Management of Anaplastic Large Cell Lymphoma

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KEYWORDS

• Anaplastic large-cell lymphoma • Treatment • Brentuximab vedotin
• Stem cell transplant

KEY POINTS

- Anaplastic large cell lymphoma (ALCL) is the second most common peripheral T-cell lymphoma, and the incidence is higher in blacks than non-Hispanic whites.
- ALK (anaplastic lymphoma kinase)-positive and ALK-negative ALCL are distinct subtypes that have different characteristics and clinical outcomes; ALK-positive ALCL is more common in younger patients and has a better overall survival.
- Breast implant–associated ALCL is a rare lymphoma that has very good survival outcome, and recent study indicates that total capsulectomy is essential for treatment of this disease.
- Brentuximab vedotin (BV) is a standard therapy for relapsed or refractory ALCL.
- Overall response rate is about 80% to 90%; however, once a patient's disease progresses on BV, survival outcome is very poor with median overall survival of less than 2 months.

INTRODUCTION

Anaplastic large cell lymphoma (ALCL) is a distinct subtype of peripheral T-cell lymphoma (PTCL). ALCL accounts for 3% to 5% of all non-Hodgkin lymphoma and 10% to 20% of childhood lymphomas and consists of about 10% to 15% of PTCLs.[1] The age-adjusted incidence in the United States. for ALCL is 0.2 to 0.25 per 100,000 person-years.[2,3] Recently, a large study using population-based registry data suggested racial differences in the incidence of ALCL.[4] Asian/Pacific Islanders have significantly lower incidence compared with non-Hispanic whites (incidence rate ratio: 0.59, 95% confidence interval [CI]: 0.49–0.70), while blacks have significantly higher incidence of ALCL compared with non-Hispanic whites (incidence rate ratio: 1.17, 95% CI: 1.03–1.32). In the most recent World Health Organization classification,

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3 types of noncutaneous ALCL are recognized.[5] One type associated with translocations involving the ALK gene leading to ALK overexpression (ALK + ALCL) is well established. The other category is morphologically and phenotypically similar to ALK + ALCL but lacks ALK abnormalities of overexpression, and ALK-negative ALCL (ALK − ALCL), which was previously considered a provisional category, is now defined as definite entity based on gene expression profile (GEP) studies that showed that ALK − ALCL has similar features to that of ALK + ALCL and is distinct from other CD30-positive PTCLs.[6,7] Breast implant–associated ALCL (BIA-ALCL) was first described in 1997 and is now recognized as a distinct new entity, which usually is associated with excellent outcomes.[8] Finally, primary cutaneous ALCL is a distinct subtype with a typically more indolent course and should be distinguished from systemic ALCL.

PATIENT AND DISEASE CHARACTERISTICS

ALK-Positive Anaplastic Large Cell Lymphoma

Patients with ALK + ALCL are commonly young, with a median age in the 30s; this is also one of the most common lymphoma diagnoses in children.[9,10] Patients with ALK + ALCL usually present with lymph node enlargement and have frequent extranodal involvement of skin, bone, soft tissue, lung, and liver. About 60% of cases present with advanced stage (stage III/IV) at presentation and often have B symptoms at diagnosis, particularly fever.

ALK + ALCL exhibits a wide histologic spectrum. Several morphologic patterns have been recognized: common type (60%), lymphohistiocytic (10%), small cell (5%–10%), Hodgkin-like (3%), and others as well as mixed or composite patterns (15%). The common type pattern is characterized by large lymphoma cells infiltrating sinuses and/or showing cohesive features (Fig. 1). In all variants, the lymphoma cells

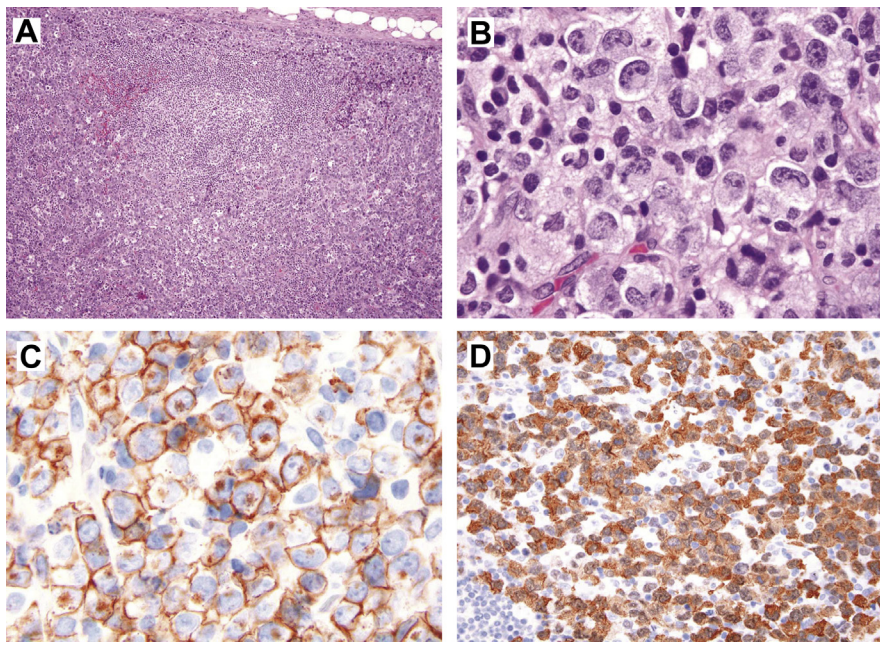

Fig. 1. (*A*) Sheets of lymphoma cells. (*B*) Atypical lymphocytes, so-called hallmark cells. (*C*) Immunohistochemical staining for CD30. (*D*) Immunohistochemical staining for ALK.