A Curious Case of Autoimmune Hepatitis and Acquired Partial Lipodystrophy

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Case description:
A seventeen-month-old boy presented with a 3-week history of fever associated with symmetrical swelling and rash over both legs which clinically resembled Henoch-Schönlein Purpura (HSP) along with a red tympanic membrane. He was admitted to hospital and extensive investigations revealed a mildly raised Alanine Transaminase (ALT; 62IU/L) and significantly raised C-reactive protein (CRP; 129mg/L) but were otherwise normal. A course of oral Co-amoxiclav was initiated for acute otitis media associated with HSP and he was discharged home with an improving CRP.

One month later...his limb swelling and rash had markedly improved but his fever persisted. His ALT remained mildly elevated and an abdominal ultrasound demonstrated a smoothly enlarged liver with abnormal echotexture. An auto-antibody screen identified anti-LKM antibodies in his serum but liver biopsy at this stage demonstrated only mild portal fibrosis and moderate giant cell transformation with no other abnormalities on staining.

Three months after first presentation...it was noted that his legs were now very slim and muscular. This appearance had been caused by a loss of lower limb adipose tissue and, while rare in this age-group, the changes were characteristic of lipodystrophy. During the same timeframe, his blood tests revealed a significant rise in his ALT (654IU/L), AST (386IU/L) and GGT (122IU/L). A repeat liver biopsy was scheduled.

Over time....the adipose tissue loss progressed to his upper limbs and trunk (figure 1). He was reviewed in clinic by the national insulin-resistance team and a diagnosis of Acquired Partial Lipodystrophy was reached. In keeping with this, his triglyceride level was slightly raised but fasting glucose and insulin profile were normal. His repeat liver biopsy, now four months after presentation, demonstrated more convincing features of chronic hepatitis (figure 2a and 2b) and a diagnosis of AIH was confirmed. Prednisolone (2mg/kg) and Azathioprine (1.5mg/kg) were started and within six months his ALT, AST and GGT had normalised. Unfortunately, no improvement was seen in his subcutaneous fat distribution though there was also no progression.

Outcome:
Five years on, the clinical features of lipodystrophy have persisted but have not progressed. He remains on dual maintenance therapy of Prednisolone and Azathioprine and a repeat liver biopsy in 2018 demonstrated mild-moderate portal inflammation with some fibrosis (figure 2c and 2d), but serial ultrasound scans have since been reassuring.

Discussion:
The development of AIH in association with APL is extremely rare. In this case, features of APL presented at a very early age and occurred in the context of a relatively mild hepatitis making both diagnosis and management more challenging. Through close monitoring, regular discussion with specialist services and effective immunosuppression, we have so far been able to manage both conditions. Until we are able to predict which children with AIH are more likely to develop lipodystrophy, or any other autoimmune condition for that matter, we recommend that these children are kept under regular clinical review.

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Background:
The lipodystrophies are a heterogeneous group of ultra-rare metabolic disorders with an estimated prevalence of between 1.3 and 4.7 cases/million. In Acquired Partial Lipodystrophy (APL), the predominant clinical feature is a progressive, symmetrical reduction of adipose tissue which typically begins during the pre-adolescent period. In a small sub-set of these patients, the development of anti-Liver/Kidney Microsomal (LKM) antibodies can lead to autoimmune hepatitis (AIH). This process differs from the liver disease caused by secondary deposition of triglycerides in the liver lobule. In this report, we describe the case of a 17-month-old boy who developed progressive features of acquired partial lipodystrophy in association with anti-LKM-1 positive autoimmune hepatitis and document his challenging path from first presentation to diagnosis and through to his ongoing management.

Figure 1. Photographs demonstrating the features of lipodystrophy in the case subject. Images a-d show loss of adipose tissue in upper and lower limbs and images e and f show abdominal adipose loss.

Figure 2. Liver histology. Panels a and b: biopsy in 2015 demonstrating portal inflammation (a) and mild steatosis (b). Panels c and d: biopsy in 2018 demonstrating persistence of portal inflammation (c) but absence of steatosis (d).