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REVIEW ARTICLE

Use of Pet/CT in different scenarios on rare and orphan diseases of autoimmune origin

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ABSTRACT

Autoimmune diseases are on the rise, likely due to many factors such as pollution, infections, dietary changes, climate modifications, and exposure to xenobiotics. These diseases impact individuals, society, and healthcare systems. Some diseases are well-known, such as type 1 diabetes, while others are orphan or rare diseases.

According to the WHO, rare diseases affect fewer than five people, 10,000 inhabitants, and over 7,000 diseases. These conditions generally have low prevalence, are mostly chronically debilitating, and typically lack treatment.

In 2013, the European Society of Nuclear Medicine and the Society of Nuclear Medicine and Molecular Imaging published guidelines for using [^{18}F]FDG (the main radiotracer) in PET/CT studies of inflammation and infection. The use of this radiotracer has expanded in recent decades.

Our objective was to describe the use of PET/CT and its various radiotracers in rare or orphan autoimmune diseases classified in ICD-11. To achieve this, we followed the methodology outlined by the Joanna Briggs Institute for scoping reviews.

Seventy-seven articles were included in the thematic analysis; 71 were case reports, while the rest were case series and cross-sectional studies. The predominant finding in the PET/CT scans of the different pathologies was an increase in the uptake of various radiotracers, with [^{18}F]FDG being the most commonly used. This diagnostic tool provided a comprehensive view of the systemic involvement of multiple conditions, such as Castleman disease and Cogan syndrome. It helped to identify the primary tumor and guide therapies for diseases like acromegaly.

Introduction

According to the World Health Organization (WHO)[1], orphan or rare diseases include around 5,500 diseases that can affect approximately 30 million people in the United States, according to the U.S. Food and Drug Administration (FDA)[2]

European Commission[3], considering rare diseases have a low prevalence of 5 per 10,000 people, are potentially fatal, chronically debilitating, and have a genetic origin.

In the United States, the National Conference of State Legislatures[4] defines them as diseases affecting fewer than 200,000 Americans, considering them neglected diseases. Their treatments are not profitable due to their cost.

This type of pathology presents a diagnosis, treatment, and follow-up challenge. The natural history of these diseases needs to be better known and studied. Their biology is complex, leading to difficulties in developing drugs, biological products, and devices to treat these conditions.

For this reason, in 1997, INSERM (French National Institute of Health and Medical Research), with subsequent support from the European Commission starting in 2002, created the Orphanet strategy[5]. This strategy includes multiple medical aspects of this type of pathology, including a comprehensive classification for the methodology explained later.

As for autoimmune diseases, the National Institute of Allergy and Infectious Diseases (NIAID)[6] and the National Cancer Institute (NCI)[7] define these pathologies as those in which antibodies are formed that attack the immune system.

The National Health and Nutrition Examination Survey (NHANES), a study program by the Centers for Disease Control and Prevention (CDC), found that approximately 32% of adults aged 60 or older may have at least four autoantibodies. Globally, an increase in the frequency of autoimmune diseases has been observed, with an estimated annual increase in incidence and prevalence of 19.1% and 12.5%, respectively[8].

In recent years, there has been a rise in the use of Positron Emission Tomography/Computed Tomography (PET/CT), as it is a non-invasive imaging study used as a diagnostic method in various clinical scenarios: detection, classification, staging, prognosis, treatment planning, evaluation of response to therapy, and surveillance in oncological, cardiovascular, neurological, inflammatory, and infectious disorders, among others[9].

We did not find a specific list of autoimmune and orphan diseases; therefore, we combined the lists to identify orphan autoimmune diseases.

For this reason, this scoping review aims to describe the different PET/CT tracers used in rare or orphan diseases of autoimmune origin, as defined in the ICD-11 classification.

Methodology

REVIEW QUESTION

What utility and characteristics are reported in the literature regarding using PET/CT with its different tracers in autoimmune orphan diseases?

The databases of available orphan diseases from Orphanet and autoimmune diseases from the Global Autoimmune Institute were cross-referenced, resulting in a list of orphan autoimmune diseases.

The study employed the broad population, concept, and context (PCC) framework indicated by the Joanna Briggs Institute for scoping reviews, as illustrated in Figure 1.

Figure 1. PCC framework in this study.

ELIGIBILITY CRITERIA

Articles were deemed eligible for inclusion if they reported case reports, case series, descriptive, or analytical observational studies published without date limitation that included the orphan autoimmune diseases from the cross-referenced list created for this study in which a PET/CT study had been conducted.

During the literature review, the following diseases were excluded due to the quantity and quality of available information, which allows for the execution of systematic reviews: polymyositis, Immune-mediated necrotizing myopathy, psoriatic arthritis, psoriasis, sarcoidosis, reactive arthritis, rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus, acute disseminated encephalomyelitis, multiple sclerosis, myopathies, myositis, myasthenia gravis, connective tissue diseases, Guillain-Barré syndrome, IgG4-related disease, giant cell arteritis, antiphospholipid syndrome, granulomatosis with polyangiitis, autoimmune hepatitis, autoimmune pancreatitis, dermatomyositis, Acute disseminated encephalomyelitis and autoimmune diseases of the nervous system.

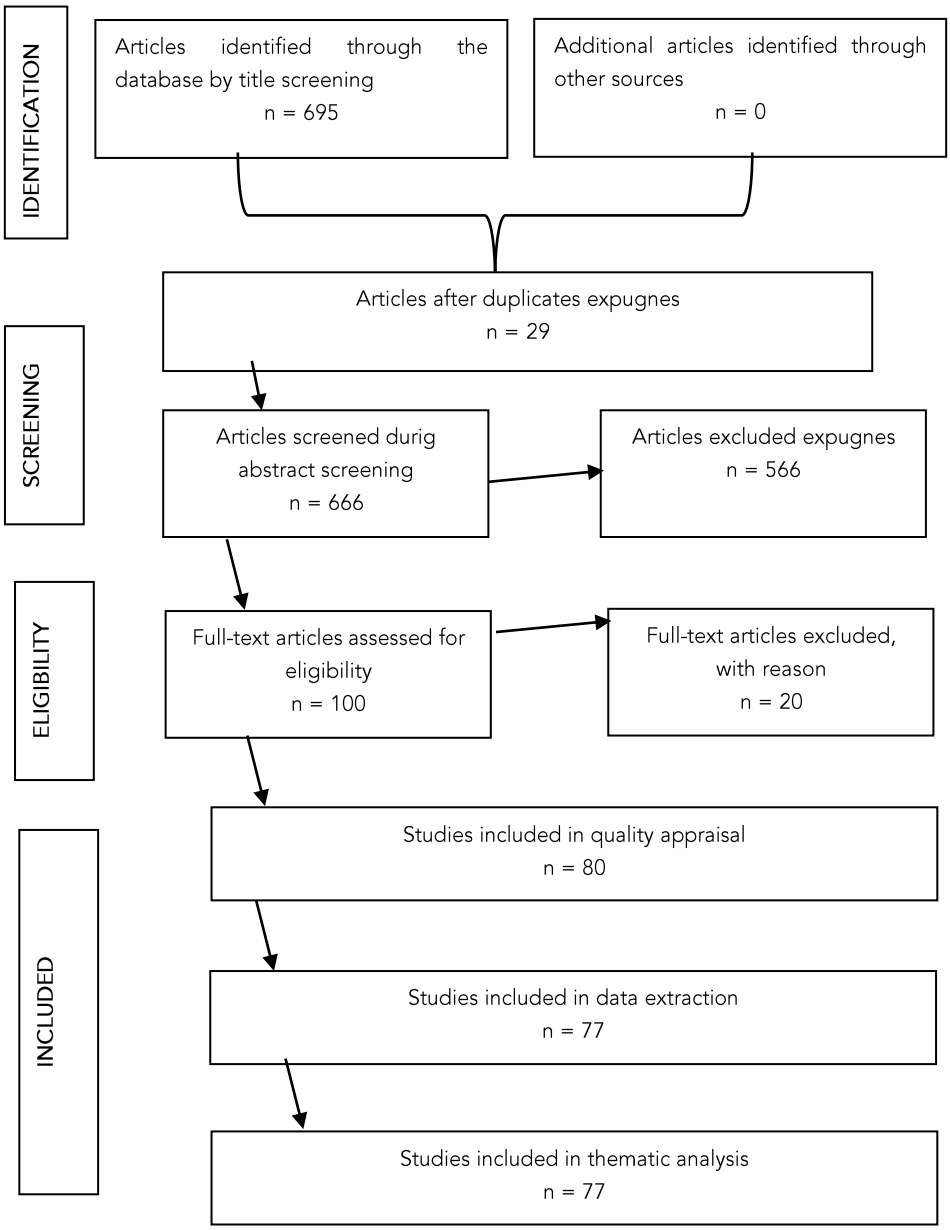
SEARCH STRATEGY.

Initially, considering the methodology described by the Joanna Briggs Institute for scoping reviews, two researchers conducted a systematical search independently in indexed databases such as MEDLINE, OVID (including Embase), Cochrane Library Epistemonikos, Scielo, LILACS, and JBI Evidence Synthesis and gray literature such as OpenGrey and GreyNet using all the keywords included in the DECS, MESH, and Entry Terms. Annex 1 contains the search methodology.

SOURCE OF EVIDENCE SELECTION.

All search results articles were uploaded to Software Mendeley, and duplicates were removed. Subsequently, two independent reviewers assessed the titles and abstracts, selecting the compositions according to the inclusion and exclusion criteria for the review. When there were disagreements between the reviewers, an additional reviewer was consulted, and an agreement was reached. This section's results are presented as a flow diagram (Figure 2) following the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRISMA-ScR) guidelines.

Figure 2. Flow diagram source of evidence.



DATA EXTRACTION.

For data extraction, two reviewers considered specific details of the articles, such as authors, year of publication, type of study, Disease, PET/CT Tracer, and Main Findings.

The items to be assessed by the two reviewers were not disagreeable, and complete information was found in the included articles to evaluate the results.

Results

The results obtained from the literature review are summarized by disease in the tables described below.

Table 1 Acromegaly

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Acromegaly				
Bashari et al. [10]	2020	Cross-sectional	L-[methyl^{11}C]-methionine or L-[carboxyl^{11}C]methionine	Focal tracer uptake in the lateral sellar and parasellar region

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Daniel et al. [11]	2021	Cross-sectional	[^{68}Ga]Ga-DOTA-TATE	A significant inverse relationship between postoperative values and the SUVmax at the sellar region
Daya et al[12]	2021	Case report	[^{68}Ga]Ga-DOTA-TATE	Receptor activity in the pituitary gland due to physiological somatostatin receptor expression
Ahsan et al[13]	2021	Case report	[^{68}Ga]Ga-DOTA-TOC	Hyperplastic left adrenal gland with increased radiotracer uptake compared to the right
Alobaid et al[14]	2023	Case report	[^{68}Ga]Ga-DOTA-PEPTIDE	Intense focus on the uptake of the pituitary gland
Haberbosch et al [15]	2023	Case report	L-[methyl^{11}C]-methionine	Uptake on the left side of the sellar region
Chiloiro et al[16]	2024	Case report	[^{18}F]FDG	Excluded the presence of cancer
Bakker et al[17]	2024	Case series	[^{18}F]FET	Suspicious para sellar tracer uptake

Table 2 Apastic Anemia, Aplastic Anemia and Systemic Lupus Erythematous and Bullous pemphigoid

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Aplastic Anemia				
Matsuki et al[18]	2024	Case report	[^{18}F]FDG	Uptake of [^{18}F]FDG pleura and lung
Disease: Aplastic Anemia AND Systemic Lupus Erythematous				
Dudek et al[19]	2024	Case report	[^{18}F]FDG	Hypometabolic bone marrow activity
Disease: Bullous Pemphigoid				
Shrestha et al[20]	2022	Case report	[^{18}F]FDG	Left mediastinal lymphadenopathy and lung lesion
Grünig et al[21]	2022	Case report	[^{18}F]FDG	Multiple small lesions of the skin distant from the known primary tumor locations

Table 3 Chagas Disease

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Chagas Disease				
Moll-Bernardes et al [22]	2020	Case report	[^{18}F]FDG AND [^{68}Ga]Ga-DOTA-TOC	Increased radiotracer uptake in the mid inferoseptal, mid anteroseptal, and basal inferolateral walls of the left ventricular
de Oliveira et al[23]	2023	Cross-sectional	[^{18}F]FDG AND [^{68}Ga]Ga-DOTA-TOC	[^{18}F]FDG AND [^{68}Ga]Ga-DOTA-TOC uptake useful for the detection of myocardial inflammation [^{68}Ga]Ga-DOTA-TOC uptake may be associated with the presence of malignant arrhythmia

Table 4 Castleman's disease

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Castleman's disease				
Reddy et al[24]	2018	Case series	[^{18}F]FDG	Uptake cervical, mediastinal, and pelvic lymph nodes. Sclerotic bone lesions
Liu et al[25]	2023	Case report	[^{18}F]FDG	Uptake mesenteric lymph node and multiple lung nodules with slight FDG uptake.
Zhang et al[26]	2023	Case report	[^{18}F]FDG	Uptake abdominal cavity
Maqbool et al[27]	2023	Case report	[^{18}F]FDG	Uptake right-sided neck mass and other lymph nodes of the head and neck
Yamauchi et al[28]	2023	Case report	[^{18}F]FDG	[^{18}F]FDG uptake in idiopathic multicentric Castleman disease was significantly lower than that in the Hodgkin lymphoma
Zuo et al[29]	2024	Case report	[68Ga]Ga-DOTA-TATE [68Ga]Ga- Pentixafor	Positive uptake in the retroperitoneal mass
Aher P et al[30]	2024	Case report	[^{18}F]FDG	Mixed-density mass with uptake in the right cardiogenic region

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Mashal et al[31]	2024	Case report	[^{18}F]FDG	Uptake in the supraclavicular, mediastinal, and retroperitoneal lymph nodes, along with diffuse uptake in the spleen and soft-tissue nodules in the inferior and medial gluteal regions
Hu et al[32]	2024	Case report	[^{18}F]FDG	Uptake in lymph nodes, spleen, bones, bone marrow, and nasopharynx, associated with multicentric Castleman disease.

Table 5 Castleman's disease AND POEMS Syndrome And Cogan’s Syndrome

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Castleman's disease AND POEMS Syndrome				
Choe et al[33]	2024	Case report	[^{18}F]FDG	Multiple lymph nodes, L1 sclerotic lesion, edema, and hepatosplenomegaly
Disease: Cogan’s Syndrome				
Balink et al[34]	2007	Case report	[^{18}F]FDG	Uptake in the wall of the aortic arch, the aorta descends into the lateral wall.
Örsal et al [35]	2014	Case report	[^{18}F]FDG	Uptake in the walls of the arteries and knees
Cabezas-Rodríguez et al[36]	2019	Case report	[^{18}F]FDG	Increased metabolic activity of thoracic aorta and subclavian arteries
Matsui et al[37]	2021	Case report	[^{18}F]FDG	Uptake in the aorta, bilateral carotid, iliac arteries, and celiac artery
Hafner et al[38]	2021	Case report	[^{18}F]FDG	Multiple liver abscesses and abdominal aortitis
Na et al[39]	2024	Case report	[^{18}F]FDG	Uptake in the subclavian and common carotid arteries, aortic arch, thoracic aorta, and coronary
Lu et al[40]	2024	Case report	[^{18}F]FDG	Uptake the walls of the right head and arm, the left common carotid artery, and the starting segment of the left subclavian artery.

Table 6 Cold Agglutinin Disease and Churg-Strauss syndrome

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Cold Agglutinin Disease				
Nakamoto et al[41]	2019	Case report	[^{18}F]FDG	Splenomegaly with diffuse uptake in bone marrow
Hayashi et al[42]	2023	Case report	[^{18}F]FDG	Uptake vertebral body, iliac bone and spleen
Disease: Churg-Strauss syndrome				
Horiguchi et al[43]	2014	Case report	[^{18}F]FDG	Uptake in lymphadenopathy in the mediastinal and hilar region

Table 7 Eosinophilic fasciitis

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Eosinophilic fasciitis				
Narváez et al[44]	2019	Case report	[^{18}F]FDG	Diffuse and symmetrical uptake in the fascia of the legs and thighs
Barlet et al[45]	2020	Case report	[^{18}F]FDG	Uptakes in the shoulders, wrists, knees, and ankles.
Song et al[46]	2021	Case report	[^{18}F]FDG	Uptakes in subcutaneous fat and muscle
Chalopin et al[47]	2021	Case report	[^{18}F]FDG	Uptake in bone lesions
Barlet et al[45]	2021	Case report	[^{18}F]FDG	Diffuse uptake of the muscular fasciae
Laria et al[48]	2022	Case report	[^{18}F]FDG	Diffuse uptake in the muscles of the forearms and of both lower limbs
Amrane et al[49]	2022	Case report	[^{18}F]FDG	Uptake in subcutaneous nodules, muscle fascia, and diffuse on the synovial walls of both knees
Benzaquen et al[50]	2023	Case report	[^{18}F]FDG	Generalized hypermetabolism of the fasciae and foci adjacent to the muscles and subcutaneous
Fevrier et al[51]	2024	Case report	[^{18}F]FDG	Uptake of fasciae in the lower and upper limbs

Table 8 Henoch-Schonlein purpura and Immune thrombocytopenic purpura

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Henoch-Schonlein purpura				
Sabzevari et al[52]	2018	Case report	[^{18}F]FDG	Uptake in subclavian, brachiocephalic, abdominal aortic, iliac and femoral arteries
Gultekin et al[53]	2021	Case report	[^{18}F]FDG	Uptake in cavitary nodular lesions and hilar lymphadenomegaly
Disease: Immune thrombocytopenic purpura				
Razanamahery et al[54]	2021	Case report	[^{18}F]FDG	Uptake in peri-nephric fat fibrosis, mediastinal lymph nodes, and a low tracer uptake on the testis
Ren et al[55]	2023	Case report	[^{18}F]FDG	Uptake in lymph nodes in numerous regions of the body

Table 9 Neuromyelitis Optica Spectrum Disorder

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Neuromyelitis Optica Spectrum Disorder				
Alkhaja et al[56]	2021	Case report	[^{18}F]FDG	Uptake along the entire spinal cord, suggestive of extensive acute myelitis
Ding et al[57]	2021	Case report	[^{18}F]FDG	Uptake in the cervicothoracic, thoracic, and rectal wall
Fujisawa et al[58]	2023	Case report	[^{18}F]Flutemetamol [^{18}F]MK6240 (TAU) [^{18}F]FDG	[^{18}F]Flutemetamol uptake in the frontal and parietal lobes, posterior cingulate gyrus, and precuneus. [^{18}F] MK6240 (TAU) uptake in the medial temporal, parietal, and frontal lobes; posterior cingulate gyrus; and precuneus. [^{18}F]FDG showing decreased glucose metabolism from the inferior parietal lobule to the mid posterior temporal lobe, frontal association cortex, posterior cingulate cortex, and precuneus, predominantly on the left side
Vlaicu et al[59]	2023	Case report	[^{18}F]FDG	Uptake in pulmonary neoplasm with lymph node and adrenal metastases

Table 10 Paraneoplastic pemphigus

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Paraneoplastic pemphigus				
Dhull et al[60]	2016	Case report	[^{18}F]FDG	Uptake in the left paravertebral region at the level of the left renal hilum, oral cavity, and left lung upper lobe.
Lim et al[61]	2017	Case report	[^{18}F]FDG	Uptake in multiple enlarged lymph nodes
Khurana et al[62]	2020	Case report	[^{18}F]FDG	Uptake mass lesion in the middle mediastinum in the subcarinal location extending into the transverse pericardial sinus
Chen et al[63]	2020	Case report	[^{18}F]FDG	Uptake soft tissue mass in the right anterior-inferior mediastinum, right parasternal adenopathy and pleural effusion
Liska et al[64]	2022	Case report	[^{18}F]FDG	Uptake in left tonsil area
Daniels et al[65]	2023	Case report	[^{18}F]FDG	Uptake in the mediastinum
Lu et al[66]	2024	Case report	[^{18}F]FDG	Uptake in neck lymphadenopathies

Table 11 Paraneoplastic pemphigus AND Castleman's disease and Paraneoplastic Cerebellar Degeneration

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Paraneoplastic pemphigus AND Castleman's disease				
Fu et al[67]	2018	Case report	[^{18}F]FDG	Uptake in the oral lesions and a heterogeneous soft tissue mass in the lower right retroperitoneum
Liu et al[68]	2011	Cases Series	[^{18}F]FDG	Uptake in the head of the pancreas
Fu et al[69]	2018	Case report	[^{18}F]FDG	Uptake mass in the lower right retroperitoneum
Wang et al[70]	2019	Case report	[^{18}F]FDG	Uptake in the head of the pancreas
Relvas et al[71]	2023	Case report	[^{18}F]FDG	Uptake in retroperitoneal lymphadenopathies and lobulated mass
Disease: Paraneoplastic Cerebellar Degeneration				
Rodriguez Herrera et al[72]	2023	Case report	[^{18}F]FDG	Uptake in orbitofrontal hypermetabolism, mesial temporal and bilateral

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
				cerebellar hypometabolism
Takahashi et al[73]	2024	Case report	[^{18}F]FDG [^{123}I]IMP SPECT	[^{18}F]FDG uptake in lung tumor and mediastinal lymph nodes [^{123}I]IMP SPECT shows normal blood flow in the cerebellum
Kalantari et al[74]	2024	Case report	[^{18}F]FDG	Uptake in the annex
Imai et al[75]	2022	Case report	[^{18}F]FDG	Uptake in the left neck

Table 12 POEMS Syndrome

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: POEMS Syndrome				
Pan et al[76]	2015	Cross-sectional	[^{18}F]FDG	Uptake in solitary and multiple hypermetabolic bone lesions, lymph nodes, Hepatomegaly, Splenomegaly, Central nervous system, Serous cavity effusion, and Gynecomastia
Allam et al[77]	2022	Case report	[^{18}F]FDG	Uptake in axillary and retro-pectoral lymph nodes and systemic fibrosis process involving pleural spaces, mediastinum, and pelvis.
Genicon et al[78]	2022	Case report	[^{18}F]FDG	Uptake in osteolytic lesion in the right femur
Gültekin et al[79]	2023	Case report	[^{18}F]FDG	Uptake diffuses in muscle
Aderhold et al[80]	2024	Case report	[^{18}F]FDG	Uptake in osteosclerotic pelvic, vertebral, and clavicular bone lesions and hilar lymphadenopathy

Table 13 Polyarteritis nodosa and Postural Orthostatic Tachycardia Syndrome

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Disease: Polyarteritis nodosa				
Kang et al[81]	2023	Case report	[^{18}F]FDG	Uptake in lower extremities
Taimen et al[82]	2024	Case report	[^{18}F]FDG	Uptake in peri- and intramuscular arterial of the lower extremities and liver

Authors	Year of publication	Type of Study	PET/CT Tracer	Main Findings
Makiyama et al[83]	2024	Case report	[^{18}F]FDG	Uptake in nodule in the right lower lung, right pulmonary artery embolism, and precordial subcutaneous tissue nodule
Philip et al[84]	2024	Case report	[^{18}F]FDG	Uptake in soft tissues and intramuscular arterial tree
Taniguchi et al[85]	2024	Case report	[^{18}F]FDG	Uptake in medium-sized vessels
Disease: Postural Orthostatic Tachycardia Syndrome				
Khan et al[86]	2022	Case report	[^{68}Ga]Ga-DOTA-TATE	Uptake associated with the contrast agent in both adrenal glands and calcified thyroid nodules
Disease: Scleroderma				
Diaz Menindez et al[87]	2023	Case report	[^{18}F]FDG	Uptake in multifocal osseous, particularly on the spine and pelvic

Discussion

Autoimmune diseases are characterized by spontaneous hyperactivity of the immune system, leading to the production of additional antibodies, which often results in inflammation that can affect all organs and tissues of the body, especially lymphoid tissues, joints, skin, muscles, salivary glands, blood vessels, and bone marrow[88].

As established in the results section, multiple autoimmune diseases are considered within the spectrum of orphan diseases. Therefore, from the perspective of molecular diagnostic studies, this review aimed to compile the available findings in the literature so that readers can become familiar with these types of pathologies and find a diagnostic aid for these conditions in these studies.

As for the pathophysiology, inflammation is the host's initial defense against pathogens and other triggering stimuli. It plays an essential role in tissue repair and eliminating harmful pathogens. However, an inadequate response can damage normal cells adjacent to the affected tissue. In many autoimmune diseases, sterile inflammation occurs.

Molecular imaging allows for the visualization, characterization, and measurement of biological processes at the molecular and cellular levels, with PET/CT being the most widely used molecular imaging study in clinical practice[89].

The European Association of Nuclear Medicine (EANM), in conjunction with the Society of Nuclear Medicine and Molecular Imaging (SNMMI), published a guideline in 2013 on the use of [18F]FDG in inflammation and infection based on the evidence available at that time. In 2018, along with the PET Interest Group (GIP) and endorsed by the American Society of Nuclear Cardiology, they published a guideline on the use of PET/CT in the diagnosis and follow-up of patients with suspected or diagnosed large vessel vasculitis and Polymyalgia Rheumatica. Over the last 10 years, the use of this diagnostic tool has rapidly evolved, and it is now considered the most utilized imaging study in nuclear medicine for diagnosing and treating various inflammatory disorders[90].

[^{18}F]FDG is the most commonly used PET tracer; as a glucose analog, it is taken up by cells with high

energy demand, where it is phosphorylated but not metabolized, continuously accumulating within the cells, allowing for the detection of its photons by the PET equipment. (Molecular Imaging of Autoimmune Diseases and Inflammation). Inflammatory processes exhibit increased FDG uptake, as infiltrating inflammatory cells can express high levels of glucose transporters, especially GLUT1 and GLUT3. Additionally, they show greater glucose consumption than non-inflammatory peripheral cells, resulting in increased glucose metabolism due to oxidative bursts in inflammatory cells[91].

This can be evidenced in our review, as the predominant finding in all the pathologies addressed in this article was the increased uptake of FDG in the affected organs or tissues. Some reports show SUVmax values greater than 4 in Castleman disease (CD), generalized Wegener's granulomatosis, POEMS syndrome, and eosinophilic fasciitis in some cases. Additionally, PET/CT helped guide the diagnosis by identifying the primary tumor in some cases of metastatic lesions in patients with paraneoplastic pemphigus.

Cogan syndrome is a rare disease of unknown origin characterized by ocular inflammation and audiovestibular symptoms; only 5% of patients present initially with systemic manifestations such as vasculitis or aortitis (Cogan syndrome). In this context, PET/CT facilitated the diagnosis of systemic involvement, revealing increased metabolism in the walls of blood vessels such as the thoracic aorta and subclavian arteries, as reported by Cabezas-Rodríguez et al.[36], with vasculitis affecting the brachiocephalic trunk, common carotid artery, and left subclavian artery, findings also reported by Lu C and collaborators[40].

Yamauchi et al. reported a case of a patient with bilateral supraclavicular and mediastinal lymph nodes showing significant FDG uptake, some with SUVmax values of 11.5. An initial biopsy of the left supraclavicular lymph node showed no evidence suggesting malignancy. It was negative for large cells CD156 and CD30, initially diagnosed as idiopathic multicentric Castleman disease, later confirmed as Hodgkin lymphoma. PET/CT was crucial in raising doubts about the appropriateness of the initial diagnosis. Yamauchi and collaborators suggested the utility of [18F]FDG PET/CT to differentiate between the two pathologies, finding significantly lower FDG uptake and SUVmax values in the non-malignant condition compared to Hodgkin lymphoma[28].

Patients with chronic autoimmune and inflammatory diseases have been reported to have a higher risk of malignancies, with a 2.4 and 2-fold increased risk of esophageal and pancreatic cancer, respectively. For lymphoma, the risk is approximately two times higher in patients with rheumatoid arthritis, 3 to 6 times higher in patients with systemic lupus erythematosus, and 9 to 18 times higher in patients with Sjögren syndrome. In patients with dermatomyositis and polymyositis, an incidence of 7 times higher risk of cancer compared to the general population has been reported[88].

Oh JR et al. suggest that PET/CT is useful for differentiating between malignancy and inflammation in patients with systemic autoimmune diseases, especially considering the spleen/liver SUVmax ratio, which is significantly higher in patients with autoimmunity, being 1.5± 0.6 vs 0.8± 0.02 in malignancy patients[88].

In conditions such as acromegaly, Chagas disease, and Castleman Diseases, case reports have been noted where PET/CT was performed using 68 Gallium-DOTATATE and DOTATOC, showing an increased uptake of these radiopharmaceuticals. The implementation of these radiotracers is based on the overexpression of somatostatin receptors by inflammatory and immune cells in various tissues and blood vessels, among others[92].

Potential uses include amino acid-based tracers, such as L—[methyl-11C]—methionine, employed by Bashari et al[10] and Haber-Bosch et al.[15], or [^{18}F]FET, described by Bakker [17]in the case of acromegaly, with patients suspected of having residual lesions in the central nervous system, guided by the persistence of biochemical abnormalities.

In the case of [^{68}Ga]Ga-Pentixafor, Zuo et al[29] report that a higher CXCR4 expression may be present in a heterogeneous lymphoproliferative disease such as Castleman's disease.

For [^{18}F]Flutemetamol and [18F]MK6240 (TAU), neuromyelitis optica associated with Alzheimer's disease is described as characterized by a marked accumulation of amyloid beta (Aβ) and a high degree of tau deposition, respectively[58].

With the above in mind, the use of PET/CT with different tracers in the case of orphan autoimmune diseases has expanded in recent years, as it allows for imaging of the processes influencing the microenvironment of inflamed tissues, which plays a significant role in the persistence of inflammatory processes in autoimmune diseases and provides a comprehensive view of systemic involvement, which can lead to more precise guidance for the treatment and follow-up of these diseases.

Conflict of Interest:

The authors have no conflicts of interest to declare.

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