Early diagnosis and intravenous immune globulin therapy in paraneoplastic cerebellar degeneration

Moll et al., present what appears to be a well-documented case of paraneoplastic cerebellar degeneration which responded differentially to plasmapharesis and IVig. Although their synthesis of the data is consistent with the available data, another possibility exists which may explain the course of events.

In their report a 44-year-old woman developed severe dys equilibrium soon after being diagnosed and treated for breast cancer. It is clearly stated that she received 5-fluorouracil (5-FU) just before this syndrome started. In fact, 5-FU has well-documented neurotoxicity characterised by gait and appendicular ataxia, dysarthria and hyponatremia and its onset may be acute. Although this complication was originally reported with higher doses, lower ones can also cause a milder ataxia which in most cases is completely reversible. Based on clinical and serological studies, Moll et al. conclude that plasmapharesis was ineffective but immune globulin effective in this patient; it seems just as possible that the patient received 5-FU on day 20, developed an acutely severe cerebellar syndrome for the dose administered, was given plasmapheresis, received more 5-FU on day 61 while still symptomatic and only after enough time had elapsed did she finally recover. I think this situation is just as likely as the one outlined by the authors and explains why the patient’s clinical course did not correlate with her antibody titres.

Although recent studies on CNS paraneoplastic syndromes have generated much interest in the correlation between CNS reactive antibodies and neurological syndromes, it is unclear whether their presence clinches a diagnosis. Since screening for these antibodies is now readily available through commercial laboratories, it seems an opportune time for developing more rigid inclusion and exclusion criteria for these unusual CNS syndromes.

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Neuromorbidological abnormalities and schizophrenia

The recent informative review by David and colleagues’ provides a much-needed update on the epidemiological relevance of abnormalities of the corpus callosum, and in particular their implications for the pathobiology of schizophrenia. The advent of MRI has generally negated the necessity of rigid inclusion criteria in designing treatment protocols for PNS. We suggest that requirements should include an early diagnosis before irreversible neurological damage has developed together with initiating new modes of therapy within four weeks after onset of neurological symptoms.

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Moll et al. reply:

Dr Recht makes a valuable point. 5-Fluorouracil (5-FU) can indeed induce a transient cerebellar syndrome, usually together with a diffuse toxic encephalopathy leading to associated mental changes. As the medical oncologist felt it very important to continue chemotherapy in our patient, she received her third cycle of CMF three weeks after onset of symptoms: cyclophosphamide (100 mg/m², days 1-14), methotrexate (40 mg/m², days 1 and 8) and 5-FU (600 mg/m², days 1-8). As we were aware that her cerebellar symptoms which had not yet fully recovered at that time, might deteriorate, we watched her carefully and observed an increase in ataxia and tinutations with additional IVig administration. These symptoms recovered to baseline abnormalities within a few weeks, with ongoing improvement later. Further chemotherapy was continued, unsuccessfully, with cyclophosphamide (500 mg/m²), epirubicin (50 mg/m²) and prednisone (40 mg, days 1-10).

Thus for clinical reasons alone we consider it unlikely that 5-FU induced the cerebellar symptoms. Two other reasons make it also improbable. First, this complication has usually been observed with doses of 1000 mg/m² or higher which is occasionally administered to patients with colorectal carcinoma. Our patient received 600 mg/m² 5-FU, which is the standard dose for adjuvant chemotherapy in breast cancer. Second, the finding of auto-antibodies in paraneoplastic neurological syndromes (PNS) is a very specific finding. The titres of these antibodies, however, do not always correlate with the clinical course. This non-correlation does not contradict a pathogenic role for these auto-antibodies at the time the paraneoplastic syndrome develops. The detection of specific antineuronal auto-antibodies is often the only finding enabling the clinician to make a reliable diagnosis of PNS during life. Dr Recht highlights the necessity of rigid inclusion criteria in designing treatment protocols for PNS. We suggest that requirements should include an early diagnosis before irreversible neurological damage has developed together with initiating new modes of therapy within four weeks after onset of neurological symptoms.

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Brachial plexopathy after botulinum toxin administration for cervical dystonia

Sampaio et al1 favour a "causal relationship" between the local administration of botulinum toxin (BT) in distinct cervical regions and a bilateral brachial plexopathy in a 32-year-old woman, and propose either a direct effect of BT on cervical nerves, or an immune-mediated mechanism similar to serogenous peripheral neuropathy. The report raises questions of general interest.

The paper does not mention whether the BT injections were successful in those muscles into which they were injected, or whether there were side effects, local or general, other than those discussed, which could be attributed to the BT injections.

The report also does not state whether the laboratory investigations before, or those after, the plexopathy took immunological studies into consideration. The report does not state whether the laboratory investigations before, or those after, the plexopathy took immunological studies into consideration.

Since its first use, possible side effects of BT treatment have been vigorously monitored.