Potential serious immunomodulatory complications of hepatitis C therapies

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**Introduction:**

- Chronic hepatitis C (HCV) is associated with many systemic manifestations (including fatigue, myalgia, weight loss, cryptoglobinemia, vasculitis, lymphoproliferative disorders, membranoproliferative glomerulonephritis and porphyria cutanea tarda).
- Recently treatment has changed from interferon-based regimens to use of direct acting antiviral (DAA) agents.
- Interferon-free treatments produce higher rates of sustained virological response at week 12 (SVR12) as well as fewer reported side effects. (PEG-IFN/ribavirin-based regimes can cause bone marrow suppression, depression, psychosis, myalgias, arthralgias, optic neuritis, retinal thrombosis, rheumatoid arthritis, hyper/hypothyroidism, hyperglycaemia and sarcoidosis).
- We report 2 causes of serious and unusual complications from patients receiving treatment for HCV.

**Case 1**

A 54 year old male non-cirrhotic co-infected HIV and HCV genotype 3 was treated with PEG-IFN and ribavirin. After 12 weeks of treatment he developed severe progressive muscular weakness over 4 weeks leaving him bedbound and unable to swallow. Examination revealed peripheral neuropathy with LMN signs and dysphagia.

**Investigations**

| HIV | 20 copies/ml |
| WCC | 5.3x10⁹/L |
| Hb | 122g/L |
| MCV | 103.1L |
| Plts | 158x10⁹/L |
| ALT | 691U/L |
| ALP | 62U/L |
| Bil | 10μmol/L |
| GGT | 220U/L |
| INR | 1.1 |
| UEG | normal |
| CK | 4453 u/L |
| ESR | 46mm/h |

**Management:**

Muscle biopsy showed non-specific inflammatory changes.

**Conclusion:**

- Case 1 reports a significant temporal association between initiation of PEG-IFN/ribavirin and development of severe life-threatening myositis. Myositis has rarely been reported as a side effect of PEG-IFN in hepatitis C. We postulate that the immunomodulatory effect of PEG-IFN was responsible for the initiation of myositis.
- Case 2 reports cryptococcal disease developing on a PEG-sparing regimen. Very rarely an association of cryptococcal peritonitis and cirrhosis has been reported and malignancy may have played a role here too but the temporal association between these events the subsequent severity of disease is noteworthy.
- It is difficult at this stage in our understanding of these drugs to postulate a mechanism of action.