

Anaplastic Large Cell Lymphoma Mimicking a Necrotizing Granulomatous Lesion: A Case Report

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Case Report

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Abstract

Introduction: Epithelioid cell granulomas into neoplastic tissues have been reported in association with a wide series of neoplasms, including lymphomas. Epithelioid granulomas in association with non-Hodgkin's lymphomas are only rarely observed. When granulomas are present in association with lymphomas, they are usually non necrotizing, sarcoid-like. Little is known about the association of granulomatous reaction with anaplastic large cell lymphoma (ALCL) and to the best of our knowledge anaplastic large-cell lymphoma with histological features of necrotizing granulomatous lesion has not been reported previously in the literature. In this article we report a case of anaplastic large-cell lymphoma mimicking a necrotizing granulomatous lymphadenitis.

Case Presentation Section: A 55-year-old Caucasian man presented with a 3-month history of a painless, enlarged, lymph node localized on the left inguinal region. Escissional biopsy was performed. The microscopic examination led to the diagnosis of granulomatous lymphadenitis with necrosis.

Two months later the patient returned because he had note the appearance of a nodule in the right axillary region. Following the escissional biopsy, the histological examination and the immunohistochemical stains have been made the diagnosis of ALCL, ALK1 negative. The first case was reevaluated. Extensive immunophenotypic characterization (positivity for CD45RO/UCHL1 and CD-30 in the areas of necrosis), in conjunction with histomorphologic and molecular analysis (presence of a T monoclonal cell lymphoid), established diagnosis of ALCL ALK-1 negative.

Conclusions: The presence of exaggerated granulomatous reaction in tissue involved by lymphomas may mask neoplastic lymphoid cells and result in erroneous histopathologic diagnosis.

In this article we report a case of primary nodal ALCL mimicking a necrotizing granulomatous lymphadenitis.

Keywords: Anaplastic large cell lymphoma; Epithelioid cell granulomas; Misdiagnosis; Immunohistochemical; Hepatosplenomegaly

Abbreviations: ALCL: Anaplastic Large Cell Lymphoma

Introduction

Epithelioid cell granulomas into neoplastic tissues have been reported in association with a wide series of neoplasms, including lymphomas. Between lymphomas, Hodgkin's lymphoma and T-cell derived non Hodgkin lymphoma are more seen commonly [1]. The presence of non-necrotic epithelioid cell granulomas is well known findings in lymph nodes, spleen, bone marrow, and liver from patients with Hodgkin's disease [2-4]. Epithelioid granulomas in association with non-Hodgkin's lymphomas are only rarely observed [5,6].

When granulomas are present in association with lymphomas, they are usually non necrotizing, sarcoid-like [7-9]. Nevertheless, rarely necrotizing granulomas occurs.

Hall et al. reported two cases of high-grade malignant lymphoma characterized by extensive necrosis in association with granulomatous reaction mimicking tuberculosis [10,11].

Chow et al. reported three cases of lymphomas masquerading as granulomatous panniculitis from inflammatory or reactive disorders associated [12].

In these cases an infectious cause is not found and their development has been attributed to an immune or inflammatory reaction to tumour-associated antigens, probably [13-15].

Little is known about the association of granulomatous reaction with anaplastic large cell lymphoma and to the best of our knowledge anaplastic large-cell lymphoma with histological features of necrotizing granulomatous lesion has not been reported previously in the literature. In this article we report a case of anaplastic large-cell lymphoma mimicking a necrotizing granulomatous lymphadenitis.

Case Presentation Section

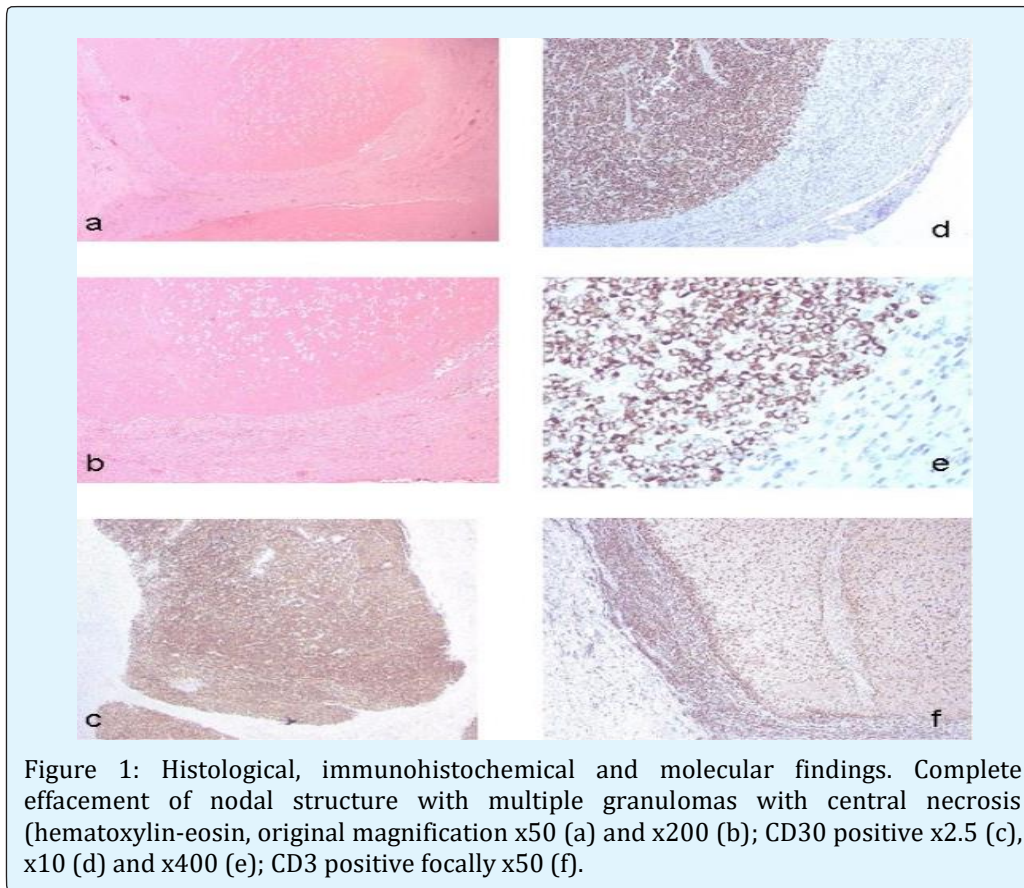
Case Report: a 55-year-old Caucasian man in otherwise good health, presented with a 3-month history of a

painless, enlarged, lymph node localized on the left inguinal region. The man had no fever, weight loss or night sweats. Physical examination revealed no other lymph node involvement. There was no hepatosplenomegaly. The chest x-ray was unremarkable. Blood-cell count, serum biochemistry and immunoglobulins, Mantoux test and Epstein-Barr virus antibody titer were either within normal limits or negative. Escissional biopsy was performed. The lymph node was 2 cm in diameter and on cut surface it showed multiple, round formations, yellow in colour.

At microscopic examination there was complete effacement of nodal structure with multiple granulomas with central necrosis (Figure 1a & 1b). Ziehl-Neelsen stain for acid fast bacilli was negative as well as the fungal stains (periodic acid-Schiff and Grocottmethenamine silver). A diagnosis of granulomatouslymphadenitis with necrosis was performed.

Two months later the patient returned because he had note the appearance of a nodule in the right axillary region, which was rapidly increasing in size. Escissional biopsy was performed. At histological examination the normal lymph node architecture was totally effaced by a diffused growth consisting of large, highly pleomorphic lymphoid cells. Immunohistochemical stains demonstrated that the neoplastic cells were positive for CD45RB/LCA (clone 2B11+PD7/26, Roche-Ventana), CD45RO (clone UCHL1, Roche-Ventana), CD30 (clone Ber-H2, Roche-Ventana), focally CD-3 (clone 2GV6, Roche-Ventana), while were negative for CD20 (clone L26, Roche-Ventana) and ALK-1 protein (clone ALK01, Roche-Ventana). Approximately 80% of the neoplastic cells reacted positively when stained with an antibody to Ki-67 (clone 30-9, Roche-Ventana). T cell receptor rearrangement was found. A diagnosis of anaplastic large-cell lymphoma ALK1 negative was performed.

The first case was reevaluated and immunohistochemical and molecular studies were performed. Immunohistochemical analysis demonstrated positivity for CD45RO, CD-30 in the areas of necrosis (Figure 1c & 1d) and CD3 focally (Figure 1e & 1f). To confirm the neoplastic feature of this cell population, the presence of rearrangement of TCR gene was investigated.



T cell clonality molecular study showed a monoclonal configuration of the TCRG and TCRB genes (Figure 2).

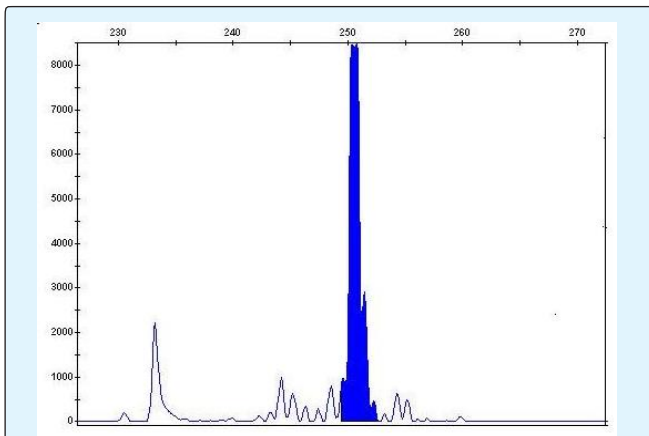


Figure 2: Clonality assessment. GeneScan results of the gene rearrangement profile in the sample patient, showing the peak clonal TCRG rearrangement with multiple primer sets in a polyclonal background. Gene rearrangement of TCRB and polyclonal tonsil biopsy FFPE control are not shown.

The T-cell clonality assay employs primers for both TCRB and TCRG, a combination that has been shown to detect clonality in essentially 100% of T-cell prolymphocytic leukemias, T-cell large granular lymphocyte disorders, and peripheral T-cell lymphomas, unspecified, with somewhat lower rates reported in angioimmunoblastic T-cell lymphomas and anaplastic large cell lymphoma [16,17].

Commercial reagents by ROCHE VENTANA, Italy were used to perform immuno-histochemical assay and by EXPERTEAM (Marghera Venezia, Italy) and INVIVOSCRIBE TECHNOLOGIES (San Diego, California USA) were used to perform beta-globin and clonality T assay, respectively. All used products are compliant to the requirements of the in vitro diagnostic directive (IVDD) 98/79/EC.

Discussion

The majority of cancer diagnoses are made on the basis of either histologic or cytologic evaluation. Generally, the error frequency and effect are poorly characterized

because there is no uniform measurement process, but, in this case, the current guide lines and the appropriated procedures have been respected.

Here, we report a case of primary nodal anaplastic large-cell lymphoma mimicking a necrotizing granulomatous lymphadenitis. Rarely, the diagnosis of a lymphoma may be masked by the presence of extensive granulomatous lesions. Lymphomas associated with marked granulomatous reaction are well documented in the literature [8].

Malignant lymphomas and solid tumours that mimic or are associated with epithelioid granulomas are a dilemma in histological materials. Granulomatous lymphadenitis may be determined by several infective agents or determined by different pathological processes, sarcoidosis and tuberculosis being the most frequent. Granulomatous lymphadenitis may also occur along haematological diseases or after chemotherapy or radiotherapy. Granulomatous reaction after chemotherapy for Hodgkin's disease has been described in the literature [14]. A prognostic relevance of the granulomatous reaction in ALCL lymphoma is not clear. Little is known about the association of granulomatous reaction with anaplastic large cell lymphoma (ALCL) [18].

The differential diagnosis of necrotizing granulomas includes chronic infections such as typical and atypical mycobacterium, fungi (e.g., histoplasmosis, aspergillosis, cryptococcosis), and Wegener's granulomatosis, as well as foreign body type granulomatous inflammations [18].

In our case an infectious cause is not found and granuloma development could be attribute to an immune or inflammatory reaction to tumor-associated antigens [1,13].

This case emphasizes the importance of a very careful microscopic evaluation of the lymph nodes with non-necrotizing granuloma searching for any large atypical cells that may represent hidden malignant cells that can be easily overlooked.

In addition, the massive necrosis found here, could call in question the veracity of the immunohistochemical and molecular assays.

Many authors reported cases of lymphomas with complete lymph node necrosis in which immunophenotypic and immunogenotypic studies were

performed successfully [19,20].

After the diagnosis, the patient underwent to oncology visit in a different hospital, so it was not possible to know the stage of lymphoma or the appropriated therapeutic treatment. Although, it should be very interesting, here we want principally to focus attention on the histological diagnosis.

We describe a case of an unusual ALCL lymphoma that was associated with exuberant granulomatous reaction and has been misdiagnosed as necrotizing granulomatous lymphadenitis.

Conclusion

The purpose of this article is to provide a strong suggestion for pathologists. In fact, the aim of this case report is to emphasize the importance of an extensive immunophenotypic characterization, in conjunction with histomorphologic and molecular analysis in all instances of the lymph nodes with granulomatous reaction. This case highlights the importance of a careful assessment of any necrosis in lymph node, using a multimodality diagnostic approach to distinguish lymphomas masquerading as granulomatous lesion from inflammatory or reactive disorders associated with such histopathologic patterns, specially, when the diagnosis should be wrong and the treatment cannot be delayed and/or imprecise.

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