Title	Diffuse large B-cell lymphoma of the central nervous system in mycophenolate mofetil-treated patients with systemic lupus erythematosus
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Expression of aldehyde dehydrogenase isoforms in acute myeloid leukaemia

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Introduction: Aldehyde dehydrogenase (ALDH) is a family of enzymes comprising 19 isoforms in human which are involved in the oxidation of both endogenous and exogenous aldehydes to the corresponding acids. ALDH activity is consistently associated with normal haematopoietic stem cells activity in mice and human and more recently leukaemia initiating activity and inferior prognosis in acute myeloid leukaemia (AML). The specific isoforms associated with the reported ALDH activity are unclear. To address this, we examined the expression of ALDH isoforms in bone marrow (BM) samples from healthy donors as well as AML patients.

Methods: Seven ALDH genes (1A1, 1A2, 1A3, 1B1, 3A1, 5A1, and 8A1)—of which 3A1 and 5A1 are involved in cyclophosphamide metabolism, 1B1 was reported to be a possible marker in granulopoiesis, and 1A1, 1A2, 1A3 and 8A1 are involved in endogenous retinoic acid biosynthesis—were examined. Purified $CD34^+$ or mononuclear cells from six normal and nine AML BM were investigated. Three AML cell lines were also studied. Reverse transcription–polymerase chain reaction was performed to amplify a specific segment of different ALDH isoforms.

Results: Among the ALDH tested, ALDH1A3 was expressed in all six normal but not in any AML BM samples or cell lines. ALDH3A1, ALDH5A1 and ALDH8A1 were not expressed in normal BM. However, they were expressed in 7/10, 8/10 and 5/10 AML samples and 1/3, 3/3 and 2/3 cell lines respectively. No differential gene expression between normal and AML samples were observed in other ALDH isoforms.

Conclusion: Specific ALDH isoforms exhibited differential gene expression between normal and AML BM. Their roles in normal and neoplastic haematopoiesis should be further evaluated.

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Diffuse large B-cell lymphoma of the central nervous system in mycophenolate mofetil–treated patients with systemic lupus erythematosus

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We report the third case of primary lymphoma of the central nervous system (PCNSL) in a patient with systemic lupus erythematosus (SLE) given long-term mycophenolate mofetil (MMF). Our 43-year-old patient has a history of lupus nephritis and has been treated with MMF 500 mg/day in addition to azathioprine (AZA) for 8 years. She presented with subacute left-sided weakness. Magnetic resonance imaging revealed a gadolinium-enhancing mass in the right parietal region which was isointense on T2-weighted imaging. Brain biopsy revealed diffuse sheets of large lymphoid cells which demonstrated strong membranous expression of CD20 by immunohistochemistry and positive signal for Epstein Bar virus (EBV)–encoded RNA by in-situ hybridisation study. Complete remission of PCNSL was achieved after discontinuation of MMF and administration of rituximab and whole brain radiotherapy.

Patients with SLE are predisposed to development of lymphoma regardless of immunosuppressive use. One meta-analysis found that non-Hodgkin's lymphoma was more common in SLE patients with a standardised incidence rate ranging from 5.2 to 44.4. However, the development of PCNSL secondary to immunosuppressive use is being increasingly recognised especially in MMF-treated renal transplant recipients with onset of PCNSL after a median of 14 months. It has also been described in some MMF-treated autoimmune conditions such as myasthenia gravis, dermatomyositis and relapsing polychondritis. Although AZA in combination with corticosteroids has been shown to predispose post-renal transplant patients to lymphoproliferative disease with a relative risk of 12.7, the association of AZA and EBV-related lymphoma is rare. The approach to management of this condition includes withdrawal of MMF and judicious use of future immunosuppressive agents.