Acta Medica Alanya

Case Report

Olgu Sunumu

Acta Medica Alanya 2023;7(2): 206-209
Doi: 10.30565/medalanya.1272707

A Diagnosis that Is Probably Missed: Rubeola Lymphadenitis, an Epidemic that Causes a Renewed Alarm

Muhtemelen Atlanılan Bir Tanı: Rubeola Lenfadeniti, Yeniden Alarm Veren Bir Salgın

Sinem Eser Polat Ünal[1], Sultan Aydın[2], Dinç Süren[1]

[1] Pathology Department, Health Science University Antalya Hospital, Antalya, Turkey

[2] Pediatric Hematology and Oncology Department, Health Science University Antalya Hospital, Antalya, Turkey

ABSTRACT

Because Rubeola (measles) infection is not observed in our country after eradication and is especially on the agenda again after migrations, pathologists may find it challenging to histopathologically recognize cases of Rubeola lymphadenitis and establish an accurate diagnosis. Here we describe the histopathological features of a rare Rubeola case. A 15-year-old Syrian migrant male patient was admitted with a complaint of lymph node swelling in the postauricular region for 2 months. Lymph node excision was performed with a preliminary diagnosis of lymphoma. The excised lymph node was subjected to a routine pathological examination in our clinic. Histopathological examination revealed that the basic structure was preserved under the thick fibrous capsule in the lymph node. Warthin-Finkeldey-type giant cells attracted attention in the interfollicular areas. The appearance compatible with lymphoproliferative neoplasia was not detected. The relevant clinic was informed that there were histological signs of Rubeola lymphadenitis upon detection of Rubeola IgM positivity in the examination, the case was evaluated as Rubeola infection. Rubeola was a common deadly infectious disease in the past century before the vaccine was developed. Today, there has been an epidemic again due to vaccine hesitancy, migration, and sociocultural conditions. Because it is exceptionally rare, we hope that the case we present will provide insights to pathologists for recognizing cases of Rubeola lymphadenitis and making precise diagnoses.

Key Words: Warthin-Finkeldey Cells, Measles, Rubeola, Hematopathology

ÖZET

Rubeola (Kızamık) enfeksiyonu, eradikasyon sonrası ülkemizde görülmediğinden ve özellikle göçler sonrası tekrar gündeme gelmesinden dolayı Rubeola lenfadenit vakalarını histopatolojik olarak tanımak ve doğru tanı koyabilmek patologlar için zorlayıcı olabiliyor. Burada nadir rastladığımız bir Rubeola vakasının histopatolojik özelliklerini tanıtmayı amaçladık. İki aydır postauriküler bölgede lenf nodlarında şişlik şikayeti olan 15 yaşındaki Suriyeli göçmen erkek hastanın lenfoma ön tanısı ile lenf nodu ekzisyonu yapıldı. Ekzisyon yapılan lenf nodu, kliniğimizde rutin patolojik sürece tabi tutuldu. Histopatolojik incelemede lenf nodunda kalın fibröz kapsül altında temel yapının korunmuş olduğu görüldü; ancak interfoliküler alanlarda Warthin-Finkeldey-tip dev hücreler dikkati çekti. Lenfoproliferatif neoplazi ile uyumlu görünüm saptanmadı. Olguda histopatolojik olarak Rubeola lenfadeniti bulgularının olduğu hastayı takip eden kliniğe bildirildi. Yapılan incelemede Rubeola IgM pozitif olarak saptanması üzerine olgu, Rubeola enfeksiyonu olarak değerlendirildi. Rubeola, geçmiş yüzyılda aşı geliştirilmeden önce yaygın bir ölümcül enfeksiyöz hastalıktı. Günümüzde aşılama karşıtı tutumdan, göçlerden ve sosyokültürel şartlardan dolayı tekrar epidemi söz konusu oldu. Oldukça nadir görüldüğünden Rubeola lenfadenit vakalarını tanımak ve doğru tanı koyabilmek adına sunduğumuz vakanın patologlara ışık tutmasını umuyoruz.

Anahtar Kelimeler: Warthin-Finkeldey Hücreleri, Kızamık, Rubeola, Hematopatoloji

Recieved Date: 28.03.2023 / **Accepted Date:** 25.08.2023 / **Published (Online) Date:** 29.10.2023

Corresponding author: Sinem Eser POLAT ÜNAL, Health Science University Antalya Hospital, Varlik, 07100, Antalya, Türkiye

Phone: 05374630088 / **mail:** sinemeserpolat@gmail.com

ORCID: 0000-0001-5566-5067

To cited: Polat Unal SE, Aydın S, Suren D. A Diagnosis That Is Probably Missed: Rubeola Lymphadenitis, An Epidemic That Causes Renewed Alarm Acta Med. Alanya 2023;7(2): 206-209 doi: 10.30565/medalanya.1272707

Acta Medica Alanya 2023;7(2): 206-209
Doi: 10.30565/medalanya.1272707

Introduction

Rubeola (measles) was a common infectious disease worldwide before vaccination, which began in 1963. Before the introduction of vaccination, approximately 3 to 4 million people were infected annually in the United States [1-3]. In Turkey, the Extended Immunization Program, which consists of rules that must be followed for managing vaccination services, was implemented in 1981. Rubeola vaccination programs were initiated in our country in 2003 and 2005. Between 2007 and 2011, the number of infected cases remained below five, whereas no cases were followed up from 2008 to 2010. However, after migrants arrived in Turkey because of the civil war in Syria in 2011 and the increase in the percentage of unvaccinated individuals, an epidemic broke out in Turkey in 2013 [4,5].

Anti-vaccination campaigns have also had a great impact on the outbreaks of eliminated diseases such as Rubeola. Vaccination rates have decreased worldwide, particularly because of the attitude adopted by parents who have been misinformed through platforms such as the Internet, social media, and television [6]. For example, the Measles, Mumps, and Rubella (MMR) vaccination rate in the United Kingdom fell from 92% in 1996 to 84% in 2002, and by 2003, in some parts of the country, this rate fell to 61% [7].

Most pathologists have little experience with Rubeola's histopathology because it is still relatively rare in our country We here aim to present the clinicopathologic features of Rubeola lymphadenitis, which is an unusual diagnosis for pathologists, and hope that these findings will shed some more light on the recognition of Rubeola infection.

Case Presentation

A 15-year-old Syrian migrant male patient with no previous medical history, was admitted to our hospital with a complaint of regional swelling in the postauricular region. Swelling had been present for 2 months. He had no complaints such as B symptoms. The patient's family history and medical and surgical history were unremarkable. No information about the patient's vaccination history was available. Physical examination revealed enlarged lymph nodes in the postauricular region. Routine laboratory tests revealed leukopenia and lymphopenia. Viral load was not detected by real-time Epstein– Barr virus (EBV) PCR or cytomegalovirus (CMV) PCR. Enzyme-linked immunosorbent assay (ELISA) was used to detect IgM and IgG antibodies in serum, including Herpes simplex type 1/2, Brucella, Varicella Zoster Virus, Mumps, Anti-HBc, Toxoplasma, and HBsAg. The ELISA test was negative for all. In the evaluation of peripheral blood smears, a normochromatic normocytic erythroid series was observed; however, atypia did not attract attention. One of the largest lymph nodes was excised and sent to our pathology department.

Histological sections revealed samples of lymph nodes containing a thick fibrous capsule. Hyalinized bands were present between secondary follicles with large and small germinal centers. Apoptotic activity was evident in lymphoid follicles. There were no signs of malignancy in the lymphocytes. In the interfollicular areas, multinucleated giant cells (Warthin-Finkeldey cells) were observed [Figure-1].

Histologically and immunohistochemically, there were no findings consistent with lymphoproliferative neoplasia.

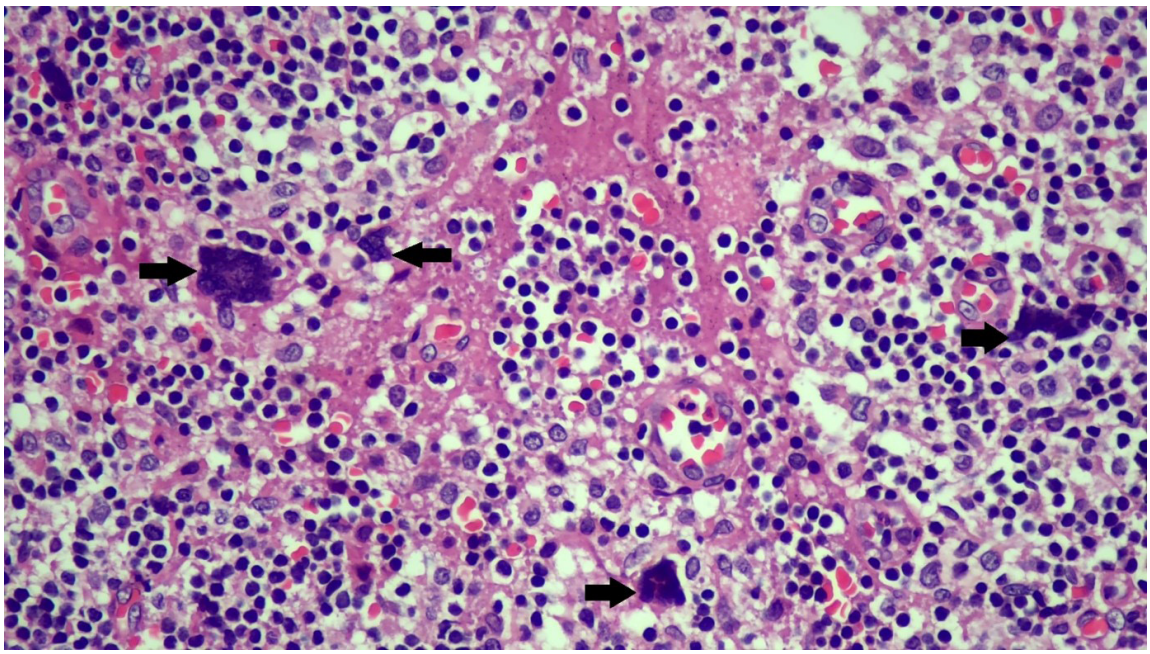

Figure 1. Warthin-Finkeldey cells (black arrows) with nonneoplastic lymphoid tissue on the background (Hematoxylin & Eosin x400)

Immunohistochemical staining for other diseases considered in the differential diagnosis (e.g., EBV infection, HIV lymphadenopathy, Hodgkin lymphoma, other B and T cell lymphomas) (CD3, CD20, PAX5, CD15, CD30, EBV) did not show significant results. The Ki67 proliferation index was within normal limits [Figure-2].

When clinical and histological findings were evaluated together, it was reported to the relevant clinic that there may be Rubeola lymphadenitis in the case, and the clinic was requested to conduct tests for Rubeola. The ELISA test was positive for Rubeola IgM, and the case was considered as "Rubeola lymphadenitis". Subsequently, the patient was isolated, and because there was no specific treatment, the patient was given supportive treatment such as antipyretics, vitamin A, and fluids. No complications have developed.

Discussion

Warthin-Finkeldey-type giant cells were first described by Dr. A. Warthin and Dr. W. Finkeldey in 1931. They named these cells in the lymphoid tissues of children with Rubeola. Warthin-Finkeldey cells (WFCs) have numerous closely packed overlapping nuclei with or without eosinophilic nuclear inclusions [8,9]. At first, WFCs were thought to be pathognomonic for Rubeola. However, these cells have been identified in many other conditions such as Kimura disease, HIV lymphadenopathy, Hodgkin lymphoma, B- and T-cell lymphomas, and nonneoplastic lymph node disorders. It is still unclear whether the cause of the formation of WFCs is intercellular fusion caused by the Rubeola virus, and whether the origin of the cells is lymphoid or dendritic cells. WFCs can be seen in malignant diseases such as various lymphomas, as well as in benign conditions such as HIV lymphadenopathy and Kimura's disease [10]. For example, in the Figure-3 cited in a study by Aladily et al., WFCs attracted attention in this case with signs of follicular lymphoma. Malignant lymphocytes on the ground were also observed in this case [11]. However, in this case, the presence of ordinary lymphocytes (morphologically recognized and immunohistochemically proven) ruled out malignant conditions.

According to Fenner's model, Rubeola is considered to develop in four stages: primary invasion, proliferation of lymphoid tissue, secondary viremia, and florid disease. Rubeola infection begins when the virus attacks the respiratory system, and then undergoes replication. Primary viremia causes the virus to spread in lymphoid tissues throughout the body. Replication of the virus in lymphoid tissue causes hyperplasia in the lymphoid tissue, and WFC

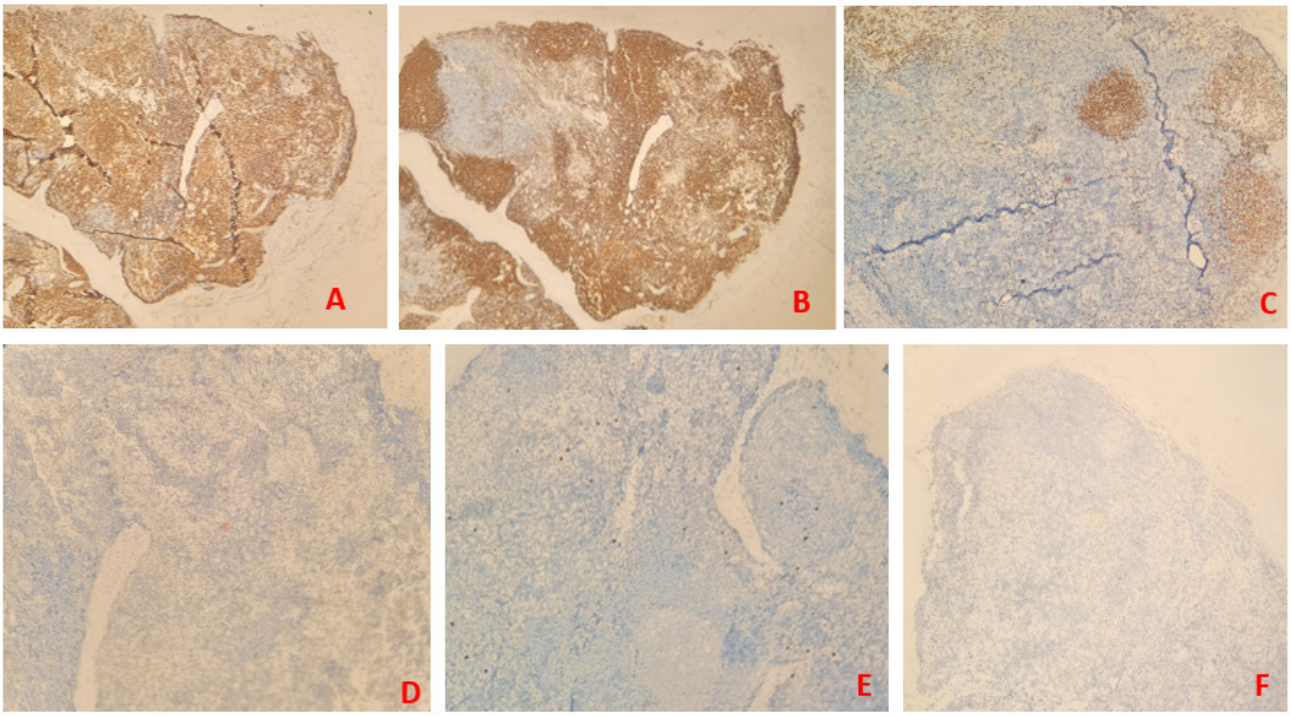

Figure 2. Immunohistochemical expression of CD3, CD20, PAX5, EBV, CD30, and CD15, respectively (A, B, C, D, E, F). A: CD3 staining was observed in nonneoplastic T lymphocytes (magnification, x100). B: CD20 staining was observed in nonneoplastic B lymphocytes (magnification, x100). C: PAX5 staining was observed in nonneoplastic B lymphocytes (magnification, x100). D, E, F: EBV, CD30, and CD15, respectively; no significant staining was observed with EBV, CD30, and CD15 (magnification, x100) (there were artificial deposits).

Acta Medica Alanya 2023;7(2): 206-209
Doi: 10.30565/medalanya.1272707

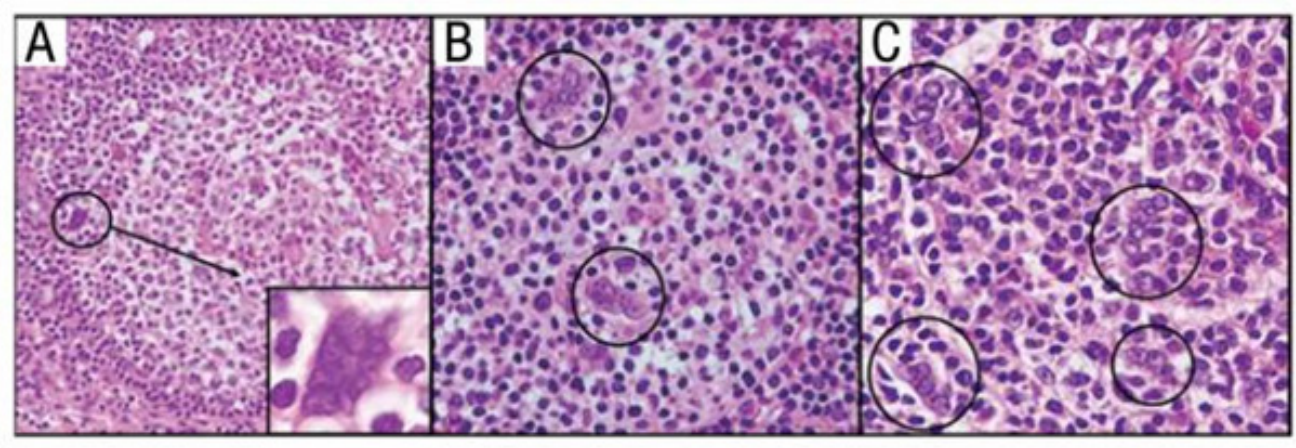

Figure 3. A: Warthin-Finkeldey cells, located on the periphery and central of the follicles (Hematoxylin & Eosin staining, magnification x200; inset at x1000). B & C: neoplastic follicles composed of small, cleaved cells of follicular lymphoma, (magnification x600) [11].

formation is induced. Immediately after this, the second stage of viremia begins. At this stage, the virus is spread to other organs by infected lymphocytes and monocytes [12]. In the prodromal and early stages of Rubeola, WFCs are often observed in germinal centers or interfollicular areas in lymph nodes [13].

Nowadays, the incidence of Rubeola is increasing, and the recognition of WFCs in routine samples by pathologists can alert clinicians to suspect Rubeola, thereby perhaps offering the potential for earlier detection. Thus, the spread of the disease can be prevented, and this re-emerging disease can be prevented from becoming an epidemic.

Conflict of Interest: No conflict of interest was declared by the author.

Funding sources: The author declares that this study received no financial support.

Ethics Committee Approval: Informed consent was obtained from the patient's parents.

ORCID and author contributions: ***S.E.P.U. (0000-0001-5566-5067):*** Literature search, writing, critical review. ***D.S.(0000-0002-1816-7816):*** Concept and design, literature search, writing, critical review. S***.A.(0000-0002-8801-7776):***Interpretation and supervision.

Peer-review: External peer review.

References

1. Centers for Disease Control and Prevention. Measles history. https://www.cdc.gov/measles/about/history.html. Accessed June 25, 2022.
2. Solomon IH, Milner DA Jr. Histopathology of vaccine-preventable diseases. Histopathology. 2017;70(1):109-22. doi: 10.1111/his.13057.
3. Centers for Disease Control and Prevention. Measles cases and outbreaks. https://www.cdc.gov/measles/cases-outbreaks.html. Accessed June 25, 2022.
4. Gulcu S, Aslan S. Vaccine application on children: a current review. Journal of Duzce University Health Sciences Institute 2018;8(1):34-43.
5. Simsek OF. An overview of the extended immunization program. Osmangazi Tip Dergisi (Sosyal Pediatri Özel Sayısı) 2020:6-14. doi: 10.20515/otd.681563
6. Hussain A, Ali S, Ahmed M, et al. (July 03, 2018) The Anti-vaccination Movement: A Regression in Modern Medicine . Cureus. 2018;10(7):e2919. doi: 10.7759/cureus.2919.
7. Murch S: Separating inflammation from speculation in autism. Lancet. 2003;362(9394):1498-9. doi: 10.1016/S0140-6736(03)14699-5.
8. Warthin AS. Occurrence of numerous large giant cells in the tonsils and pharyngeal mucosa in the prodromal stage of measles. *Arch Pathol.* 1931;11:864–74. doi: 10.7326/0003-4819-5-1-74_1
9. Finkeldey W. Ueber Riesenzellbefunde in den Guamenmandeln, zugleich ein Beitrag zur Histopathologie der Mandelveranderungen im Maserninkubationsstadium. *Vichows Arch Pathol Anat.* 1931;281:323–9.
10. Lapadat R, Nam MW, Mehrotra S, et al. Mulberry cells in the thyroid: Warthin-Finkeldey-like cells in Hashimoto thyroiditis-associated lymphoma. Diagn Cytopathol. 2017;45(3):212–6. doi: 10.1002/dc.23652.
11. Aladily T, Bustami N. Follicular Lymphoma Rich in Warthin-Finkeldey Cells. Sultan Qaboos Univ Med J. 2021;21(4):668-9. doi: 10.18295/squmj.4.2021.051.
12. Fraser KB, Martin SJ. Measles virus and its biology, The pathogenesis of measles. Academic Press, London, 1978:pp 6-11
13. Nozawa Y, Ono N, Abe M, et al. An immunohistochemical study of Warthin-Finkeldey cells in measles. Pathol Int. 1994;44(6):442-7. doi: 10.1111/j.1440-1827.1994.tb01708.x.