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CASE IMAGE

ALK+ ALCL in the setting of adalimumab-related hidradenitis suppurativa

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Abstract

This ALK-positive anaplastic large cell lymphoma (ALCL) case highlights the importance of considering ALCL in the setting of iatrogenic immunosuppression in hidradenitis suppurativa patients. Diagnosis of ALCL can be challenging in situations with very low viability/cellularity, negative CD3 and/or other T-cell markers, and immunosuppression.

KEYWORDS

adalimumab, ALCL, ALK, iatrogenic immunodeficiency-associated, *KRAS*

Anaplastic large cell lymphoma (ALCL) is an aggressive T-cell lymphoma, a subset of which is associated with genomic alterations in *ALK*, termed ALK-positive ALCL. We here describe an unusual presentation of EBV-negative, ALK-positive, *KRAS*-mutant ALCL occurring during tumor necrosis factor (TNF)-inhibitor therapy for hidradenitis suppurativa in a young patient.

An 18-year-old girl presented with worsening back pain and was found to have a 4.7-cm destructive T12 vertebral and paraspinal lesion concerning for an infectious process (Figure 1A). She was previously diagnosed with hidradenitis suppurativa (HS, Figure 1B) and treated with adalimumab for 4 months.

Resection revealed an extensively necrotic (>95% necrosis) malignant neoplasm, with rare viable foci of large dyscohesive lymphoid cells, including "hallmark cells" with kidney-shaped nuclei (Figure 1C). Initial workup was negative for CD3 (Figure 1D), CD20 (not shown), and EBER (not shown). Neoplastic cells were positive for CD30 (Figure 1E), ALK (Figure 1F), CD4 (Figure 1G), CD45 (Figure 1H), CD2 (subset; Figure 1I), and EMA (not shown). Break-apart FISH detected *ALK* gene rearrangement and next-generation sequencing revealed *NPM1*::*ALK* fusion and *KRAS* p.Q61H hotspot mutation (30% allele frequency). She received six cycles of brentuximab vedotin in combination with chemotherapy[1] and did well.

This case is a rare example of EBV-negative, ALK-positive, *KRAS*-mutant anaplastic large cell lymphoma (ALCL) rapidly emerging during TNF-inhibitor therapy. ALCL is an aggressive subtype of T-cell lymphoma that is commonly associated with genomic alterations in *ALK* on chromosome 2. ALK-positive ALCL represents approximately 3% of adult non-Hodgkin lymphomas and is more commonly seen in younger patients compared to the slightly rarer ALK-negative variant (5.5% of mature T-cell lymphomas vs. 6.6% for ALK-positive ALCL).[2] ALCL is rarely associated with iatrogenic immunodeficiency.[3] The *KRAS* hotspot mutation is an uncommon feature of ALCL.[4] Interestingly, HS is also associated with a higher risk for lymphoma.[5] Other challenges in this case include extensive necrosis and lack of expression of CD3, which particularly confounded initial frozen sections and cytological evaluation. Additionally, immunosuppressive

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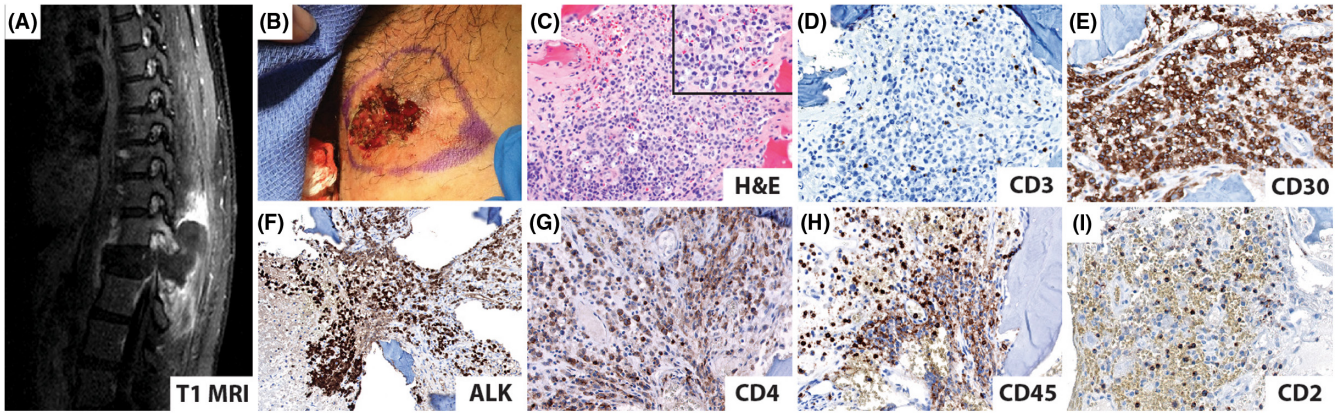

FIGURE 1 (A) MRI (T1-weighted with contrast, sagittal view) reveals a 4.7-cm destructive T12 vertebral and paraspinal lesion with involvement of vertebral bodies. (B) A representative photograph of one of patient's hidradenitis suppurativa lesions from the left thigh, taken 1 year before her presentation with back pain. (C) The lymphoma cells within rare viable foci (H&E, 200×) include classic "hallmark cells" with kidney-shaped nuclei which are better seen on high power (insert, 600×). (D) Lymphoma cells are negative for CD3 (400×). (E) Lymphoma cells are positive for CD30 (400×). (F) Lymphoma cells are positive (both nuclear and cytoplasmic) for ALK (400×). (G) Lymphoma cells are positive for CD4 (400×). (H) Lymphoma cells are positive for CD45 (400×). (I) A small subset of lymphoma cells are positive for CD2 (400×).

agents such as adalimumab exert anti-proliferative effects on lymphocytes, making diagnosis difficult. The initial clinical and radiographic impression was most suspicious for infection, and histopathologic examination was crucial to establishing the correct diagnosis of this rare neoplasm.

AUTHOR CONTRIBUTIONS

Alexander Craig: Conceptualization; writing – original draft; writing – review and editing. **Kwun Wah Wen:** Conceptualization; writing – original draft; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

We declare no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by the Institutional Review Board for human subjects research at UCSF Medical Center (IRB # 18-25787).

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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