PostScript

LETTERS TO THE EDITOR

Diagnostic relevance of anti-filamentous actin antibodies in autoimmune hepatitis

We read with interest the paper by Granito *et al*[1] reporting on the clinical and diagnostic significance of anti-filamentous actin antibodies (A-FAA) in autoimmune hepatitis type 1 (AIH-1). The authors found that A-FAA, measured by a new commercially available ELISA based on a modified cut-off of 30 instead of the manufacturer's 20 arbitary units (AU), strictly correlates with the smooth muscle antibody glomerular/tubular (SMA-G/T) pattern,[2] also known as the microfilament pattern, mostly seen in patients with AIH-1.[1] Their findings further indicate F-actin as the predominant, if not the sole, target of AIH-1-specific SMA reactivity, a notion that has been questioned in the past because of the inconsistent results obtained by several actin-based assays.[3 4]

We agree with Granito *et al*[1] that many laboratories are unfamiliar with the interpretation of the immunofluorescence patterns of AIH-specific SMA; such a problem arguably generates an urgent need for a reliable and observer-independent molecular-based SMA detection assay.[5] New commercially available A-FAA ELISAs could be viable alternatives for routine laboratories, as the likelihood of a false-negative result is relatively low, but the possibility of reporting inaccurate results by immunofluorescence remains high.

We would like to raise a few points on the basis of our recent experience with the A-FAA ELISA.

At variance with Granito *et al*[1]—and using the same ELISA and modified cut-off of 30 AU—we found A-FAA seropositivity in a considerable proportion of SMA-G/T-seronegative patients with AIH-1 (fig 1A). The increased sensitivity of the A-FAA ELISA comes to the cost of its lower specificity, as it detects A-FAA in a considerable number of SMA-seronegative pathological controls, especially in patients with primary biliary cirrhosis and chronic hepatitis C (fig 1B).

We also found through inhibition studies that AIH-1-specific SMA-G/T reactivity is not always abolished by F-actin as a solid-phase competitor; only in one of the three patients with AIH-1 were we able to absorb out immunofluorescence SMA-G/T reactivity by 70% using F-actin as a solid-phase competitor[6 7] (in the other two patients, SMA-G/T reactivity was inhibited by 23% and 47%).

Our inhibition studies suggest that F-actin is a likely, but not the only, target of AIH-specific SMA reactivity.[5] We agree with the recent consensus statement of the international autoimmune hepatitis group affirming that: (1) the basic technique of choice at present for the routine testing of SMA patterns relevant to AIH is indirect immunofluorescence on a rodent multiorgan (kidney, liver and stomach) substrate and (2) the remaining targets of the AIH-1-specific microfilament reactivity will require further identification.[5] We also think that larger studies are needed to consider the performance of the newly established A-FAA ELISA in terms of specificity and sensitivity.

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References

1 **Granito A**, Muratori L, Muratori P, *et al*. Antibodies to filamentous actin (F-actin) in type 1 autoimmune hepatitis. *J Clin Pathol* 2006;**59**:280–4.
2 **Bottazzo GF**, Florin-Christensen A, Fairfax A, *et al*. Classification of smooth muscle autoantibodies detected by immunofluorescence. *J Clin Pathol* 1976;**29**:403–10.
3 **Bretherton L**, Brown C, Pedersen JS, *et al*. ELISA assay for IgG autoantibody to G-actin: comparison of chronic active hepatitis and acute viral hepatitis. *Clin Exp Immunol* 1983;**51**:611–16.
4 **Leibovitch L**, George J, Levi Y, *et al*. Anti-actin antibodies in sera from patients with autoimmune liver diseases and patients with carcinomas by ELISA. *Immunol Lett* 1995;**48**:129–32.
5 **Vergani D**, Alvarez F, Bianchi FB, *et al*. Liver autoimmune serology: a consensus statement from

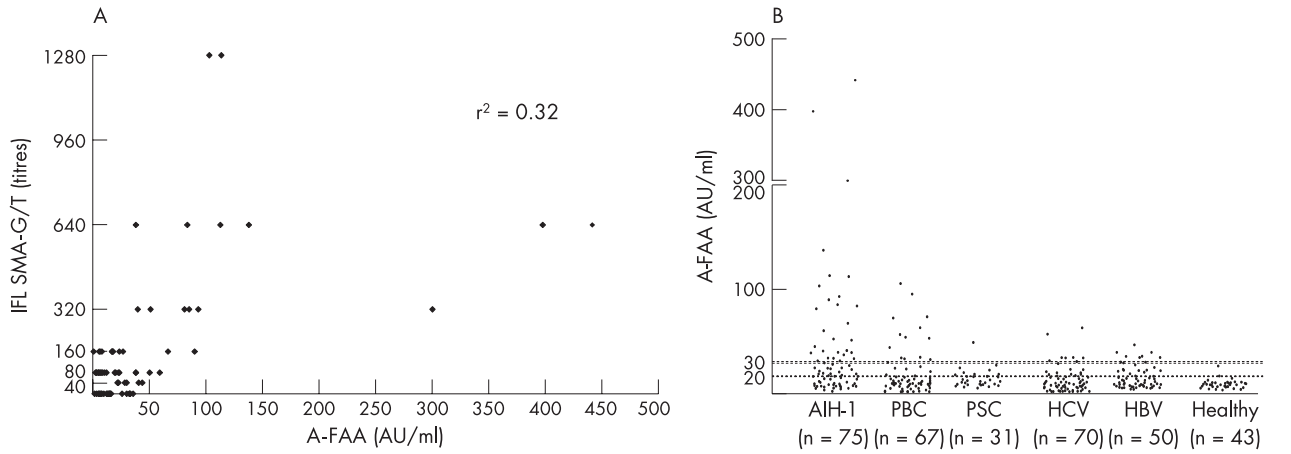

Figure 1 (A) Scatter plot representation of the correlation between the ELISA titres (arbitary units, AU) of the anti-filamentous actin antibodies (A-FAA; x axis) and the titres of smooth muscle antibody glomerular/tubular (SMA-G/T) pattern by indirect immunofluorescence (IFL; y axis). (B) ELISA titres for A-FAA in 75 patients with autoimmune hepatitis type 1 (AIH-1), 67 with primary biliary cirrhosis (PBC), 31 with primary sclerosing cholangitis (PSC), 70 with chronic hepatitis C virus (HCV) infection, 50 with hepatitis B virus (HBV) infection and 43 healthy controls. According to the manufacturer's instructions, a test is strong positive when the ELISA titre is >30 AU; weak positive between 20 and 30 AU; and negative at <20 AU. In agreement with Granito *et al*,[1] the mean (standard deviation) optical density at 450(5) nm in our 50 controls corresponds to 29.6 AU.

the committee for autoimmune serology of the International Autoimmune Hepatitis Group. *J Hepatol* 2004;**41**:677–83.
6 **Bogdanos DP**, Baum H, Gunsar F, *et al*. Extensive homology between the major immunodominant mitochondrial antigen in primary biliary cirrhosis and *Helicobacter pylori* does not lead to immunological cross-reactivity. *Scand J Gastroenterol* 2004;**39**:981–7.
7 **Bogdanos DP**, Baum H, Okamoto M, *et al*. Primary biliary cirrhosis is characterized by IgG3 antibodies cross-reactive with the major mitochondrial autoepitope and its *Lactobacillus* mimic. *Hepatology* 2005;**42**:458–65.

Enteropathy type T cell lymphoma with an unusually late relapse: a case report

Enteropathy type T cell lymphoma (ETTL) is a rare subtype of T cell lymphoma that is strongly associated with coeliac disease.[1] The overall prognosis is poor. In one study, 15 of 19 (79%) patients relapsed within 60 months after the initial diagnosis (median, 6 months), and the overall survival rate at 5 years was 24%.[2] We describe a case of ETTL with an unusually late relapse. The patient was a 50-year-old woman who developed an ulcerated gastric tumour in 1992, with no associated lymphadenopathy or hepatosplenomegaly. A partial gastrectomy was performed, and at the time of surgery, the tumour was found grossly infiltrating into the peritoneum, posterior rectus sheath and the liver. The pathological diagnosis was diffuse large cell lymphoma of mature T cell lineage (fig 1). On immunohistochemical analysis, the neoplastic cells were found to be CD3+, CD4−, CD5−, CD7+/− and CD8−, and positive for CD56, TIA 1 and granzyme B. She received a full course of VACOP-B (etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin). Shortly after the diagnosis of T cell lymphoma was made, she was diagnosed with coeliac disease. In view of this finding, the T cell lymphoma was reclassified as ETTL. She was in complete remission and her gastrointestinal symptoms were under control with a gluten-free diet. In 2003, she experienced symptoms of progressive nasal obstruction. Excisional biopsy of a left nasal mass was performed and the pathological diagnosis was diffuse large cell lymphoma of mature T cell phenotype. The immunohistochemical results from the tumour of 1992 and those of 2003 were identical. Molecular analysis of the T cell receptor γ gene also showed an identical rearrangement between these two neoplasms (fig 1), supporting the fact that they were derived from the same neoplastic clone. She was treated with eight cycles of CHOP+R (cyclophosphamide, vincristine, doxorubicin, prednisone, rituxan), followed by additional surgical excision, radiation therapy to the nasal cavity (3600 cGy over 20 fractions) and three cycles of prophylactic intrathecal chemotherapy (methotrexate and cytarabine). After a short remission, she presented with swelling of her right nipple in 2005, which was confirmed to be relapsed T cell lymphoma. She received two cycles of intensive chemotherapy and autologous stem cell transplantation. After a brief remission, she developed jaundice and thrombocytopenia. Circulating malignant cells were found in the peripheral blood (fig 1). She was placed under home palliative care. In summary, our patient represents a highly unusual case of ETTL that relapsed after a long latency time period.

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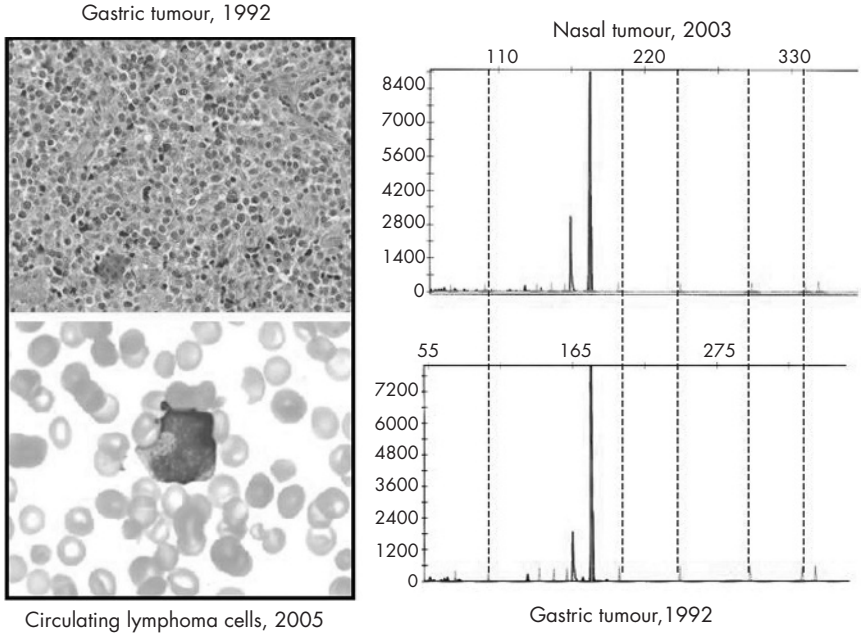

Figure 1 Left upper panel: gastric enteropathy type T cell lymphoma diagnosed in 1992, composed of a monotonous population of lymphoid cells with a medium cell size, a moderate amount of pale-staining cytoplasm and a round vesicular nucleus. Left lower panel: a circulating large lymphoma cell with a few azurophilic granules in the cytoplasm. Right panel: molecular studies showed that both the gastric and the relapsed nasal tumour had an identical T cell receptor gene arrangement, TCR γ 2, detectable using an automated gene sequencer (AB13100, Applied Biosystems, Foster City, California, USA).

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References

1 **Isaacson P**, Wright D, Ralfkiaer E, *et al*. Enteropathy-type T-cell lymphoma. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, eds. *WHO classification of tumors*. Lyon: IARC Press, 2001:208–9.
2 **Gale J**, Simmonds PD, Mead GM, *et al*. Enteropathy-type intestinal T-cell lymphoma: clinical features and treatment of 31 patients in a single center. *J Clin Oncol* 2000;**18**:795–803.

Anaplastic large cell lymphoma presenting with paraneoplastic pemphigus

Paraneoplastic pemphigus is an autoimmune acantholytic mucocutaneous disorder that rarely accompanies an overt or occult neoplasm. Typical features include painful mucosal erosive lesions and pruritic papulosquamous eruptions that often progress to blisters. The antibody is a unique immunoglobulin G that recognises epidermal proteins. We discuss the case of a 23-year-old woman who presented with anaplastic large cell lymphoma complicated by paraneoplastic pemphigus, rapidly resulting in fatal multiorgan failure.

A 23-year-old woman presented with 1 week of fever and a disseminated erythrodermic rash with desquamation of the hands and feet, and erosions in the mouth. A local doctor started treatment with ciprofloxacin and prednisolone.

A diagnosis of toxic epidermal necrolysis was made. On day 4, she required intubation, ventilation and transfer to a tertiary referral centre. A skin punch biopsy showed features of Staphylococcal toxic shock syndrome.

By day 9, multiorgan failure developed and a laparotomy was performed for acute abdominal distension. Retroperitoneal lymphadenopathy, hepatomegaly and splenomegaly were noted, and splenectomy and lymph node biopsy performed.

The histological examination of the spleen and splenic hilar lymph node showed replacement by a nodular infiltrate of small lymphoid cells with vesicular nuclei, multiple nucleoli and a moderate amount of eosinophilic