The usefulness of FDG-PET/CT in evaluating the disease activity, distribution and treatment response of IgG4-related disease

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Learning objectives

1. Recognize the contribution of a positive PET finding on the diagnosis of IgG4-related disease.

2. Realize the usefulness of PET/CT in the monitoring of corticosteroid therapy.
Background

IgG4-related disease (IgG4-RD) is an increasingly recognized clinicopathological disorder with immune-mediated inflammatory lesions mimicking malignancies.¹,²,³

F¹⁸-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is used for an accurate identification of this systemic disease in a single session.

IgG4-related disease combined with organ-specific criteria

Consensus statements from a multinational, multidisciplinary group of experts on IgG4-RD describe guidelines for the diagnosis of the disease and the histopathologic findings important in making the diagnosis. (Figure1)

The histopathological findings of a dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliteratorive phlebitis are critical features for establishing the diagnosis.

The presence of these findings, often together with mild tissue eosinophilia, is strongly suggestive if accompanied by increased numbers of IgG4-positive plasma cells.

PET/CT imaging revealed the enlargement and an increase in the FDG uptake of the salivary gland, lachrymal gland, lymph node, lung, thyroid gland, pancreas, spleen, kidney, pericardial artery and retroperitoneum in 19 patients.

The maximum standardized uptake value (SUVmax) was 7.4 (median, range 2.5 - 9.9).

The PET/CT findings were useful for making a differential diagnosis of other malignancies with typical uptake patterns. (Figure2)

Autoimmune pancreatitis

Type 1 (IgG4-related) AIP is the prototypical form of IgG4-RD.⁵,⁶

It often presents as a pancreatic mass or as painless obstructive jaundice and can be mistaken for pancreatic cancer.

AIP is frequently associated with diabetes mellitus.

Elevated serum IgG4 levels (>135 mg/dL) can also be seen in some patients with pancreatic cancer, although they are usually less than twice the upper limit of normal;
thus, increased IgG4 serum levels alone cannot be used to exclude a diagnosis of pancreatic malignancy.

Radiologic features of type I AIP include diffuse enlargement of the pancreas, leading to the descriptor "sausage-shaped" pancreas, and a halo of edema surrounding the organ. Both of these features are appreciated most readily on abdominal CT scanning. #Figure3#

**Salivary and lacrimal gland involvement**

Salivary gland disease, which can present as major salivary gland enlargement or as sclerosing sialadenitis. #Figure4#

The constellation of lacrimal, parotid, and submandibular gland enlargement was formerly termed "Mikulicz disease." Isolated submandibular gland swelling was termed "Küttner's tumor."

These were often erroneously considered to be subcategories of Sjögren's syndrome (SS).

Many of the patients previously described as having in association with AIP and IgG4-RD may have had one of these conditions rather than true SS.

**Retroperitoneal fibrosis and related disorders**

Retroperitoneal fibrosis, which frequently occurs in the larger context of chronic periaortitis and can often affect the ureters, leading to hydronephrosis and renal injury. #Figure5#

In some cases, the syndrome is responsive to steroid therapy. The diagnosis of IgG4-RD in this setting can be challenging because of the advanced fibrotic changes typically observed in this condition.

Figure5: Retroperitoneal fibrosis and related disorders

**Aortitis and periaortitis**

IgG4-RD has been recognized as one of the causes of noninfectious aortitis. #Figure6#

A series of patients with thoracic lymphoplasmacytic aortitis or with inflammatory abdominal aortic aneurysms and abdominal periaortitis has been identified in retrospective pathologic studies of patients who had undergone aortic resections.
**Thyroid disease**

Two forms of thyroid involvement in IgG4-RD have been described, including Reidel’s thyroiditis (IgG4-related thyroid disease) and the fibrous variant of Hashimoto’s thyroiditis.  

#Figure7#  

**Lung and pleural disease**

Multiple reports have documented IgG4-related pulmonary disease, which may be asymptomatic or present with cough, hemoptysis, dyspnea, pleurisy, or chest pain; pseudotumors and interstitial pneumonia have been associated with AIP.

Visceral or parietal pleural thickening may occur.

Four patterns of lung involvement have been described.*15,16

- Solid nodular (Figure8)
- Bronchovascular (with thickening of bronchovascular bundles and interlobular septa)
- Alveolar interstitial (with honeycombing, bronchiectasis, and diffuse ground-glass opacities) (Figure9)
- Round-shaped, ground-glass opacities

IgG4-RD may mimic sarcoidosis.

**Renal disease**

The most common finding is tubulointerstitial nephritis (TIN). (Figure10)

Affected patients are primarily middle-aged and older men, and histopathology and other laboratory characteristics are similar to those observed in patients with autoimmune pancreatitis (AIP).*17-20

Immunohistochemistry of renal biopsy tissue demonstrates increased numbers of IgG4-positive plasma cells.

Nodular lesions mimicking renal cell carcinoma may be seen.
Figure 1: Diagnostic algorithm for comprehensive diagnostic criteria for IgG4-related disease combined with organ-specific criteria.

4. Mechanisms and assessment of IgG4-related disease: lessons for the rheumatologist

Fig. 1


Figure 2: Systemic organ involvement in IgG4-related disease

Mechanisms and assessment of IgG4-related disease: lessons for the rheumatologist; Motohisa Yamamoto et al.: Nature Reviews Rheumatology 10, 148–159 (2014) doi:10.1038/nrrheum.2013.183 Published online 03 December 2013:

Figure 3: Autoimmune pancreatitis (AIP)

Fig. 3
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Figure 4: Salivary and lacrimal gland involvement

Fig. 4

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Figure 5: Retroperitoneal fibrosis and related disorders

Fig. 5

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Figure 6: Aortitis and periaortitis

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Fig. 6

Figure 7: Thyroid disease

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Fig. 7
Figure 8: Lung and pleural disease

Fig. 8
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Figure 9: Lung and pleural disease

Fig. 9
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Figure 10: Renal disease

Fig. 10

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Findings and procedure details

We analyzed the correlation among the serum IgG4 concentration, the number of FDG-avid lesions, and the SUVmax of the lesions and investigated the value of PET/CT.

No significant correlation was identified among the serum IgG4 concentration, number of FDG-avid lesions, and SUVmax of the lesions. (Case1,2)

On a follow-up study, after performing steroid therapy, FDG-PET could detect the disease activity as a change in the degree and distribution of the FDG uptake.(Case3)
Case1: 70s Male
slgG4 2970mg/dl
SUVmax4.8
SUVmax5.2
SUVmax2.0

Fig. 11
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Case2: 80s Male
slgG4 99.4mg/dl
SUVmax9.9
SUVmax6.9
SUVmax8.2

Fig. 12
Case 3: 80s Male

Serial Imaging Changes During Treatment of Immunoglobulin G4–Related Disease With Multiple Pseudotumors: Circulation. 2015; 131: 1882-1883

Fig. 13

Case 3: 80s Male

Serial Imaging Changes During Treatment of Immunoglobulin G4–Related Disease With Multiple Pseudotumors: Circulation. 2015; 131: 1882-1883

Fig. 14
Conclusion

FDG PET/CT is thus considered to be a potentially useful tool for assessing organ involvement, monitoring the disease activity, evaluating the therapeutic response, and for selecting the optimal interventional treatment for IgG4-RD.
References


