False-Positive Somatostatin Receptor Scintigraphy: Really?

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• 50-yr old female
• Was diagnosed with a right paravertebral pulmonary mass obstructing the inlet to the middle lobe.
• Surgical treatment: resection of middle lobe and right inferior lobe.
• Upon sectioning the right intermediate bronchus a mechanical suture was used to close the stump.
• Final diagnosis: non-functioning well-differentiated bronchial neuroendocrine tumor.
Staging post surgical somatostatin receptor scintigraphy.

Radiopharmaceutical:
\(^{99m}\text{Tc-HYNIC-Tyr}^3\)-octreotide

Administered activity:
18 mCi

Findings:
Well defined, high focal uptake in the right hilum.
SPECT CT software fusion.
Post surgical volume loss in right hemithorax
No parenchymal lesion
No intrabronchial mass
Visible metal clips in surgical bed
Focal uptake in intermediate bronchus stump
• Fiberoptic bronchoscopy: otherwise unremarkable right bronchial stump.
• Bronchoalveolar lavage: no infectious agents, no tumor cells. Moderately reactive inflammatory process in respiratory epithelium (polymorphonuclear cells: 90%).
• Bronchial stump biopsy: negative for tumor involvement.
• Serum chromogranin A: 16 ng/ml.
Follow-up scintigraphy shows no interval variation in right hilar uptake. No new lesions are depicted. Direct testing and sequential imaging results point out to a false-positive induced by chronic inflammation around surgical clips.
Teaching Points

To adequately determine that a localization result is a false-positive or true-positive requires either direct examination (by surgery, cytology or biopsy), other imaging studies to clarify the lesion or extensive follow-up and careful comparison to the clinical context to determine the true nature of the lesion.
Example of a false positive result.

28-year old male with a well-differentiated neuroendocrine tumor of the jejunum.

Staging In-111 pentetreotide depicted bilateral diffuse pulmonary uptake.

The patient had concealed information about being under treatment for active tuberculosis.
Teaching Points

Granulomatosis disease (sarcoidosis, tuberculosis, Wegener's) as well as both benign and malignant breast diseases are reported to possess high-affinity somatostatin receptors that bind octreotide and to be imaged on somatostatin receptor scintigraphy.
Example of a false positive result. 55-year old male with a well-differentiated neuroendocrine bronchial carcinoma of the left lung with liver metastases. A follow-up somatostatin receptor scintigraphy was practiced one year after left partial pneumonectomy and partial right hepatectomy. There is visible uptake in the thoracotomy scar (*straight arrow*). Notice focal uptake in a liver metastasis (*arrow head*).
Teaching Points

Operative sites have been reported to result in false-positive localization on somatostatin receptor scintigraphy, perhaps because of activated lymphocytes or inflammatory cells that are known to possess somatostatin receptors and, in some patients, remain positive on SRS for several months after surgery.
Example of a false positive result.

48-year old male with a well-differentiated neuroendocrine bronchial carcinoma that was initially mistaken for an adenocarcinoma and treated with mediastinal radiotherapy before referral to a specialized institution.

A staging somatostatin receptor scintigraphy performed shortly after revisited diagnosis showed uptake in mediastinal pleura. Repeated imaging 2 years later shows very little interval resolution.
Teaching Points

Radiation pneumonitis can occur 1-8 months after treatment. From 8 months onwards, lung fibrosis may appear.

Indium-111-pentetreotide scans are strongly or moderately positive in symptomatic patients examined 2-5 months after radiotherapy.

The uptake mechanism of In-111-pentetreotide in areas of radiation pneumonitis remains to be elucidated. Radiation pneumonitis has been explained by early vascular alterations followed by epithelial changes and ablation of type II alveolar cells which will eventually also result in early surfactant release into the alveoli. Enhanced production and release of cytokines from alveolar macrophages has been postulated as a component in the mechanism of radiation injury.
Discussion

True false-positive results are neither false (because they represent somatostatin receptor-positive lesions) nor positive (because they are not related to the pathology under scrutiny).

Despite its increased use, there has been only one systematic study of the occurrence of false-positive somatostatin receptor analogue localization (Gibril et al).

Although several large studies report that somatostatin receptor scintigraphy has excellent specificity it is nevertheless important that these points be systematically examined.
Newer radiolabeled somatostatin analogs which can be used in PET imaging, and which have a higher affinity for the somatostatin receptor, especially receptor subtype-2, have been developed.

The most likely candidates to become the new standard for somatostatin receptor imaging are $^{68}$Ga-DOTA$^0$-Tyr$^3$-octreotate and $^{68}$Ga-DOTA$^0$-Tyr$^3$-octreotide.
Teaching Points (II)

The most common causes for ‘false positive’ results are: radiation pneumonitis, accessory spleen, surgical scar tissue, nodular goitre, ventral hernia, bacterial pneumonia, respiratory infections, common cold (nasal uptake), cerebrovascular accident, concomitant granulomatous disease, diffuse breast uptake and concomitant second primary tumour.

False positive readings can be induced by the tracer’s physiologic pathways or contamination: focal collection of stools, gallbladder uptake, adrenal uptake and urine contamination.
References

