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Intracerebral Abscess: An Uncommon Infection in a Psoriatic Arthritis Patient under Long-Term Certolizumab Pegol Treatment

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Abstract

The treatment of autoimmune disorders like psoriatic arthritis, include anti-tumor necrosis factor biological agents, such as Certolizumab Pegol, which presents notable efficacy, however at the same time elicits concerns regarding susceptibility to infections.

In our case study, a 49-year-old male with psoriatic arthritis treated with Certolizumab Pegol and oral glucocorticosteroids, developed unilateral paresthesia prompting neurological evaluation.

Magnetic Resonance Imaging (MRI) of the cerebrum revealed a lesion suggestive of an intracerebral abscess. Despite negative cultures, he underwent tooth extraction, received antibiotics and glucocorticosteroids with full clinical and paraclinical recovery.

Rheumatologists should consider a brain abscess as a differential diagnosis in patients receiving immunosuppressive medication with the onset of neurological symptoms. Intracerebral abscesses, albeit rare as a complication, necessitate prompt diagnosis, effective treatment, and vigilant monitoring to optimize patient outcomes and quality of life.

Keywords: Intracerebral Abscess; Infection; Psoriatic Arthritis; Certolizumab Pegol; Immunodeficiency.

Introduction

Infections pose a significant concern for patients undergoing treatment with biological agents for inflammatory diseases, given the immunosuppressive effects they induce. Typically, infections associated with anti-tumor necrosis factor (anti-TNF) biological agents, such as Certolizumab Pegol, manifest as upper and lower respiratory tract infections [1,2]. Central nervous system infections are relatively uncommon in this context [3].

Case Presentation

A 49-years old male patient was followed in the outpatient clinic of the Danish Hospital for Rheumatic Diseases, diagnosed with peripheral erosive psoriatic arthritis with primarily involvement of the feet since 2011. The patient had a family history of psoriatic arthritis and was human leukocyte antigen B27 (HLAB27) positive without any radiographic signs of spondylarthritis.

His treatment included Certolizumab Pegol 200 milligrams (mg) every 10 days, combined with a daily dosage of 5 mg oral prednisolone since 2013. While on this treatment, he experienced only partial clinical remission with Disease Activity index for Psoriatic Arthritis (DAPSA) scores ranging between 14.2 and 19.2 indicating moderate disease activity [4].

The patient had known comorbidities including sleep apnea and underwent cholecystectomy in December 2017 due to cholecystolithiasis.

In the summer of 2018, he presented with unilateral paresthesia of the upper and lower right extremities and was referred for neurological evaluation suspecting anti-TNF induced polyneuropathy. However, clinical examination, electroneurography, and MRI scan of the cerebrum in November 2018 were unremarkable.

On February 6, 2019, he was admitted to the neurological emergency department under suspicion of cerebral stroke due to reduced strength and paresthesia in the right upper extremity, accompanied by severe headache radiating to the back of the head. He did not report nausea, vomiting, visual disturbances or fever. The neurological examination revealed reduced strength in the right arm. A Computed Tomography (CT) of the cerebrum showed a 2 cm large cystic lesion in the left frontoparietal side with approximately 1 cm of perifocal edema. Subsequent CT scans of the thorax and abdomen showed no signs of malignancy or infection, as the lesion was suspicious of metastasis. Blood tests revealed elevated C-reactive protein (CRP) of 106 mg/L (normal range: under 5,0 mg/L).

On February 8, 2019, the patient experienced a 30-second-long generalized tonic/clonic seizure with eye and head turning to the left and subsequently initiated levetiracetam treatment (500 mg, 2 times daily). A MRI of the cerebrum revealed a 26 mm intraaxial lesion on the left frontoparietal side exhibiting peripheral contrast enhancement and adjacent leptomeningeal contrast enhancement (Figure 1). The leading differential diagnosis was an intracerebral abscess. After consulting with neurosurgeons from the Odense University Hospital (OUH), who concluded that due to the abscess's localization, drainage and cultivation of the material were not feasible and thus found no indication for the surgery, the patient was transferred to the infectious medical department at OUH.

Blood, urine and sputum cultivations showed no bacterial growth. Human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), QuantiFERON test (QFT) for tubelculosis bacteria, Toxoplasma gondii immunoglobulin M (IgM) and immunoglobulin G (IgG), Cytomegalovirus IgM and IgG, Aspergillus galactomannan antigen tests were all negative.

Immunoglobulin levels were normal, apart from slightly elevated immunoglobulin A (IgA). The patient underwent extraction of infected teeth (26 and 27) as confirmed by facial CT on February 12, 2019. A positron emission tomography-computed tomography (PET-CT) scan on February 13, 2019, did not reveal any additional evidence of infection or malignancy.

The patient started a triple combination therapy of intravenous antibiotics according to the national guidelines with Benzylpenicillin (Penicillin G) 5 million international units (MIU) 4 times daily, Metronidazole 500 (mg) 3 times daily and Ceftriaxone 4 grams (g) 1 time daily from February 8, 2019, to March 8, 2019, supplemented with oral prednisolone at 50 mg daily for 5 days. Biological treatment with Certolizumab Pegol was paused upon admission.

The patient exhibited notable paraclinical improvement, as evidenced by follow-up cerebral MRI image (Figure 2 and Figure 3). Despite persistent headache, its intensity gradually diminished with the administration of opioid therapy, necessitated by liver toxicity resulting from paracetamol and non-steroid anti-rheumatic drugs. Considering adverse effects to levetiracetam, the preventive antiepileptic treatment was changed to lamotrigine, to manage focal muscle contractions observed in the right arm. The patient ultimately achieved complete recovery, prompting a gradual tapering and discontinuation of antiepileptic treatment.

During subsequent follow-up, immunodeficiency investigations unveiled normal subtypes of thymus derived cells (T cells), bursa derived cells (B cells), and natural killer cells (NK cells) but indicated low to immeasurable levels of mannose-binding lectin (MBL). Consequently, the patient was classified as being at high risk for severe future infections and was counselled to undergo prophylactic antibiotic therapy prior to any invasive procedures.

To manage his psoriatic arthritis, the patient was prescribed a regimen consisting of Sulfasalazine at a dosage of 2 g daily in conjunction with oral prednisolone at 5 mg daily. This treatment approach maintained his DAPSA score within the range of 10.6 to 16.9, which is low to moderate disease activity.

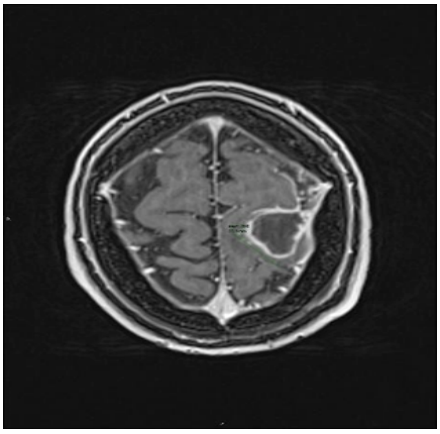

Figure 1: MR of cerebrum February 2019 with intravenous contrast agent. Showing a 26 mm intraaxial lesion on the left frontoparietal side exhibiting peripheral contrast enhancement and adjacent leptomeningeal contrast enhancement. Furthermore, changes show restricted diffusion which indicate an abscess (not shown).

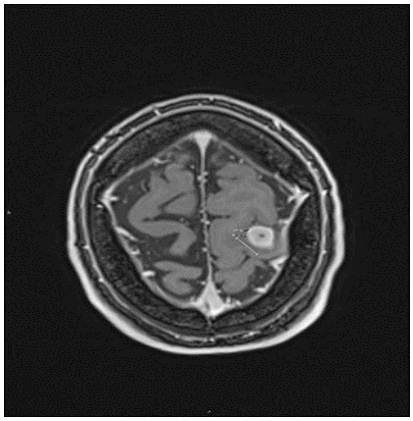

Figure 2: MR of cerebrum June 2019 with intravenous contrast agent. Showing progressive regression of the abscess compared to the initial MRI scanning (lesion diameter13,0 mm).

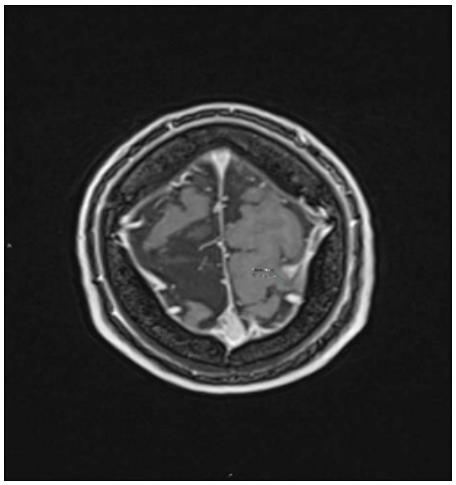

Figure 3: MR of cerebrum December 2019. Showing progressive regression of the abscess compared to the initial MRI scanning (lesion diameter 5,0 mm).

Discussion

Biological agents, including tumor necrosis factor inhibitors like Certolizumab Pegol, are widely utilized with success in the management of autoimmune diseases such as axial spondyloarthritis, psoriatic arthritis, psoriasis, and inflammatory bowel disease, and are typically regarded as safe. Nonetheless, their use is associated with an increased risk of infections, predominantly upper and lower respiratory tract infections [1,2,5,6]. Additionally, in some cases, they have been linked to opportunistic and severe infections with adverse outcomes [1-3,5,6].

An intracerebral abscess denotes a localized collection of pus within the brain parenchyma from direct inoculation, contiguous dissemination from adjacent anatomical sites, or hematogenous seeding from a distant infectious focus [7]. Brain abscesses occur at an annual incidence rate of 0.3 to1.3 per 100,000 individuals [8]. There have previously been described cases of patients diagnosed with rheumatic diseases, such as psoriatic arthritis, receiving treatment with tumor necrosis factor inhibitors, who have developed intracerebral abscesses [3,9].

Clinically, the presentation of a brain abscess can vary. Approximately one-fifth of patients present with the classic triad of headache, fever, and focal neurological deficits [7]. More commonly, patients solely exhibit signs and symptoms of

raised intracranial pressure, such as confusion, decreased level of consciousness, headache, nausea, and vomiting, which can mimic presentations of various intracranial pathologies [7]. Long-term sequelae have been observed in about 45% of patients at 6 months after discharge, typically encompassing focal neurological deficits corresponding to the anatomical location of the brain abscess and neurocognitive impairment [10].

Neurosurgery plays a pivotal role in achieving source control in patients with brain abscesses. Pus samples extracted from the abscess should undergo both aerobic and anaerobic cultures, along with histopathological analyses. Although blood cultures yield positive results in 28% of patients, they should always be obtained [10]. Furthermore, consideration should be given to conducting tests for tuberculosis and HIV in patients presenting with non-traumatic brain abscesses [10].

A limitation inherent in our case is the inability to ascertain the microbial etiology of the infection, which can be attributed to the abscess's location and the absence of positive findings from blood bacterial cultures. The possibility of an odontogenic origin for the infection warrants consideration. Despite the patient undergoing a dental examination prior to commencing biological treatment in 2013, subsequent dental records were not documented in the patient's medical dossier. However, a facial skeleton CT scan revealed radiolucency around the apices of certain tooth roots, prompting the extraction of two affected teeth.

Only 2 to 5% of brain abscesses originate from odontogenic sources [8]. Mortality rates from odontogenic brain abscesses range from 8.3% to 16% in reported studies [8,11]. These abscesses typically localize in the frontal lobe in 45% of cases followed by the parietal lobe [8]. They are commonly caused by pathogenic species of the Streptococcus Milleri family in 32% of cases [8]. Prompt tooth extraction, once the patient's medical condition allows, is often necessary and recommended as the primary treatment [8,10].

Conclusion

Prior to commencing treatment with biological agents such as Certolizumab Pegol, it is essential to engage in thorough discussions with the patient, providing comprehensive orientation regarding the risks of infections and other potential adverse events. An intracerebral abscess remains a rare yet critical infection that, if not promptly diagnosed, can result in disability or even fatality.

Considering an intracerebral abscess as a potential cause for unilateral neurological symptoms, even in the absence of clinical or paraclinical signs of infection, is crucial. Increased awareness can facilitate screening and prevention of such occurrences.

Conducting a meticulous dental screening by specialists and addressing any identified issues before commencing treatment with biological agents is highly recommended and should be integrated into routine clinical practice.

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Ethical Considerations: Our institution does not require ethics approval for reporting individual cases or case series. Written informed consent was obtained for anonymized patient information to be published in this manuscript.

Conflict of Interest: The authors report no funding or conflicts of interest.

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