A non-chemotherapy treatment of a primary effusion lymphoma: durable remission after intracavitary cidofovir in HIV negative PEL refractory to chemotherapy

A 78-year-old male of Italian heritage was evaluated for progressive shortness of breath over two months and recurrent pleural effusions. He had a 5-year history of fluctuating anemia and mild lymphadenopathy and had previously undergone a bone marrow examination that was normal. An excisional lymph node biopsy revealed only reactive changes.

Upon evaluation, he had bilateral pleural effusions, a small pericardial effusion, pericardial thickening, axillary lymphadenopathy and splenomegaly. An FDG PET study revealed increased uptake in axillary, mediastinal and mesenterial lymph nodes. Bilateral thoracenteses yielded exudative pleural fluid containing atypical large lymphocytes. The lymphocytes weakly expressed CD30 and strongly expressed CD45, MUM-1 and HHV-8 and were negative for other markers, including CD20, CD79a, CD138, CD3, CD30, ALK-1 and kappa and lambda immunoglobulin light chains. A diagnosis of primary effusion lymphoma (PEL) was made. A bone marrow examination showed no involvement by lymphoma. Serology for HIV-1 was negative but there was evidence of past infections with human herpes virus 8 (HHV-8) and Epstein–Barr virus.

The patient received two cycles of conventional CHOP chemotherapy with substantial improvement of the pleural effusions. Unfortunately, the effusions recurred after the third cycle. Repeated thoracenteses showed persistent PEL. One cycle of salvage DHAP chemotherapy was administered without improvement. A short course of interferon alpha also failed to control the disease. Having failed conventional treatments and not willing to pursue further cytotoxic therapy he underwent therapy with intrapleural cidofovir hypothesizing that anti-viral therapy directed against HHV-8 would abort PEL relapse. Intrapleural cidofovir was administered into the right pleural space on five occasions. The initial dose was 3 mg/kg and the subsequent doses were 5 mg/kg. The treatment was well tolerated except for mild uveitis. He also received intensity-modulated radiation therapy radiation therapy of 3060 cGy to a localized field in the right hemithorax. The treatment successfully halted further accumulation of pleural fluid and the patient’s performance status improved substantially. He has now been monitored for 15 months since having the last intrapleural cidofovir injection. He remains in a complete remission and his most recent CT scan only shows a minimal right pleural effusion, pleural thickening and a small segmental atelectasis. The respiratory and performance status were much improved.

PEL is a rare entity, usually described in HIV-infected patients. It is invariably associated with Kaposi sarcoma-associated herpesvirus/human herpes virus 8 (KSHV/HHV-8) [1]. The prognosis of PEL in HIV patients is poor [2, 3]. PEL has been described in HIV-negative patients, frequently elderly males from the Mediterranean region or immunocompromised patients [4]. Chemotherapy in these patients is generally unsatisfactory, partly because of advanced age and frequent comorbid conditions.

Cidofovir is an antiviral agent with a broad activity against multiple DNA viruses. In vitro studies have shown efficacy against HHV-8 and PEL cell lines [5, 6]. Recently, Luppi et al. reported three cases of elderly men with HIV negative PEL who received intracavitary cidofovir. All three patients responded and the duration of response was 5–15 months. Intracavitary cidofovir may represent a reasonable choice of therapy in frail, elderly patients or in patients refractory to conventional chemotherapy. In our patient, the chemotherapy transiently controlled the PEL but with repeated treatments, progressive immunosuppression possibly allowed further proliferation of the virus leading to rapid recurrence. Inhibition of viral replication and a direct pro-apoptotic effect on lymphoma cells by the cidofovir appears to have successfully controlled the malignant process [5, 6]. The cidofovir concentration needed to exert the pro-apoptotic effect is not achievable with intravenous use of the drug, but sufficient concentration may be achieved when the drug is delivered directly in the pleural cavity. Therapy directed at the putative infectious agent driving the malignant transformation may be of significant clinical relevance, not only in bacterial but also in viral associated lymphomas [7, 8].

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