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Published in:

Amyloid: Journal of protein folding disorders

DOI:

[10.3109/13506129.2014.881796](https://doi.org/10.3109/13506129.2014.881796)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2014

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Noordzij, W., Glaudemans, A. W. J. M., van Rheenen, R. W. J., Dierckx, R. A., Slart, R. H. J. A., & Hazenberg, B. P. C. (2014). Additional diagnostic value of SPECT/CT to planar Iodine-123 labeled serum amyloid P component scintigraphy in a patient with pulmonary nodular amyloidosis. *Amyloid: Journal of protein folding disorders*, 21(2), 131-133. <https://doi.org/10.3109/13506129.2014.881796>

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To cite this article: Walter Noordzij, Andor W. J. M. Glaudemans, Ronald W. J. van Rheenen, Rudi A. Dierckx, Riemer H. J. A. Slart & Bouke P. C. Hazenberg (2014) Additional diagnostic value of SPECT/CT to planar Iodine-123 labeled serum amyloid P component scintigraphy in a patient with pulmonary nodular amyloidosis, *Amyloid*, 21:2, 131-133, DOI: [10.3109/13506129.2014.881796](https://doi.org/10.3109/13506129.2014.881796)

To link to this article: <https://doi.org/10.3109/13506129.2014.881796>

Published online: 30 Jan 2014.

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LETTER TO THE EDITOR

Additional diagnostic value of SPECT/CT to planar Iodine-123 labeled serum amyloid P component scintigraphy in a patient with pulmonary nodular amyloidosis

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Localized pulmonary amyloidosis is a rare disease [1]. According to the Mayo Clinics experience, pulmonary amyloidosis can be divided into four types: tracheobronchial amyloidosis, nodular amyloidosis, infiltrating interstitial amyloidosis and lymph node amyloidosis [2]. The exact incidence of nodular pulmonary amyloidosis is not known; however, the amount of case reports and case series indicate that this diagnosis is well established [3,4]. In cases of nodular pulmonary amyloidosis and lymphocytic interstitial pneumonia, the presence of Sjögren's disease should be considered [5,6]. Histopathological confirmation remains the gold standard for the diagnosis. The nodules appear heterogeneous on conventional chest X-ray images and contrast enhanced CT [7]. However, four types of CT findings are considered to be characteristic for the disease: sharp, lobulated contours; calcifications (in approximately half of the patients); varying size; and slowly progressive growth over years [8]. Despite these typical CT features, amyloidosis cannot be differentiated from granuloma, primary or spread neoplasms, or infection at the time of first presentation of such a patient.

Nuclear medicine imaging techniques may provide additional information with regard to organ involvement, size and potential sites for biopsy to eventually acquire a definite diagnosis. Our group previously showed that Fluorine-18 labeled fluorodeoxyglucose positron emission tomography (¹⁸F-FDG PET/CT) has potential to discriminate localized from systemic amyloidosis, and in addition may be an interesting tool for therapy evaluation [9,10]. However, ¹⁸F-FDG uptake in a lesion has a wide differential diagnosis, and is therefore non-specific for amyloidosis and should only be performed after amyloidosis has been diagnosed to further differentiate between localized and systemic types. In patients with nodular pulmonary amyloidosis, tracer accumulation on ¹⁸F-FDG PET/CT scans is frequently reported; however, this modality also lacks potential to discriminate [11].

Keywords

¹⁸F-FDG PET, nuclear medicine, pulmonary nodular amyloidosis, serum amyloid P scintigraphy

History

Received 29 July 2013
Revised 19 December 2013
Accepted 28 December 2013
Published online 30 January 2014

Iodine-123 labeled serum amyloid P component (¹²³I-SAP) scintigraphy is the best validated nuclear medicine imaging modality to visualize specific organ involvement and therapy evaluation in amyloidosis [12]. For lung lesions, however, conventional planar ¹²³I-SAP scintigraphy may be falsely negative, due to physiological blood pool accumulation in the mediastinum, relative high background activity in the lungs, and limited spatial resolution. Complementary single photon emission computed tomography combined with low-dose computed tomography (SPECT/CT) can be used to visualize in more detail smaller lesions in organs of interest and may therefore have additional diagnostic value in small lung lesions. In this report, we describe the additional use of ¹²³I-SAP SPECT/CT for an identification of pulmonary involvement in localized amyloidosis, illustrated by a clinical case that turned out to have underlying Sjögren's disease.

Patient A is a 56-year-old woman who was referred to our amyloidosis referral center because of amyloid deposits in pulmonary tissue. Approximately six months before referral, she suffered from a persistent non-productive cough. Her general practitioner treated her for possible bronchitis, however without improvement. Conventional X-ray image of the thorax showed bilateral pulmonary consolidations, which was interpreted as metastases of an unknown primary malignancy. This assumption was further supported by contrast enhanced CT and ¹⁸F-FDG PET/CT scan (Figure 1). However, both modalities did not show a primary tumor. An open lung biopsy was performed and histological examination revealed lymphocytic interstitial pneumonia, with nodular AL amyloidosis accompanied by calcifications,

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Figure 1. Maximum intensity projection of ^{18}F -FDG PET/CT scan (A) before referral, with multiple lesions with elevated glucose metabolism. Physiological uptake in the brain, tonsils, oral cavity, myocardium, breast tissue, liver, spleen, and digestive and urogenital tract. CT only (B) and fused PET/CT (C) image, showing multiple pulmonary nodules both with and without ^{18}F -FDG accumulation.

Figure 2. Maximum intensity projection of ^{18}F -FDG PET/CT scan (A) after 5-year follow-up, with multiple metabolically avid lesions in both lungs. Physiological uptake in the brain, tonsils, oral cavity, myocardium, breast tissue, liver, spleen, and digestive and urogenital tract. Anterior planar view of ^{123}I -SAP scintigraphy (B) showing normal tracer distribution in the nasal mucosa, salivary glands, thyroid gland, mediastinum, liver, spleen, stomach and rest of the bowel, and urine bladder. No focal lesions with increased tracer accumulation in the lungs.

multinuclear giant cells, and monoclonal plasma cells with restriction for immunoglobulin light chain lambda.

The usual diagnostic approach for patients with amyloidosis in our hospital was followed by planar ^{123}I -SAP scintigraphy that showed no specific organ involvement and normal extravascular retention of ^{123}I -SAP [13]. SPECT/CT was not performed at that time. Congo red staining of abdominal adipose tissue aspiration was negative for amyloid deposits. No

M-protein was found and serum levels of immunoglobulin free light chains were within reference ranges. The antinuclear antibodies, ENA antibodies SSA and SSB, and IgM rheumatoid factor were all positive. These serologic findings in combination with dryness of the eyes and mouth and a positive Schirmer test enabled us to conclude to underlying primary Sjögren's disease. Pulmonary function tests showed normal lung volumes and slightly reduced diffusion capacity.

Figure 3. Axial reconstructions of low-dose CT only in lung setting (A), fused ¹⁸F-FDG PET/CT (B), and ¹²³I-SAP SPECT/CT (C, at the same thoracic level as A and B). The low dose CT shows multiple consolidations in both lungs, with varying ¹⁸F-FDG and ¹²³I-SAP accumulation. The consolidation in lateral part of the middle lobe (right lung, solid black arrow) shows both ¹⁸F-FDG and ¹²³I-SAP uptake. Some nodules do not accumulate any of both tracers (left lung, dashed black arrow).

The diagnosis was considered to be local nodular pulmonary amyloidosis, associated with monoclonal plasma cells producing lambda light chains and on the other hand giant cells held responsible for the assembly of amyloid derived from these light chains [14]. We decided to carefully monitor the course of the disease without further specific treatment. During the next five years of follow-up, the disease was slowly progressive, leading to minimal further decrease in pulmonary diffusion capacity. After five years, the patient was re-evaluated using both ¹⁸F-FDG PET/CT scan and ¹²³I-SAP scintigraphy, now with the addition of SPECT/CT of the thorax and abdomen. Both modalities showed an essentially unchanged situation, with multiple nodular ¹⁸F-FDG positive lesions in both lungs (Figure 2A) and no ¹²³I-SAP specific organ involvement on the planar images (Figure 2B). Axial reconstructions of low-dose CT revealed multiple consolidations in the parenchyma of both lungs, with heterogeneous ¹²³I-SAP uptake visible on the SPECT images. Several lesions were both ¹⁸F-FDG and ¹²³I-SAP positive (Figure 3); however, some lesions showed ¹⁸F-FDG uptake but no ¹²³I-SAP accumulation. Abdominal subcutaneous adipose tissue analysis did again not show any evidence for systemic amyloidosis. Since the pulmonary function testing parameters were only slightly decreased, we decided to continue the policy of watchful waiting.

The use of ¹²³I-SAP scintigraphy, and especially additional SPECT/CT, to visualize nodular pulmonary amyloidosis has not been reported thus far. As mentioned above, planar images do not seem to have enough potential to visualize uptake in the pulmonary nodules. Complementary SPECT/CT can provide three-dimensional reconstructions, which have potential to overcome the majority of limitations of planar images.

The amount of amyloid nodules remained unchanged as judged by several different imaging techniques, a finding that supported the clinical policy of watchful waiting.

This case does show some limitations for the general application of ¹²³I-SAP scintigraphy and SPECT/CT for the detection of pulmonary amyloidosis. Despite the fact that ¹²³I-SAP accumulation in pulmonary nodules was detected, this neither improved the detection of the nodules over time nor did this provide a measure of treatment response beyond the findings on contrast enhanced CT. Further justification for the use of ¹²³I-SAP SPECT/CT should be supported by larger experience and a clear indication of therapeutic or diagnostic utility that exceeds the present potential of CT as the modality of choice for nodular pulmonary amyloidosis.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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