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Rapid progression of angioimmunoblastic t cell lymphoma after Covid-19 vaccination (Chadox1-S): A case report

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Abstract

We present the case of a 57-year-old male patient from Ukraine who developed tonsillitis and generalized lymphadenopathy approximately one week after receiving the first dose of the ChAdOx1 (AstraZeneca) anti-SARS-CoV-2 vaccine. A total body computerized tomography scan revealed pronounced lymphadenopathy above and below the diaphragm, and enlargement of the spleen. Histologic examination of the left inguinal lymph node revealed revealed lack of a clear separation of the cortical and paracortical areas. Expanded proliferation of vessels (postcapillary venules) around which atypical lymphoid cells of small and medium size were located. The most of atypical lymphoid cells expressed CD3, CD4, PD1, blc-6, and Ki-67 antigens, some cells also CD10-, CD30-positive. Diagnosis of angioimmunoblastic T-cell lymphoma (AITL), IVB Ann Arbor stage, was established. The patient received six courses of therapy CHOEP regimen. According to the results of treatment clinical and hematological remission is achieved. Thus, this article describes the second case of the development of AITL after vaccination. The accumulation of such data and their analysis will allow to make appropriate conclusions about the relationship of anti-SARS-CoV-2 vaccination with development of oncohematological diseases.

Introduction

SARS-Cov-2 virus infection is widespread throughout the world. By May 2023, the number of infected cases raised to 765,903,278 persons and a total 13,350,530,518 vaccine doses have been administered [1]. Vaccination is an effective mean of preventing infection and the development of severe forms of the disease. Eleven vaccines were recommended by World Health Organization for vaccination: Pfizer-BioNTech, Oxford-AstraZeneca, Sinopharm BIBP, Moderna, Janssen, CoronaVac, Covaxin, Novavax, CovoVax (Novavax formulation), Convidecia, Sanofi-GSK; a number of vaccines are under consideration [2]. Oxford-AstraZeneca, CoronaVac, Pfizer-BioNTech, and Moderna were used for vaccination against SARS-CoV-2 in Ukraine [3].

Vaccination leads to the development of protective antiviral immunity [4, 5]. In oncological patients, this may have ambivalent influence on tumor growth. Two cases of spontaneous tumor regression after SARS-Cov-2 vaccination have been described: shrinking of the cervical lymph node and resolution of the diffuse lung lesions in patient with a recurrent primary cutaneous anaplastic large-cell lymphoma one week after having received the first COVID-19 vaccination (BioNTech/Pfizer) [6]; and spontaneous regression of metastatic salivary

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gland myoepithelial carcinoma in patient one month after vaccination of mRNA-1273 COVID-19 (Moderna) vaccine [7]. Anti-cancer effect of COVID-19 vaccines (a decrease in tumor size, a decrease in the expression of tumor markers (VEGF, Ki-67, MMP-2/9), CD4/CD8 ratio, and metastasis to the vital organs) has been shown in 4T1 mice models [8].

On the other hand, cases of progression of oncohematological diseases after vaccination have also been described. Goldman et al. described rapid progression of angioimmunoblastic T cell lymphoma following BNT162b2 mRNA vaccine booster shot [9]. Cavanna et al. presented a case of anaplastic large-cell lymphoma that developed in a patient approximately 10 days after receiving the third dose of the BNT162b2 vaccine and summarized eight additional cases identified in the available literature [10]. There were four cases of diffuse large-B-cell lymphoma [11-13], one case of extranodal NK/T-cell lymphoma [12], one patient with subcutaneous panniculitis-like T-cell lymphoma [14], one case of marginal zone B-cell lymphoma [15] and one primary cutaneous anaplastic large-cell lymphoma (developed at the SARS-CoV2 vaccine injection site) [16].

In this article, we report a case of angioimmunoblastic T-cell lymphoma developed shortly after SARS-CoV2 vaccination.

Case report

The patient is a 57-year-old Caucasian man with no previous history of disease. On May 6, 2021, he received the first dose of the ChAdOx1 (AstraZeneca). A few days later, he noted a flu-like syndrome and a sore throat. A diagnosis of tonsillitis was established. Antibacterial therapy was ineffective and within two weeks patient noted rapid increase of cervical, axillary, and inguinal lymph nodes. On May, 28, 2021, trephine biopsy of the left inguinal lymph node was performed.

Pathological examination revealed lack of a clear separation of the cortical and paracortical areas. Expanded proliferation of vessels (postcapillary venules) around which atypical lymphoid cells of small and medium size were located. Mitotic figures, single plasma cells, macrophages, neutrophils and eosinophils were present. The most of atypical lymphoid cells expressed CD3, CD4, PD1, blc-6, and Ki-67 antigens, some cells also CD10-, CD30-positive. Small clusters of CD20-positive cells were found between tumor cells. CD21- and CD23-positive follicular dendritic cells wrapped around postcapillary venules. Conclusion (8.06.2021): morphological changes in the lymph node and the immunophenotype of tumor cells correspond to diagnosis of angioimmunoblastic T cell lymphoma.

CT scan (29.05.2021) revealed pronounced lymphadenopathy above and below the diaphragm (diameters of cervical lymph nodes 10-24 mm, paratracheal lymph nodes 8-18 mm, bifurcation lymph nodes 14-25 mm, right axillary lymph nodes up to 20 mm, left axillary lymph nodes up to 15 mm, inguinal lymph nodes 8-28 mm), enlargement of the spleen (5.8x12.0x11.3 cm).

On June, 11, 2021 patient referred to the hematological department of National Research Center for Radiation Medicine. Complaints of the patient upon admission: fever (up to 380C) in the second half of the day, weakness, severe fatigue, enlargement of tonsils and lymph nodes. At examination: ECOG2 performance status. Weight 72 kg. Height 174 cm. Skin is pale. Peripheral lymph nodes are palpable: submaxillary up to 6 cm, cervical 4-6 cm, axillary up to 4 cm, inguinal up to 4 cm in diameter. The liver is not enlarged. The spleen is not palpable. Breathing is vesicular. Systolic murmur over the cardiac apex. The heart rhythm is correct. Blood pressure is 115/75 mm Hg, heart rate is 80 per min. There are no edema.

Bone marrow aspiration (11.06.2021) showed hypercellular marrow, dysplasia in erythropoiesis and megakariocytopoiesis, absence of blast cells, 5.6% of lymphocytes, no cytological signs of leukemic involvement. Among all nuclear bone marrow cells 1.68% with phenotype CD45dim+CD34+CD7+CD5+CD1a-TdT- were quantified by flow cytometry.

Except high level of blood lactate dehydrogenase (1249 units/L), and C-reactive protein (29.8 mg|L) other results of laboratory test of blood and urine were unremarkable.

Diagnosis of angioimmunoblastic T-cell lymphoma (AITL), IVB Ann Arbor stage, was established, and CHOEP (cyclophosphamide, vincristine, doxorubicin, etoposide and prednisone) regimen was initiated. The patient received six courses of therapy CHOEP regimen. According to the results of treatment clinical and hematological remission is achieved: hemodynamic parameters are stable, peripheral lymph nodes are not palpable, the spleen is not enlarged, and the size of the tonsils has decreased significantly. At the time of this report the patient continues to be in clinical and hematological remission.

Discussion

The most exciting, intriguing question is: can vaccines induce the development of tumors, in particular, lymphoproliferative diseases?

So far, only the development of fibrosarcomas in cats after vaccination is known. This has been proven for killed adjuvanted virus vaccines (vaccination against rabies and feline leukemia virus). An inflammatory process with the formation of granulomatous nodules, only 5% of which subsequently undergo transformation, preceded tumor

development. The interval between vaccine administration and detection of sarcoma varied from 4 months to several years [17]. In human, we found three similar cases in the literature: the development of lymphoma and undifferentiated, pleiomorphic high-grade sarcoma at the site of anti-SARS-CoV-2 vaccine administration [16, 18], and peripheral T-cell lymphoma at the injection site of influenza vaccination [19]. However, the interval between vaccine administration and tumor development was short, which does not fit into the classical scheme for the development of the oncological process (initiation, promotion, progression). Thus, it is unclear whether there is a true association between vaccination and the development of malignancy.

For the case described in this article, progression of preceding lymphoma under the influence of the vaccine seems more likely. Anti-SARS-CoV-2 vaccines cause a powerful immune response and stimulation of T- and B-lymphocytes, as well as the production of numerous cytokines [20]. Cases of post vaccine benign lymphadenopathy are described [21]. Today, AITL is recognized as a neoplasm derived from T-follicular helper cells [22, 23]. Up to 75% of AITL patients had a mutation RHOA G17V that facilitates proliferation and activation of several signaling pathways [24]. Since T-follicular helper cells are one of the main targets of mRNA vaccines [25], the Goldman et al. suggested that their stimulation under the influence of the vaccine can accelerate the development of AITL. In their case the malignant cells of patient had a mutation RHOA G17V that could make them especially sensitive to anti-SARS-CoV-2 vaccines [9]. Unfortunately, molecular genetic studies have not been performed in our patient.

Thus, this article describes the second case of the development of AITL after vaccination. The accumulation of such data and their analysis will allow to make appropriate conclusions about the relationship of anti-SARS-CoV-2 vaccination with development of oncohematological diseases. It will contribute to our better understanding of the possible negative consequences of anti-SARS-CoV-2 vaccination and their prevention as well.

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