**18 F-FDG PET/CT in Relapsing Polychondritis (RP): Role for diagnosis and therapy monitoring in a case series of 6 patients**

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Learning objectives

• To become familiar with the rare multi-systemic inflammatory disease of Relapsing Polychondritis (RP)
• To outline the typical pattern of RP in $^{18}$F-FDG-PET/CT
• To evaluate the potential role of $^{18}$F-FDG-PET/CT for diagnosis and therapy management of RP
Background

Definition

Recurrent polychondritis (RP) is a rare multi-systemic inflammatory disease (3:100.000; Lahmer et al. 2010) potentially affecting all types of cartilage tissues and connective tissues in the body. Without therapy inflammation can result in severe tissue destruction. As RP often presents with non-specific symptoms (e.g. ataxia, joint pain, neuropathies) and is associated with diseases such as vasculitis and myelodysplastic syndrome (MDS) diagnosis is impeded. Thus it still takes a long time to be diagnosed (mean time 2.9 years; Pol et al. 2009) and therapy is started.

Epidemiology

Although RP is an autoimmune disease, men and women are equally affected with a peak in the fifties. Only rare cases of RP in childhood are depicted in literature.

Pathophysiology

Although the etiology of RP is still unknown a positive genetic association has been reported for HLA-DR4. Immunohistological analysis revealed that antibodies probably directed against collagen-type II might play an essential role in the pathogenesis of RP (Kern et al. 2013).

Clinical diagnosis of RP

Clinical diagnosis should encompass at least three of the following five criteria according to McAdam et al. (1976):

- cartilage inflammation of the respiratory tract
- cartilage inflammation of the otolaryngeal tract
- impairment of the audio-vestibular organ
- inflammation of the visual system
- sero-negative polyarthritis
Fig. 1: Clinical findings of RP. Swelling of the right auricular cartilage also called "cauliflower ear" (A); after therapy no proof of any residua (B)


**Diagnostics**

In some cases patients show clinically evident swelling and redness of auricular and nasal cartilage. In almost every patient laboratory results are elevated concerning non-specific inflammation values such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Diagnostic imaging with CT shows thickening (in acute stages) or destruction (in chronic stages) of the affected tissue. Case reports have demonstrated that PET/CT can reveal the full extent of the affected tissue, even if morphological changes are minimal in CT.

**Therapy**

The standard therapy in acute stages is an i.v. immunosuppressive medication with steroids, whereas therapy in chronic stages consists of Methotrexate, Azathioprine and Biologicals. In few and severe cases stem cell transplantation is delineated in literature.
Findings and procedure details

Patient population

Between 2004 and 2013 eight whole body $^{18}$F-FDG-PET/CT examinations were performed in six patients with suspected or prior diagnosed RP, two females and four males, mean aged 54 years (range 28-78 years). One patient had two additional $^{18}$F-FDG-PET/CT examinations for therapy monitoring.

PET/CT examination

The protocol of the PET/CT examination was a standard one with 60 minutes uptake time after administration of mean 350 MBq $^{18}$F-FDG. The examinations were performed with a modern PET/CT scanner consisting of a high-resolution 3D LSO PET and a 128-row multi-detector CT. Most $^{18}$F-FDG-PET/CT scans included a contrast-enhanced CT to obtain diagnostic CT data.

Findings

The value of PET/CT for primary diagnosis of RP includes the depiction of affected tissues, in some cases even the diagnosis itself and the detection or exclusion of RP associated diseases, which is essential for therapy management (Figures 2-4).

The benefit of PET/CT in the course of RP consists mainly in the assessment of disease activity. This can be difficult due to inconsistency between clinical symptoms and laboratory findings (Figures 5-9).

Manifestations

As collagen-type II is present nearly everywhere in the body, the potential tissues for an affection of RP are various ranging from eyes with recurrent episcleritis and keratitis to indistinct symptoms such as dizziness and nausea. However, the main affected tissues of RP encompass the elastic cartilage of the ear (Figure 1). Hyaline cartilage is also affected by RP, resulting in a saddle deformation of the nose.

Another affection of the hyaline cartilage concerns the tracheal-bronchial-system (Figure 4-6). Pathognomonic for RP is the manifestation mainly in larynx and upper trachea although inflammation can also spread into the subsegmental bronchial system without including the posterior tracheal membrane (Prince et al. 2002). Patients with RP of the airway system have poor prognosis due to recurrent pneumonias resulting in respiratory insufficiency, which is the most common complication of RP. As a consequence functional
airway abnormalities (e.g. air trapping or malacia) are common and best diagnosed in expiratory chest CT (Lin et al. 2010).

The manifestations of RP affected hyaline cartilage of joints vary between monoarthritis and polyarthralgia, which can occur transient and migratory affecting mainly the small and large peripheral joints (Figure 3); (Trentham et al. 1998).

**Associated diseases**

30% of RP patients also suffer from vasculitis. Following inflammation of the vessels the second common complication of RP concerns the cardiovascular system with aortic or mitral regurgitation and aortic aneurysms (Figure 9); (Selim et al. 2001).

The myelodysplastic syndrome (MDS) is diagnosed in some RP-patients probably as a paraneoplastic syndrome (Figure 2); (Heo et al. 2003).

**CT and PET/CT findings of RP**

In CT acute manifestations of RP include diffuse or localized tissue thickening, sometimes combined with contrast enhancement of the affected tissues (circular swelling of the trachea; Figure 4). In chronic stages and associated diseases of RP CT may reveal calcifications (e.g. vessels and bronchia; Figure 8), fibrosis and destruction of the affected tissues (e.g. thoracic aneurysm; Figure 9). In the PET scan manifestations of active RP show an elevated $^{18}$F-FDG-uptake indicating an increased glucose metabolism, which can be quantitatively measured by the standard uptake value (SUV). Because elevated glucose metabolism can be found in both, inflammatory and malignant processes, for further differentiation the localization and corresponding morphological information by CT is essential.

**Images for this section**

**PET/CT for primary diagnosis of RP**
PET/CT for primary diagnosis of RP after negative conventional diagnostics in a 77-year old male patient with clinically singular swelling of the right ear, resistant to antibiotic therapy, fever, loss of weight and anaemia. Native CT shows symmetric swelling of the right auricular cartilage (a) with focally increased FDG-uptake in PET (b), suspect for an inflammatory process. This finding is a typical manifestation of RP. The same patient shows normal presentation of the pelvis in CT (d) but diffuse, elevated metabolism in the whole skeleton (c and e), suspect for MDS in the context of RP.

References: Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE.
**Fig. 3:** PET/CT for evaluation of disease extent in a 28-year-old male patient with known RP under steroid therapy. CT shows symmetrically thickened cartilage of both ears and nose (b) with intensive FDG-uptake in PET/CT (c). CT also shows thickening of the proximal trachea without stenosis (d) but marked elevated glucose metabolism (e). PET/CT revealed one further positive lesion in the left sacroiliac joint (g), with focal subchondral sclerosis in CT (f) accordable to an inflammatory process, resulting in an extent of therapy with MTX.

**References:** Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE

**PET/CT for differential diagnosis**
**Fig. 4:** PET/CT in a 40-year old female patient with dyspnea and croakiness, suspicious for lymphoma in previously performed CT. CT and PET/CT (a, b) showed enlarged metabolically active cervical lymph nodes. In addition CT revealed a circular swelling and narrowing of the upper part of the trachea with contrast enhancement of the margin (d). PET showed corresponding intensive, focal FDG-uptake (c, e). After PET/CT RP was included in differential diagnoses. Lymphoma was excluded after bone marrow puncture. Under therapy with high dose steroids symptoms declined.

**References:** Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE

**PET/CT for therapy monitoring of RP**
Fig. 5: PET/CT for initial examination of RP in a 69-year old male patient with fever, night sweat and swelling of the right ear after negative conventional diagnostics. Clinical differential diagnosis included vasculitis or a malignant tumour. The first PET/CT excluded any involvement of the vascular system and did not show any signs for a malignancy. PET/CT examination revealed FDG-uptake in the right swollen auricular cartilage (a-c) and outlined the distinct involvement of the tracheal-bronchial system (a, d-g), consistent for active RP.

References: Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE
**Fig. 6**: Follow-up PET/CT of the a 69-year old male patient with active RP (same patient of Figure 5) after 3 months of immunosuppressive therapy but persisting fever and elevated values of laboratory parameter of inflammation. After three months of therapy PET/CT revealed an impressive decline in all aforementioned lesions despite clinically persisting symptoms: reduced thickening of the right auricular cartilage without FDG-uptake (b, c). Concordant decline of the wall-thickening in the tracheal-bronchial-system (d, f) and metabolism (e, g). No new manifestations of RP were identified and thus no change in therapy was necessary.

**References**: Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE
Fig. 7: Second follow-up PET/CT of the 69-year old male patient with active RP (same patient of Figure 5 and 6) after therapy and diminishing of clinical symptoms. PET/CT demonstrated a mild swelling of the right auricular cartilage (b) with a slight FDG-uptake again (a, c), suspect for a relapse of RP in absence of clinical symptoms. To prevent any further progression of disease, patient was put under constantly immunosuppression and maintained remission.

References: Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE

PET/CT for exclusion of active RP
**Fig. 8:** PET/CT for assessment of disease activity in a 78-year old male patient with known RP under immunosuppressive medication, clinically suspect for relapse (elevated CRP). CT showed calcifications in trachea (b) and main bronchi (d) without any wall thickening. No elevated FDG-uptake could be detected (c, e), thus imaging findings were consistent with non-active RP. No change in therapy management of RP had to be performed.

**References:** Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE

PET/CT for exclusion of associated diseases of RP
Fig. 9: PET/CT for exclusion of vasculitis pre-operatively in a 43-year old female patient with known RP and elevated CRP-values. PET/CT was performed before planned aorta replacement to exclude any vascular involvement of known RP. Examination revealed dilated aorta descendens with pronounced circular sclerosis (b) but without any FDG-uptake of the vessel wall (c). Thus PET/CT excluded vasculitis and confirmed non-active RP.

References: Diagnostic and Interventional Radiology, University of Tuebingen - Tuebingen/DE
Conclusion

RP is a rare multi-systemic inflammatory disease often combined with a significant delay in diagnosis and therapy due to non-specific clinical symptoms and uncharacteristic findings in conventional imaging. So far, there are only single case reports available about the benefit of PET/CT in the management of RP. This case series provides further evidence that $^{18}$F-FDG PET/CT plays an important role in the diagnosis and management of RP.

In patients with symptoms suspicious of RP PET/CT helps to establish the correct diagnosis, especially if clinical and laboratory findings are inconsistent. In this way the number of additional diagnostic tests could be reduced.

In patients with known RP $^{18}$F-FDG-PET/CT is useful to define the extent and activity of disease throughout the body thereby enabling an adequate individual therapy.
References


