Transplant International

LETTER TO THE EDITORS

Successful treatment of systemic *de novo* sarcoidosis with cyclosporine discontinuation and provision of rapamune after liver transplantation

doi:10.1111/j.1432-2277.2011.01256.x

Sarcoidosis is a granulomatous disease of unknown aetiology that has rarely been documented after liver transplantation (LT) [1,2]. We herein present a case of systemic, *de novo* sarcoidosis complicating LT.

A 53-year-old man underwent LT for HCV-related liver cirrhosis. Maintenance immunosuppression consisted of cyclosporine monotherapy from day 0. Postoperative course was uneventful.

Seventy-two months after LT, patient developed stenosis of the common bile duct, which required the insertion of an endoluminal stent. Six months later, he was readmitted for a new episode of jaundice, fever and asthenia. Imaging revealed recurrent cholangitis so stent replacement and antibiotic therapy were performed. During hospitalization, dyspnoea, nonproductive cough and purpuric rash at the extremities developed. Chest imaging showed atelectasis of the inferior lobe of the right lung, mediastinal widening, moderate right pleural effusion and enlarged lymph nodes in peribronchial and carinal areas. As the general condition of the patient showed no improvement, biopsies were taken of the liver and mediastinal lymph nodes.

Pathology of the mediastinal lymph nodes showed parenchyma completely scattered with multiple, well-defined, non-necrotizing, sarcoidosis-like granulomas containing CD68+ epithelioid histiocytes and some multinucleated giant cells (Fig. 1). Granulomas were surrounded by a halo of CD3+ positive small T lymphocytes associated with clusters of CD20+ B lymphocytes and mature plasma cells with polyclonal kappa and lambda light chains and rare CD30+ activated CD30+ immunoblasts. Ziehl-Neelsen staining was negative. Polymerase chain reaction analysis ruled out mycobacterium tuberculosis.

Liver biopsy showed mild chronic hepatitis consistent with HCV disease recurrence. Importantly, necrotizing granulomas containing Langhans-like multinucleated giant cells were present in hepatic lobules. Ziehl-Neelsen staining was also negative here.

Overall, the clinical pattern was suggestive of sarcoidosis. Corticosteroids (CS) are considered the drug of choice for sarcoidosis, however, there exists little evidence of any improvement in lung function after 6 months of treatment and no data are available beyond 2 years to indicate whether CS have any impact on long-term outcome [3]. Therefore, we did not administer CS for two reasons: (i) CS favour progression of HCV disease recurrence by upregulating cell-entry factors occludin and scavenger receptor class B type I [4]; (ii) it is our policy not to administer CS to our LT recipients [5]. Moreover, as literature shows that sarcoidosis patients treated with cyclosporine may encounter significant adverse events [5–8], we decided to discontinue cyclosporine and introduce rapamune (blood trough levels 5–6 ng/ml). Patient general condition dramatically improved thereafter.

Two years after this episode, patient is doing well. Chest imaging is normal and liver biopsy shows HCV recurrence but no granuloma-like lesions. Notably, patient never received any antiviral treatment as graft function, serum HCV-RNA, and degree of disease recurrence did not justify it.

To the best of our knowledge, this is the first case of *de novo* systemic sarcoidosis after LT. Although rapamune introduction resulted in disease elimination, it should be noted that this association does not necessarily equate to causality. Nonetheless, our report questions the efficacy of CS and CsA and highlights the potential of rapamune in the armamentarium of sarcoidosis treatment.

Funding

Giuseppe Orlando, MD, PhD is recipient of the Marie Curie International Outgoing Fellowship POIF-GA-2008-221850, financed by the European Commission under the 7th Framework Program for Research and Development.

Conflicts of Interest

None.

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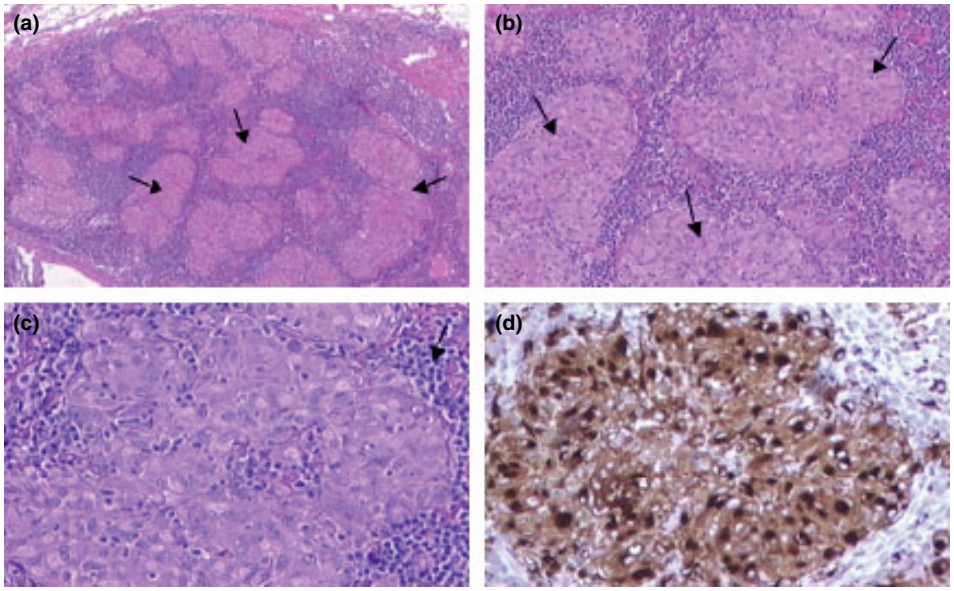

Figure 1 Pathology of the mediastinal lymph node depicting histological features of pulmonary sarcoidosis. (a, b) Multiple, well-defined, non-necrotizing, focally coalescing granulomas (arrows). (c) Granulomas are mainly composed of epithelioid cells (arrow) and (d) multinucleated CD68+ Langhans giant cells.

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