Short communication

Multifocal central nervous system demyelination and Lhermitte's phenomenon secondary to combination chemotherapy for chronic lymphocytic leukaemia

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Abstract

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1. Introduction

Chemotherapy can occasionally cause central neurological toxic effects. The CRF (cyclophosphamide, rituximab, fludarabine) regime is used widely for the treatment of chronic lymphocytic leukaemia (CLL). Fludarabine is the only agent in this regimen reported to cause a demyelinating encephalopathy at high doses [1]. Rituximab and cyclophosphamide have not been associated with central nervous system demyelination, even though cyclophosphamide is frequently used at much higher myeloablative doses. We report a case of disseminated central nervous system (CNS) demyelination from the CRF regime.

2. Case report

A 54 year old man with chronic lymphocytic leukaemia (CLL) received 2 × 6 cycles of cyclophosphamide (250 mg/m2 days 1–3), rituximab (700 mg day 1) and fludarabine (25 mg/m2 days 1–3) some 3 years apart. Two months after the last cycle, he received lenalidomide (5 mg/day). Soon after, he developed Lhermitte-like phenomena precipitated by neck flexion. He became impotent and had urinary hesitancy. There was patchy pinprick sensory loss below T4, over C5/6 dermatomal regions bilaterally and over the malar regions of the face, but no weakness or ataxia. Ankle jerks were mildly depressed and the plantar responses were flexor. Blood tests, including autoimmune studies, VRDL and B12 levels, were all normal. Cerebrospinal fluid revealed only a minor elevation of protein (0.56 g/L) and oligoclonal bands were not detected. Magnetic resonance imaging (MRI) of the brain and whole spine revealed non-specific periventricular fluid attenuated inversion recovery (FLAIR) hyperintense lesions and subtle hyperintensity in the ventral medulla (Fig. 1).

Peripheral nerve conduction studies showed mild slowing of median motor conduction velocity in the forearm segment (46 m/s; N > 49 m/s) only with no evidence for more widespread demyelination. Somatosensory evoked potentials (SSEPs) of the upper and lower limbs were normal but there were abnormalities noted in motor evoked potentials (MEPs; central motor conduction time 8 ms; N < 8 ms for the right abductor digiti minimi; and 24.5 ms; N < 14 ms for the right tibialis anterior muscle), visual evoked potentials (VEPs; central field latency – right eye 120 ms, left eye 128 ms; N < 112 ms) and brainstem auditory evoked potentials (BAEPs; wave III–V latencies – right ear 2.24 ms, left ear 2.32 ms; N < 2.2 ms). Lhermitte's phenomenon took several months to resolve and his sensory symptoms improved with no long term consequences at one year.

3. Discussion

This is the first report of diffuse CNS demyelination in a patient on CRF and lenalidomide. We believe the most likely culprit in this case is...
but again usually in myeloaabitive doses. Our patient had only mild changes on large fibre peripheral nerve studies, which may be secondary to lenalidomide. This drug is not known to produce CNS abnormalities but it can uncommonly cause a peripheral neuropathy at high doses [14].

In conclusion, CNS demyelination is an uncommon complication of chemotherapy and has not been described previously in patients receiving CRF or lenalidomide. Central neurophysiological abnormalities may be helpful in identifying this complication. Lhermitte’s phenomenon due to chemotherapy is rare but may alert clinicians to the possibility of CNS demyelination.

Conflict of interest

The authors report no conflicts of interest related to this work.

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References