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Eosinophilic lymph node abscesses following a COVID-19 vaccination: A case report

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All authors meet the ICMJE authorship criteria.

Abstract: In this paper, we reported a 37-year-old man who developed several lymphadenopathies after using the second dose of Pfizer-BioNtech vaccination against SARS-CoV-2. The excisional lymph node biopsy showed eosinophil-rich inflammation with micro-abscesses. Although eosinophilic dermatosis and eosinophilic myocarditis have been described previously following COVID-19 vaccinations, eosinophilic lymph node abscess was not reported in the literature. In our case, all lesions were completely recovered with steroid treatment. The patient has been doing well and no recurrence has been observed for six months.

Keywords: COVID-19 ■ Eosinophilic abscess ■ Vaccination

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<https://doi.org/10.1016/j.jnma.2023.01.003>

1. INTRODUCTION

COVID-19 is a viral infection causing serious morbidity and mortality. In order to prevent the disease, a wide range of vaccines have been developed and administered to people all over the world.^{1,2} Though most of them show a high level of efficacy and safety, many different side effects have been reported. These adverse events include fever, myalgia, pain at the injection site, hypercoagulability and acute myocarditis.¹ Lymphadenopathy following a COVID-19 vaccination is one of the common side effects, occurring in about 3–16% of patients.¹ Generally, it is observed ipsilateral to the intramuscular injection site and axillary and/or supraclavicular lymph nodes are commonly involved.^{3,4} Most lymphadenopathies are benign and resolved spontaneously within the following days to weeks.

2. CASE

A 37-year-old man was admitted to an outside clinic with a mass in the left axillary region. Two days later, another

swelling appeared in left epitrochlear area. The masses were developed following a Pfizer-BioNtech vaccination against SARS-CoV-2 and he noticed after ten days of the injection. On initial evaluation, both masses were appeared on the same side of the injection. Ultrasound revealed an epitrochlear lymphadenopathy and several axillary lymphadenopathies, the largest of which was 26 × 20mm. The lesions were attributed to a general side effects of the vaccination and no treatment was administered. On follow-up, as no improvement was observed, his physician prescribed a course of amoxicillin-clavulanate (daily/2 gram) for 2 weeks. Despite the administration of antibiotics, no reduction in lymph nodes size was observed. An excisional biopsy was performed from the axillary ones. On histopathologic evaluation, eosinophil-rich inflammation with micro-abscesses was observed (Fig. 1). Possible drug reaction was considered by the pathologist. Later, the patient was referred to our hospital for further investigations. On admission, he did not have concomitant fever, weight loss and night sweats and her complaints began after the second shot and continued for 2 months. She had no comorbidities except for allergic asthma. 2 years ago, the patient was diagnosed with allergic asthma but was not on any treatment. The patient had also no immunosuppressive disease and no history of trauma including cat scratch. On medical history, he received all childhood vaccinations and did not experience any serious side effects. On physical examination, the axillary mass slightly regressed following the operation but residual swelling was present with palpation. Epitrochlear lymph node was more enlarged, painful and fluctuating. Both ultrasound and magnetic resonance imaging of the epitrochlear mass showed suppurative lymphadenitis measuring 40 × 20 mm (Fig. 2). The laboratory values showed a total white blood cells count of 7400 cells/McL, with 1.8% eosinophils, sedimentation rate was 20 mm/hour and C-reactive protein was 15 mg/L (0-5). Total IgE, urinalysis, basic chemistry, and thoracic imaging were all normal. Serologies for syphilis, brucellosis, Hepatitis B Virus, Human Immunodeficiency Virus, Epstein-Barr Virus, Toxoplasmosis, Cytomegalovirus, Tularemia and Bartonellosis were unremarkable. Peripheral smear was normal and no hematologic disorder was considered by

Figure 1. A biopsy material showed inflammatory tissue consisting of eosinophilic infiltration and micro-abscesses.

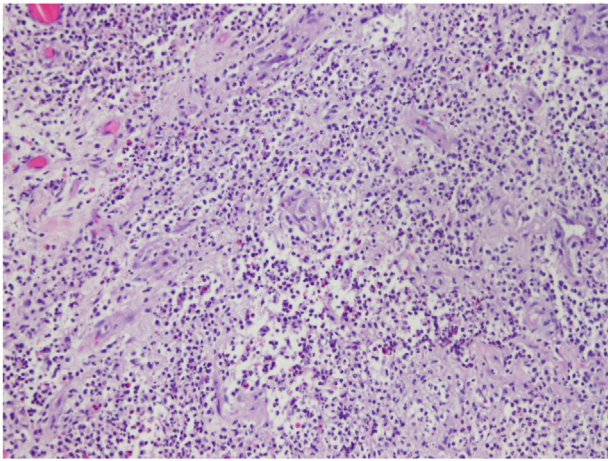


Figure 2. A contrast-enhanced elbow MRI showing subcutaneous edema and suppurative epitrochlear lymph node. (arrow)



a hematologist. The epitrochlear mass was drained completely under ultrasonography (Fig. 3). The gram staining of the material revealed abundant leukocytes but no microorganisms. The solid and liquid cultures of the material remained negative. The abscess aspirate was also negative for acid fast bacteria and tuberculosis culture and PCR. Cytological investigation revealed no atypical cell and the Giemsa staining of the material showed a plenty of eosinophils. As no specific etiology was reached, no antimicrobial treatment was initiated. Finally, the patient was considered as an immune mediated inflammatory disorder due to the COVID-19 vaccination. A total of 6 weeks of steroid treatment was planned. Steroid treatment (Methylprednisolone 48 mg /days) was initially administered for 3 weeks and stopped by tapering the dose within 3 weeks.

Figure 3. Macroscopic appearance of the material compatible with abscess including a plenty of polymorphonuclear eosinophils.



All lymphadenopathies were improved. The patient has been doing well and no recurrence has been observed for six months.

3. DISCUSSION

Lymphadenopathy is not a rare condition in clinical practice. There are many potential causes including infection, autoimmune disorders, malignancy, vaccinations and medications.⁵ Generally, the diagnosis is based on complete history and physical examination. However, biopsy is needed if the underlying etiology is uncertain and LAP persists. In most patients, it is benign and self-limited within days to weeks.

Vaccination-related reactive lymphadenopathy is considered a local adverse reaction to vaccination and is more commonly seen following receipt of the COVID-19 mRNA vaccines compared with other vaccines.^{6,7} Like many vaccines, mRNA vaccines depend on antigen presenting cells from regional lymph nodes to induce both a cellular and humoral immune response. When compared to protein-based vaccines, mRNA vaccines provide a more robust and rapid B-cell proliferation in the germinal center of the lymph node, thereby increasing the incidence of lymphadenopathy.⁸ Cohen et al. found a high correlation between the presence of hypermetabolic lymph nodes after COVID-19 vaccine and serologic antibody testing after vaccination and also describe that the characteristics of hypermetabolic lymphadenopathy following the first and second vaccine doses were reported to be different⁹.

In literature, although there are some eosinophilic disorders following COVID-19 vaccinations, eosinophilic lymph node abscess has not been reported to date. Cinotti et al. reported an eosinophilic dermatosis a 70-year-old man.¹⁰ Skin eruptions developed after the first dose of AstraZeneca vaccination. De Montjoye et al. presented eosinophilic cellulitis following the second dose of Pfizer/BioNTe mRNA COVID-19 vaccine.¹¹ Peripheral blood eosinophilia was observed in both cases. Ameratunga et al. reported a patient with fulminant necrotizing eosinophilic myocarditis.¹² It developed after the first dose of Pfizer/BioNTe mRNA COVID-19 vaccine. There was no eosinophilia and she died from myocarditis in hospital.

The mechanism of eosinophilic inflammation is not well understood. Some theories were postulated. Possible mechanism is that activation of T helper 2 induces IL 4 and IL 5, resulting in eosinophil-related disease.¹³

In conclusion, eosinophilic inflammation is one of the possible adverse reactions to an mRNA COVID-19 vaccine. Its mechanism is likely mediated by protein release and it responds to short-term steroid administration.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020;383:2603–2615.
2. Jackson LA, Anderson EJ, Rouphael NG, Roberts PC, Makhene M, Coler RN, et al. An mRNA vaccine against SARS-CoV-2 — preliminary report. *N Engl J Med*. 2020;383:1920–1931.
3. Granata V, Fusco R, Setola S, Galdiero R, Picone C, Izzo F, et al. Lymphadenopathy after BNT162b2 COVID-19 vaccine: preliminary ultrasound findings. *Biology*. 2021;10:214.
4. Tu W, Gierada DS, Joe BN. COVID-19 vaccination-related lymphadenopathy: what to be aware of. *Radiol Imaging Cancer*. 2021;3:e210038.
5. Ferrer R. Lymphadenopathy: differential diagnosis and evaluation. *Am Fam Physician*. 1998;58:1313–1320.
6. Cohen D, Krauthammer SH, Wolf I, Even-Sapir E. A sigh of relief: vaccine-associated hypermetabolic lymphadenopathy following the third COVID-19 vaccine dose is short in duration and uncommonly interferes with the interpretation of [(18)F]FDG PET-CT studies performed in oncologic patients. *Eur J Nucl Med Mol Imaging*. 2021;49:1338–1344.
7. Tan NJH, Tay KXJ, Wong SBJ, Nga ME. COVID-19 post-vaccination lymphadenopathy: report of cytological findings from fine needle aspiration biopsy. *Diagn Cytopathol*. 2021;49:E467–E470.
8. Lam DL, Flanagan MR. Axillary lymphadenopathy after COVID-19 vaccination in a woman with breast cancer. *JAMA*. 2022;327:175–176.
9. Cohen D, Krauthammer SH, Cohen YC, Perry C, Avivi I, Herishanu Y, et al. Correlation between BNT162b2 mRNA Covid-19 vaccine-associated hypermetabolic lymphadenopathy and humoral immunity in patients with hematologic malignancy. *Eur J Nucl Med Mol Imaging*. 2021;48:3540–3549.
10. Cinotti E, Perrot JL, Bruzziches F, Tognetti L, Batsikosta A, Sorrentino E, et al. Eosinophilic dermatosis after AstraZeneca COVID-19 vaccination. *J Eur Acad Dermatol Venereol*. 2022;36:e171–e172.
11. De Montjoye L, Marot L, Baeck M. Eosinophilic cellulitis after BNT162b2 mRNA Covid-19 vaccine. *J Eur Acad Dermatol Venereol*. 2022;36:e26–e28.
12. Ameratunga R, Woon ST, Sheppard MN, Garland J, Ondruschka B, Wong CX, et al. First identified case of fatal fulminant necrotizing eosinophilic myocarditis following the initial dose of the Pfizer-BioNTech mRNA COVID-19 vaccine (BNT162b2, Comirnaty): an extremely rare idiosyncratic hypersensitivity reaction. *J Clin Immunol*. 2022;42:441–447.
13. Lindsley AW, Schwartz JT, Rothenberg ME. Eosinophil responses during COVID-19 infections and coronavirus vaccination. *J Allergy Clin Immunol*. 2022;146:1–7.