Case Report

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An Exceptional Case of a Supra-tentorial Streptococcus Salivarius Brain Abscess—A Case Report

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Abstract

Introduction: During the COVID-19 pandemic, incidence of brain abscesses is difficult to assess. Numerous studies reported benign and severe post SARS-CoV-2 vaccine side effects, including rare cases of brain abscesses associated with COVID-19 or Anti-SARS-CoV-2 vaccines. Here in, we report what we believe to be, up to date, the fourth known case in the medical literature of a *streptococcus salivarius* brain abscess, the first intra parenchymatous or supra-tentorial *streptococcus salivarius* brain abscess and also the first that occurs following an anti-SARS-CoV-2 vaccine.

Case presentation: We describe the case of a north african 63-year-old man with an unremarkable medical history except for recent anti-SARS-CoV-2 vaccinations. Following the administration of a third anti-SARS-CoV-2 booster vaccine, the patient developed neurological symptoms, including left hemiparesis, facial palsy, vertigo, and balance issues. Imaging studies revealed a right temporo-parietal lesion consistent with intracranial suppuration. Stereotaxic cerebral biopsy confirmed the presence of purulent content, indicating a brain abscess caused by multi-sensitive *streptococcus salivarius*.

Conclusion: Sepsis-induced immunodepression appears to be a consequence of severe inflammatory state, as it dysregulates leukocytes population and results in serious infections. A plausible hypothesis is that a previous stress such as anti-SARS-CoV-2 vaccination could lead to the development of a *streptococcus salivarius* septicemia. In light of the available evidence and research findings, no definitive conclusion can be drawn regarding any potential link between anti-SARS-CoV-2 vaccines and the physiopathology of sepsis-induced immunodepression.

Keywords

Brain abscess, nervous system, SARS-CoV-2, *Streptococcus salivarius*, sepsis, immunodeficiency

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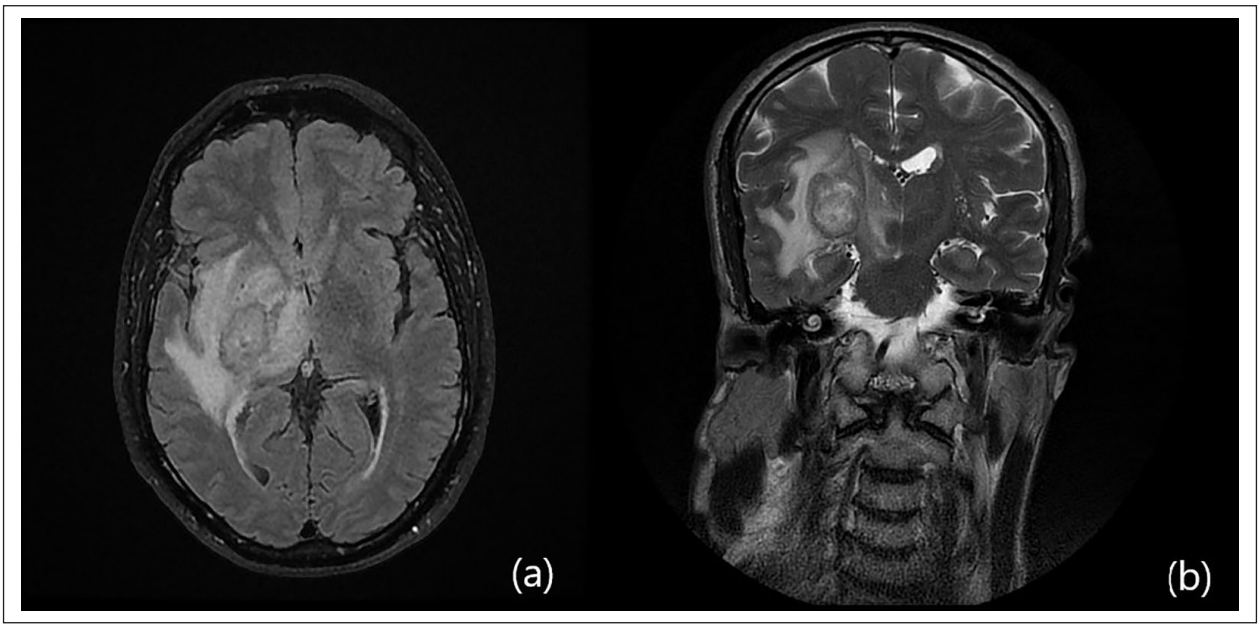

Figure 1. Cerebral MRI showing a right temporo-parietal round heterogenous lesion in hypersignal axial T2 Flair (a) and coronal T2 (b).

Introduction

Brain abscesses are a formation of suppurative intracranial infections in a focal area. It is a rare pathology often linked to immunodepression or post-operative period[1] and it can result in significant morbidity and mortality, making early diagnosis and treatment crucial.[1]

During the COVID-19 pandemic, incidence of brain abscesses was difficult to assess. Numerous studies reported benign and severe post SARS-CoV-2 vaccine side effects,[2-4] including rare cases of brain abscesses associated with COVID-19 or Anti-SARS-CoV-2 vaccines.[5,6]

In terms of COVID-19 pandemic management, morocco stood out as a good example worldwide, particularly with the swift implementation of the anti-SARS-CoV-2 vaccine strategy.[7] According to WHO, in April 2022, 63.29% of the moroccan population (versus 58% globally) was fully vaccinated with the last dose of primary series, with a total vaccine doses administered per 100 population of 147.135 (versus 143.47 globally).[8]

Here in, we report what we believe to be, up to date, the fourth known case in the medical literature of a *streptococcus salivarius* brain abscess and the first intra-parenchymatous or supra-tentorial *streptococcus salivarius* brain abscess; that occurs following an anti-SARS-CoV-2 vaccine.

Case Presentation

We report a case of a north-african 63-year-old man, who has no relevant medical history beside a series of recent anti-SARS-CoV-2 vaccinations, starting with two first doses of ChaAdOx1 nCoV-19 vaccine (AZD1222), followed by a third BNT162b anti-SARS-CoV-2 vaccine dose. The patient reported the onset of symptomatology one day upon the administration of a third anti-SARS-CoV-2 vaccine dose.

At the admission, the patient was conscious: Glasgow coma scale (GCS) was at 15/15 and well oriented in time and space. The neurological examination found a left hemiparesis: motor power was grade 4 out of 5 on the medical research council (MRC) scale in the left body, a central facial palsy, a rotary vertigo, and a balance disorder. No sensitive or sensorial deficit was found. The patient was afebrile and the rest of the physical examination was normal.

Further questioning reported the progressive beginning of the symptomatology 48 hours before the admission, 6 days after the administration of the third BNT162b anti-SARS-CoV-2 booster vaccine.

Cerebral contrast-enhanced computed tomography (CT) was performed one day before the admission, revealing an oval right temporal lesion measuring $27 \times 30 \times 20$ mm with a necrotic center, and a thickened wall enhanced after the contrast product injection.

A cerebral magnetic resonance imaging (MRI) was requested at the admission, revealing a right temporo-parietal round lesion measuring $34 \times 21 \times 31$ mm in iso-signal T1, heterogenous hypersignal T2 and flair, with some a-signal zones T2*, hypersignal in diffusion with a drop in apparent diffusion coefficient sequence (Figure 1). The multi-voxel magnetic resonance spectroscopic imaging (MRSI) showed significant elevation of the lipid/lactate (LL) peaks especially in the central portion of the lesion. Neural markers like N-acetyl aspartate (NAA) and creatine (Cr) were significantly decreased, with a slight elevation of choline (Cho) (Figure 2). All those imaging characteristics were compatible with an intracranial suppuration.

Moreover, a cardiovascular evaluation was conducted using a transthoracic echocardiography and transesophageal echocardiography. An aspect of hypertensive heart disease, with a preserved ventricular ejection fraction indicating good left ventricular function, was observed. No

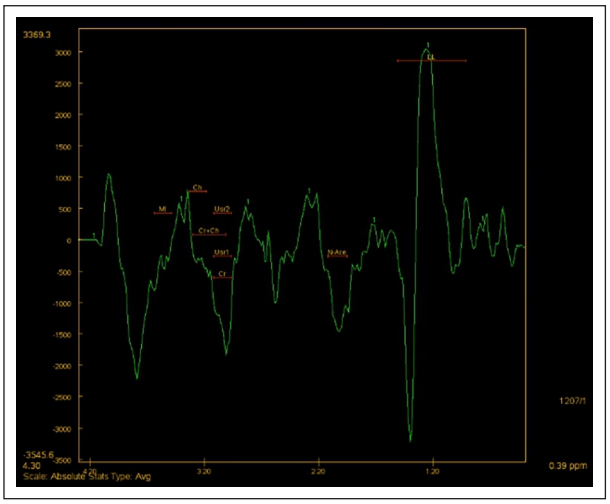

Figure 2. Multi voxel MRSI showing a lipid/lactate (LL) peak, with decreased neural markers (Cr and NAA).

sign of endocarditis or other abnormality were observed (no evidence of vegetations and no valvular or paravalvular regurgitation).

Blood tests were normal except for a lymphopenia at 480/mm^3.

Three potential diagnoses have been raised: glioblastoma, metastatic secondary lesion and brain abscess.

Given the accessibility of the lesion, we decided to do a stereotaxic cerebral biopsy, directly to the superficial right temporal lesion, finding a purulent content. Microbiological and pathological assessment of the pus revealed a multisensitive *streptococcus salivarius.*

Further evaluation was undertaken to determine a potential source of entry for the brain abscess. A thoraco-abdomino-pelvic computed tomography (CT) was negative and CT of sinus was normal. Oro-dental examination realized by the oral surgeon failed to find any source of entry.

The patient was treated empirically with metronidazole (500 mg three times daily), gentamycin (320 mg once a day), and ceftriaxone (2g three times daily). After revealing the *streptococcus salivarius* resistance pattern, antibiotic treatment was narrowed to ceftriaxone for 6 weeks and combined to corticosteroid therapy with prednisone (40 mg once a day).

Regarding lymphopenia, an immunological screening panel was requested and resulted in the following: HIV serology (P24 antigen and anti-HIV 1 and 2 antibodies) was negative twice in a row, in addition to a negative HIV viral load. Moreover, HBV serology profile was entirely negative and considered then as host-susceptibility to HBV infection. HCV serology, TPHA and VDRL were all negative.

An initial immunophenotyping of peripheral blood lymphocytes test, with dosage of complement and immunoglobulins were performed, as shown in Table 1.

The patient was discharged from the hospital at day 10 of hospitalization, against medical advice, expressing a preference for home-based care. Nine days later, he was readmitted in the emergency unit, where we found a conscious but somnolent patient, suffering from strong headaches with deeper motor deficit than the first admission (hemiplegia with a muscular strength evaluated at 2 out 5 on the Medical Research Council (MRC) scale; in both left extremities.

Cerebral CT scan revealed an increase of brain abscess volume, measuring $36 \times 27 \times 29$ mm, a thickened wall enhanced after the injection of the contrast product, associated with a range of moderate perilesional edema.

A second stereotaxic cerebral biopsy was performed, directly to the superficial right temporal lesion, finding a serous content. Microbiological study and culture of the serous sampling was sterile.

Then, the patient benefited of 6 weeks of intravenous neuro-meningeal antibiotics (ceftriaxone) and corticosteroids (methyl-prednisone) therapy, in addition to continuous physiotherapy sessions.

After assessing the oral health and ENT sphere searching for entry points, we found no abnormality other than a dental amalgam next to 26, and an aspect of chronic mandibular periodontal disease at the dental panoramic X-ray. A cone beam computed tomography revealed decay of the 18, associated with a global periodontal disease.

Three months after the first episode, the patient was recovering well, and was found to be almost autonomous in his everyday life. He was still pursuing his physiotherapy sessions, and kept a persistent left hemiparesis with a muscular strength evaluated at 4 out 5 on the medical research council (MRC) scale; in both left extremities.

Control cerebral CT revealed a complete resorption of the cerebral abscess, and no other abnormality other than demyelination lesions classified as grade 1 according to Fazekas' classification.

A control immunophenotyping of peripheral blood lymphocytes was performed, as shown in Table 1.

Discussion

Brain abscesses are suppurative collections developed within the cranial parenchyma. It is a rare pathology with an estimated incidence of 0.3-1.3 per 100,000 people per year but can increase in certain risk groups like immunocompromised patients.[9] Their location is essentially supra-tentorial.

There are two known mechanisms by which a brain abscess can be formed: either by contiguous spread from an adjacent infection like nasopharyngeal and otologic infections, periodontal or dental disease, following a cranial trauma or iatrogenic following brain surgery; or by hematogenous spread because of heart diseases like right to left cardiac shunts or endocarditis. In 10 to 20% of cases, the mechanism is not known,[10] as is the case of our patient, although a dental entry point seems to be plausible. Therefore, the clinician must make a good history investigation in front of any cerebral abscess to find the etiology.

Microbiology of brain abscesses varies according to the mechanism. In the previously mentioned meta-analysis, the most frequent family of pathogen found was streptococci

Table 1. Initial and control Immunophenotyping of peripheral blood lymphocytes tests.

Immune profile markers	Initial Immunophenotyping of peripheral blood lymphocytes	Control Immunophenotyping of peripheral blood lymphocytes	Normal range
Lymphocyte count	↓ 310/mm^3	2130/mm^3	1000-4800/mm^3
T CD3 count	↓ 126/mm^3	1623/mm^3	900-1900/mm^3
T CD4 count	↓ 46/mm^3	1056/mm^3	500-1200/mm^3
T CD8 count	↓ 65/mm^3	462/mm^3	200-800/mm^3
CD4/CD8 ratio	↓ 0.70	2,29	> 1
NK CD16+ count	↓ 40/mm^3	170/mm^3	90-600/mm^3
NK CD56+ count	↓ 37/mm^3	85/mm^3	90-600/mm^3
B CD19+ count	↓ 84/mm^3	277/mm^3	100-500/mm^3
IgA count	2.45g/l	-	0.845-4.99 g/l
IgG count	7.77g/l	-	6.103-16.16 g/l
IgM count	1.16g/l	-	0.40-2.30 g/l
Complement C2	34.24mg/l	-	18.93-42.68 mg/l
Complement C3	0.78g/l	-	0.82-1.85 g/l
Complement C4	0.19g/l	-	0.15-0.53 g/l

(34%) followed by staphylococci (18%). In this patient's case, we isolated a *streptococcus salivarius*, a gram-positive coccus belonging to the viridans streptococci group. The bacteria of viridans group of streptococci are commensal organisms, usually known as nonpathogenic, and especially since some studies reported their important role in the oral and digestive tract ecology as they may impact the stability of microbiota composition[11]. Nevertheless, they were incriminated in some local and systemic infections such as endocarditis, peritonitis and even meningitis.[11]

At present, there are limited reported cases of cerebral abscesses due to *streptococcus salivarius*. To the best of our knowledge, we found only Three cases described in the literature, and all of them were infra-tentorial pontic localization, which makes our case, the first described *streptococcus salivarius*-associated brain abscess of supra-tentorial localization and the fourth of any cerebral localization combined. In only one case, it was due to infectious endocarditis; in the other cases, like our patient, no evident source of infection was identified.[12-14] The clinical outcome was favorable in the four cases.

Surprisingly, our patient, who barely reported any previous infectious episodes, was at the admission considered as immunocompromised. This conclusion was drawn based on the initial blood count which included a lymphopenia of 480 cells/mm^3. An immunological screening confirmed the lymphopenia and a severe decrease of approximately all lymphocyte subpopulations. However, the patient recovered from the immunocompromised state and reached a normal lymphocyte count.

Sepsis-induced immunodepression (also called sepsis-induced leukocyte "deactivation" or "immuno-paralysis") appears to be a consequence of a severe inflammatory state resulting of a serious infection.[15,16] Given the fact that *streptococcus salivarius* isn't notoriously known to be the cause of serious infections,[11] a plausible hypothesis is that a previous stress related to the anti-SARS-CoV-2 vaccine could explain the immunosuppression that led to the development of a *streptococcus salivarius* septicemia prior to its progression into a brain abscess.

Recent studies proved that leukocyte populations are quantitatively and functionally defective in patients with serious illnesses.[15,17-19] Trauma, post-operative course, burn injury and sepsis are notably known to be the major architects of leukocytes dysregulation. From a physio-pathological point of view, sepsis results in a shift in T cell cytokine response favoring a Th2- over a Th1-phenotype response. Decrease in production of IFN-γ, IL-2, IL-12 and TNF are usually observed. Contrariwise, there is an increase of IL-4 and IL-10 synthesis given the dysregulated Th2-phenotype shift.[15] According to the literature, the SARS-CoV-2 BNT162b2 vaccine could modulate both B and T cells. T cell response to SARS-CoV-2 spike protein, particularly the IFN-γ and IL-2 responses after the first dose of vaccine were similar to those found after a natural infection.[20]

Several research groups reported different factors regulating Th differentiation. One of them is very low and very high antigen doses which have been suggested to promote a Th2 response, while moderate antigen levels predispose naïve T cells to become Th1 cells.[21] This characteristic may explain the immunocompromised state of our patient, after the administration of the anti-SARS-CoV-2 vaccine, and leading to the development of a *streptococcus salivarius* brain abscess.

In light of the available evidence and research findings, it is imperative to emphasize that no definitive conclusion can be drawn regarding any potential link between anti-SARS-CoV-2 vaccines and the physiopathology of sepsis-induced immunodepression. While anti-SARS-CoV-2 vaccines have proven to be effective in eliciting immune responses against the SARS-CoV-2 virus, their direct involvement in the intricacies of sepsis-induced immunodepression remains uncertain. Rigorous scientific research is necessary to explore the underlying mechanisms of both anti-SARS-CoV-2 vaccines and sepsis-induced immunodepression.

Conclusion

Streptococcus salivarius, typically known as a nonpathogenic germ, can in some particular cases lead to a serious infection, rarely described in the literature.

In this case report, we document what we believe to be, up to date, the first intra-parenchymatous or supra-tentorial *streptococcus salivarius*-associated brain abscess, and the first reported brain abscess potentially associated with an anti-SARS-CoV-2 vaccine.

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Abbreviations

COVID-19: Corona Virus Disease 2019
UM6SS: Mohammed VI University of Health Sciences
SARS-CoV-2: Severe Acute Respiratory Syndrome Corona Virus 2
WHO: World Health Organization
GCS: Glasgow Coma Scale
MRC: Medical Research Council
CT: Computed Tomography
MRI: Magnetic Resonance Imaging
HIV: Human Immunodeficiency Virus
HBV: Hepatitis B Virus
HCV: Hepatitis C Virus
TPHA: Treponema Pallidum Hemagglutination Assay
VDRL: Veneral Disease Research Laboratory
NK: Natural Killer cell
CD: Cluster of Differentiation
ENT: Ear, Nose and Throat
Th1: T helper type 1 cell
Th2: T helper type 2 cell
IFN-γ: Interferon gamma
IL-2: Interleukin 2
IL-4: Interleukin 4
IL-10: Interleukin 10
IL-12: Interleukin 12
TNF: Tumor Necrosis Factor
MRSI: Magnetic Resonance Spectroscopic Imaging
LL: Lipid/Lactate
NAA: N-Acetyl Aspartate
Cr: Creatine
Cho: Choline

Statements and Declarations

Ethical approval

Not applicable

Consent to participate

Written and informed consent taken.

Consent for publication

Written and informed consent taken.

Author's contributions/CRediT

- Abderrahim Bourial, Wahib Lahlou and took part in taking care of the patient, researching the bibliography and writing the article.
- Fadila Guessous took part in the design, editing the article and approved the final manuscript.
- Mounir Rghioui, Sidi Mamoun Louraoui, Abdessamad El Azhari approved and participated in the process of validating the final manuscript.

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Availability of data and material

On request, email the corresponding author.

Code availability

Not applicable

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