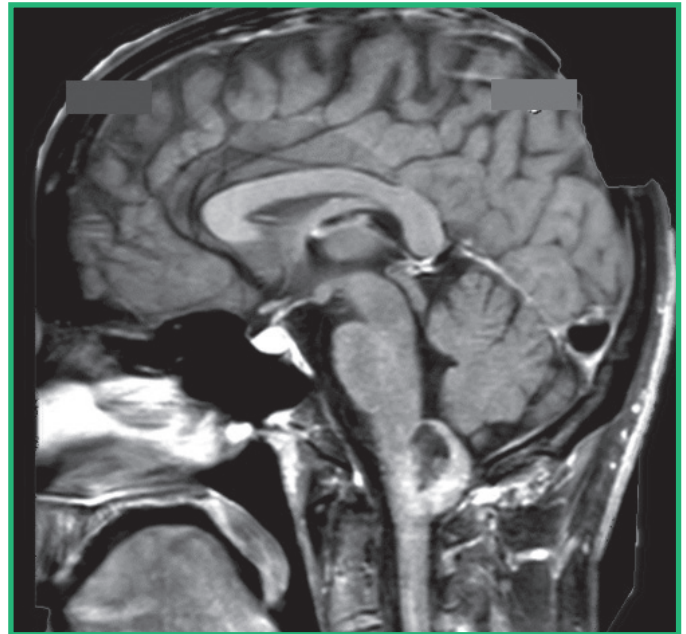
Treatment plan

Radiation and chemotherapy

Post-contrast sagittal FLAIR



Post-contrast T1 FSE



- Partially enhancing, complex dorsally exophytic lower brainstem lesion



PRESCRIBING INFORMATION CLARISCAN™ – gadoteric acid

Please refer to full national Summary of Product Characteristics (SmPC) before prescribing. Further information available on request.

PRESENTATION Clariscan 0.5 mmol/mL solution for injection. Solution for injection containing 279.3 mg/mL gadoteric acid (as gadoterate meglumine) equivalent to 0.5 mmol/mL.

INDICATIONS For diagnostic use only. Clariscan should be used only when diagnostic information is essential and not available with unenhanced magnetic resonance imaging (MRI). Contrast agent for contrast enhancement in MRI for a better visualisation/delineation. Adult and paediatric population (0-18 years): lesions of the brain, spine, and surrounding tissues. Adults and children over 6 months Whole body MRI. Non-coronary angiography in adults only.

DOSAGE AND METHOD OF ADMINISTRATION This medicinal product should only be administered by trained healthcare professionals with technical expertise in performing and interpreting gadolinium enhanced MRI. The lowest dose that provides sufficient enhancement for diagnostic purposes should be used. The dose should be calculated based on the patient's body weight, and should not exceed the recommended dose per kilogram of body weight detailed in this section.

MRI of brain and spine: Adults: The recommended dose is 0.1 mmol/kg BW, i.e. 0.2 mL/kg BW. In patients with brain tumours, an additional dose of 0.2 mmol/kg BW, i.e. 0.4 mL/kg BW, may improve tumor characterisation and facilitate therapeutic decision making. **Children (0-18 years):**

The recommended and maximum dose of Clariscan is 0.1 mmol/kg body weight. Do not use more than one dose during a scan. Careful consideration in neonates up to 4 weeks and infants up to 1 year of age. Lack of information on repeated administration, Clariscan injections should not be repeated before 7 days. **Whole body MRI (including lesions of the liver, kidneys, pancreas, pelvis, lungs, heart, breast, and musculoskeletal system): Adults and children over 6 months:**

The recommended dose is 0.1 mmol/kg BW, i.e. 0.2 mL/kg BW. **Angiography: Adults only:** The recommended dose, IV injection is 0.1 mmol/kg BW, i.e. 0.2 mL/kg BW. **Impaired renal function:**

Clariscan should only be used in patients with severe renal impairment (GFR < 30 mL/min/1.73 m²) and in patients in the perioperative liver transplantation period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. If it is necessary to use Clariscan the dose should not exceed 0.1 mmol/kg body weight.

Clariscan injections should not be repeated before 7 days. **Impaired hepatic function:** The adult dose applies. Caution recommended, especially in perioperative liver transplantation period.

Elderly (aged 65 years and above): No dosage adjustment, but exercise caution.

CONTRAINDICATIONS Hypersensitivity to gadoteric acid, to meglumine or to any medicinal products containing gadolinium.

WARNINGS AND PRECAUTIONS Appropriate facilities should be readily available for any complication, as well as for emergency treatment of severe reaction to the contrast agent (e.g. hypersensitivity, seizures). The usual precaution for MRI examination should be taken. Regarding any metallic object such as exclusion of patients with pacemakers, vascular clips, infusion pumps, nerve stimulators, cochlear implants, or suspected intracorporeal metallic foreign bodies, particularly in the eye.

Not for intrathecal use: For intravenous injection only. Clariscan must not be administered by subarachnoid (or epidural) injections. **Extravasation:** In the event of extravasation local intolerance reactions may be observed, necessitating short term local treatment. **Hypersensitivity reactions:** Hypersensitivity reactions can occur, including life-threatening, and may be either allergic or non-allergic. They can be either immediate (less than 60 minutes), or delayed (up to 7 days).

Anaphylactic reactions can occur immediately and can be fatal. Symptoms of an existing asthma may be aggravated. Hypersensitivity reactions can be aggravated in patients on beta-blockers, particularly those with bronchial asthma. These patients may be refractory to standard treatment of hypersensitivity reactions with beta-agonists. Caution in patients with a history of allergy (e.g. fish and seafood allergy, hay fever, hives), sensitivity to contrast media and bronchial asthma and premedication with antihistamines and/or glucocorticoids may be considered. Appropriate support measures should be available. **Nephrogenic Systemic Fibrosis (NSF):** Reports of NSF associated with use of some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 mL/min/1.73 m²). Incidence of acute renal failure is high in patients undergoing liver transplantation. Clariscan should only be used in patients with severe renal impairment and in patients in the perioperative liver transplantation period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. Prior to administration of Clariscan, it is recommended that all patients are screened for renal dysfunction. **CNS disorders:** Special precaution is necessary in patients with a low threshold for seizures. **Cardiovascular disease:** Clariscan should only be administered after careful benefit assessment. **Patient preparation:** Nausea and vomiting are known possible undesirable effects when using MRI contrast agents. The patient should therefore refrain from eating for 2 hours prior to the investigation.

UNDESIRABLE EFFECTS NSF [see Warnings and Precautions]. **Clinical Studies Experience:** **Immune system disorders:** Uncommon: Hypersensitivity, anaphylactic reaction, anaphylactoid reaction. **Psychiatric disorders:** Very rare: Agitation, anxiety. **Eye disorders:** Rare: Conjunctivitis, ocular hyperaemia, vision blurred, lacrimation increased, eyelid oedema. **Nervous system disorders:** Very common: Paraesthesia, headache. Rare: Dysgeusia. Very rare: Coma, convulsion, syncope, presyncope, dizziness, parosmia, tremor. **Cardiac disorders:** Very rare: Cardiac arrest, bradycardia, tachycardia, arrhythmia, palpitations. **Respiratory, thoracic and mediastinal disorders:** Very rare: Respiratory arrest, Rare: Pulmonary oedema, bronchospasm, laryngospasm, pharyngeal oedema, dyspnoea, nasal congestion, sneezing, cough, dry throat. **Gastrointestinal disorders:** Common: Nausea, vomiting. Very rare: Diarrhoea, abdominal pain, salivary hypersecretion. **Skin and subcutaneous system disorders:** Common: Pruritus, erythema, rash. Rare: Urticaria, hyperhidrosis. Very rare: Eczema, angioedema. Isolated cases of NSF have been reported with gadoteric acid, most of which were in patients co-administered other gadolinium-containing contrast agents. **Vascular disorders:** Very rare: Hypotension, hypertension, vasodilatation, pallor. **Musculoskeletal and connective tissue disorders:** Very rare: Muscle contracture, muscular weakness, back pain. **General disorders and administration site conditions:** Common: Feeling hot, feeling cold, injection site. Very rare: Chest discomfort, fever, chills, face oedema, asthenia, injection site discomfort, back pain, malaise, thoracic pain, superficial phlebitis, decreased oxygen saturation. Injection site reaction, injection site oedema, injection site extravasation, injection site inflammation (in case of extravasation), injection site necrosis (in case of extravasation). See full SmPC for adverse reactions reported with other intravenous MRI contrast agents. **Postmarketing experience:** The most commonly reported adverse reactions following administration are nausea, vomiting, pruritus and hypersensitivity reactions. The most frequently observed hypersensitivity reactions are localised, extended or generalised skin reactions which most often occur immediately (during the injection or within one hour after the start of injection) or sometimes delayed (one hour to several days after injection). Immediate reactions include one or more effects, which appear simultaneously or sequentially, which are most often cutaneous, respiratory and/or cardiovascular reactions. Each sign may be a warning sign of a starting shock and go very rarely to death. **DRUG INTERACTIONS** No formal studies. No interactions with other medicinal products have been observed. Beta-blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists: These medicinal products induce decreased efficacy of cardiovascular compensation mechanisms of blood pressure. Contrast media may increase the incidence of hypersensitivity reactions in patients taking beta-blockers. **PREGNANCY AND LACTATION** No data in pregnant women. Clariscan should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteric acid. **Nursing Mothers:** At clinical doses, no effects on the infant are anticipated due to the small amount excreted in milk and poor absorption from the gut. Continuing or discontinuing breast feeding for a period of 24 hours after administration, should be at the discretion of the doctor and lactating mother. **Fertility:** no clinical data. **SPECIAL POPULATIONS: Neonates and infants:** Clariscan should only be used in neonates up to 4 weeks of age and infants up to 1 year age after careful consideration. **Elderly (aged 65 years and above):** Patients should be screened due to age related decline in renal function. **OVERDOSE** Clariscan can be removed by haemodialysis. However, there is no evidence that haemodialysis is suitable for prevention of NSF. **EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES** No studies. Ambulant patients while driving vehicles or operating machinery should take into account that nausea may incidentally occur. **INSTRUCTIONS FOR USE AND HANDLING** For single use. The solution for injection should be inspected visually prior to use. Only clear solutions free of visible particles should be used. In neonates and infants the required dose should be administered by hand. The peel-off tracking label on the syringes/vials/bottles should be stuck onto the patient record. The dose used should also be recorded. See SmPC for full instructions. **MARKETING AUTHORISATION HOLDER** GE Healthcare AS, P.O. Box 4220 Nydalen, NO-0401 OSLO, NORWAY. **MARKETING AUTHORISATION NUMBER** PL 00637/0065 and PL 00637/0066. **CLASSIFICATION FOR SUPPLY** Subject to medical prescription. **DATE OF REVISION OF THE TEXT** May 2018. **Cost 10x15mL: £666**

Adverse events should be reported.

Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk/>. Adverse events should also be reported to GE Healthcare at gpv.drugsafety@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: 469-90.
3. Clariscan Summary of Product Characteristics (UK), April 2022.

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