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What are the common SPECT imaging agents that cross the blood brain barrier?

Tc99m ECD and Tc99m HMPAO for epilepsy, brain death, and potentially dementia imaging. Also, I123-iodoflupane for dopamine transporter imaging. Remember that Tc99m DTPA can be used for brain perfusion imaging but does not cross the blood brain barrier.

True or false? A seizure focus will be hot on Tc99m ECD or HMPAO imaging in the inter-ictal state.

False. When imaging with these agents in the inter-ictal (between seizure) state, uptake is expected to be less than normal brain uptake. When imaged in the ictal (active seizure) state, higher uptake than normal for brain is expected. Imaging in the ictal state requires that radiotracer is injected during or nearly immediately following a seizure for most accurate results.

True or false? Kaposi sarcoma typically shows thallium uptake.

True.

True or false? CNS lymphoma typically shows thallium uptake.

True.

True or false? CNS toxoplasmosis is typically thallium positive?

False. Remember, thallium uptake requires active human sodium potassium pumps as thallium behaves like a potassium analogue. Therefore, human derived tumors will show thallium uptake in most cases, while non-human parasites such as toxoplasmosis will not.

True or false? Brain parenchymal necrosis is typically thallium positive?

False. Remember, thallium is a viability marker in the myocardium and the same principle holds true within the brain. Therefore, necrosis would be predicted to not show increased thallium uptake, whereas entities such as CNS lymphoma would be predicted to show thallium uptake.

**We will now discuss a few key concepts pertinent to nuclear medicine brain death studies for board exam questions. Note that the interpretation of a brain death study in clinical practice is complex and is beyond the scope of our brief review here, and should only be made by trained professionals, given the gravity and importance of the clinical situation and imaging interpretation.*

What radiotracers may be considered for use with a nuclear medicine brain death study?

Tc-99m ECD, Tc-99m HMPAO and Tc-99m DTPA. Less common tracers include Tc-99m pertechnetate and glucoheptonate. Note that Tc-99m ECD and Tc-99m HMPAO are more widely utilized as they cross the blood brain barrier into the brain parenchyma, therefore supporting brain perfusion via uptake within the brain parenchyma.

True or false? Tc-99m DTPA can cross the blood brain barrier.

False. Tc-99m DTPA does not cross the blood-brain barrier—this is a frequently tested concept. Tc-99m DTPA therefore only shows information regarding presence of tracer within the vessels around the brain, therefore allowing evaluation of whether the vessels around the brain are patent, but not directly showing diffusion or presence of radiotracer into the brain parenchyma itself.

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What are nuclear medicine imaging findings that support a diagnosis of brain death?

According to the Society of Nuclear Medicine Practice Guideline for Brain Death Scintigraphy (please refer to most recent version), interpretation of a brain death study includes that the study is technically adequate/diagnostic for interpretation. A positive scan for brain death generally involves absence of demonstrable radionuclide activity within the brain but this alone is not sufficient for this diagnosis and must be correlated with all available clinical and imaging findings.

Nuclear medicine brain death imaging typically includes flow images from the anterior projection and delayed images, often with SPECT or SPECT/CT imaging about 5-10 minutes after the injection. On a normal exam, images will show tracer from the level of the carotid arteries to the skull vertex. In brain death intracranial blood flow is completely absent. In brain death, the hot nose sign may be seen which results from blood shunting away from the brain with apparent increased uptake in the region of the nose on the frontal view. Classic teaching is that this results from increased flow in the external carotid circulation with subsequent increased perfusion in the nasal region. That is probably the most likely potential explanation to be tested. However, I've also seen some reports that this sign can result from increased perfusion to the brain stem/spinal cord, and appear over the nose on the frontal view, also because of blood shunting away from the cerebral hemispheres. The hot nose sign is a commonly tested finding on board exam questions about brain death, and it is key to realize that this is the result of shunting of blood away from the cerebral hemispheres and this finding can be seen but with but alone does not confirm brain death.

One must be careful not to misattribute scalp uptake via the external carotid arteries as brain uptake from the internal carotid arteries. Lack of superior sagittal sinus activity helps confirm lack of brain perfusion, but presence of superior sagittal sinus activity needs to be interpreted with caution as low-level sagittal sinus activity can come from the scalp even if brain death is present.

Other imaging tests for evaluation of brain death include cerebral angiography evaluating for blood flow beyond the internal carotid arteries which is considered by many to be the gold standard test but, from my experience at least, is less commonly tested than the nuclear medicine brain death studies on board exams.

One more word of caution that my discussion of brain death interpretation here is for board exam prep only to help prepare for commonly tested concepts. The complete clinical performance and interpretation of brain death studies is beyond the scope of what is covered here.

What are classic clinical features of normal pressure hydrocephalus?

Three classic clinical features to remember for radiology board exams are ataxia, urinary incontinence, and mental impairment/dementia.

What is the underlying mechanism of classic normal pressure hydrocephalus?

Impaired absorption of CSF due to some sort of subarachnoid space obstruction, for example related to prior subarachnoid hemorrhage, leptomeningitis, or meningeal-based malignancy.

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What nuclear medicine agent is classically injected into the CSF for evaluation of CSF flow/normal pressure hydrocephalus?

Indium111-DTPA injected via lumbar puncture into the subarachnoid space. Note that Indium111-DTPA has favorable imaging characteristics for evaluation of NPH including a longer half-life at 67 hours to allow delayed imaging for several days following injection into the CSF, the fact that DTPA which is not lipid soluble, so activity remains within the CSF without entering the brain parenchyma, lack of metabolism, ability to be absorbed by arachnoid villi, and generally inert nature making a chemical meningitis unlikely. Given the intrathecal injection, sterile preparation of radiopharmaceutical must be assured. Note that this agent can also be utilized for evaluation of ventriculoperitoneal shunt patency where one injects the radiotracer into the VP shunt reservoir and monitors the course of tracer into the peritoneal cavity to confirm patency.

What are classic nuclear medicine findings of normal pressure hydrocephalus?

On board exams, expect early visualization of radiotracer within lateral ventricles which may show a somewhat blunted or heart-shaped appearance compared to normal, lack of radiotracer migration to the superior aspect of the cerebral convexities, retrograde flow of CSF into the lateral ventricles, and delayed absorption of radiotracer with persistent visualization within ventricles beyond 24-48 hours. A typical normal study following lumbar puncture will show cephalad radiotracer migration which reaches the basal cistern within about 1 hour, the Sylvian fissure by about 6 hours, and the cerebral convexities by about 12 hours with uptake in the superior sagittal sinus by about 24 hours. Uptake that remains at the site of lumbar puncture may be related to inadequate lumbar puncture with injection of radiotracer external to the sub-arachnoid space including muscles/subcutaneous tissues.

A classic positive study for NPH on a board exam question would be a case that shows persistent ventricular activity beyond 24-48 hours with lack up uptake reaching the cerebral convexities/superior sagittal sinus.

True or false? Brain tumors on FDG-PET may show as either areas of focal increased or areas of focal decreased metabolic activity.

True. Because the brain cortex is so metabolically active and takes up quite a bit of FDG, brain tumors may have either increased, equal, or decreased activity to the normal cortex, and therefore areas of increased and decreased metabolism must be evaluated as potential manifestation of brain tumors. Additionally, tumors that have co-existing vasogenic edema may present with a larger region of decreased FDG-uptake as uptake within regions of vasogenic edema is often low or absent.

What other PET tracers beyond FDG can be used to evaluate for metastatic disease in the brain?

Multiple additional tracers for PET imaging exist that can potentially identify brain tumors beyond FDG PET with several key studies discussed here. Fluoroestradiol (FES) PET imaging can show uptake with estrogen receptor positive brain metastases, such as with ER+ breast cancers. Note that FES can also show uptake in meningiomas. PSMA-PET can evaluate for metastatic prostate and other PSMA-avid brain tumors. Dotatate and similar somatostatin-receptor PET imaging studies can evaluate for somatostatin receptor positive brain metastases. Fluciclovine PET imaging can also identify brain tumors via mechanisms that include increased amino acid transportation. Other new and emerging PET agents are also being studied for evaluation of brain malignancy.