‘Out of blue’ Lhermitte’s sign: three cases due to low cumulative doses of oxaliplatin

Lhermitte’s sign (LS) or ‘Baber’s chair sign’ consists of a sudden electric shock-like sensation that shoots down the back and into the limbs when the neck is flexed. In patients with cancer, LS has been associated with spinal cord involvement, postirradiation phenomenon, and chemotherapy:
specifically reported in association with cisplatin [1] and docetaxel [2].

To our best knowledge, seven cases of LS have been previously reported in association with oxaliplatin. Brienza et al. [3] reported the first two cases in a pooled retrospective analysis of the peripheral neuropathy (PN) due to oxaliplatin, and De Gramont et al. [4] described one more, without any physiopathology discussion. Taieb et al. [5] reported three more cases, in all of them LS appeared with cumulative doses of at least 1200/mg² and were always accompanied by persistent paresthesias or sensory ataxia. Ciucci et al. [6] reported LS in a cisplatin-pretreated patient with a prior mild PN and LS appeared after a cumulative dose of 450 mg/m² with a severe PN worsening. In addition, the patient also received concomitant paclitaxel; despite its potential neurotoxicity, it was not associated with LS. However, another taxane, docetaxel, has been reported in association with LS [2]. No cases of LS have been reported in MOSAIC or FLOX trials to our knowledge. We report three new cases of LS in association with oxaliplatin, a widely used antineoplastic agent in metastatic colorectal carcinoma.

case-1

A 33-year-old woman, with a metastatic colon adenocarcinoma at diagnosis, received treatment with FOLFOX4 [4]. During the first four cycles of chemotherapy, the patient experienced only a mild and transitory fingers dysesthesias. After a cumulative dose of 765 mg/m², the woman described LS without other new neurological symptoms. Under this situation, the oxaliplatin was discontinued and the LS completely resolved after 2 months.

case-2

A 53-year-old woman, with a metastatic colon adenocarcinoma at diagnosis, received treatment into a clinical trial with FOLFOX4 [4] plus PTK787 (1250 mg/day). After the fifth cycle, the woman experienced only a moderate and transient paresthesia and mild fingers hypoesthesias. At the fourth cycle, a 20% oxaliplatin and 5-fluorouracil dose reduction was needed for a persistent severe neuropenia. After a cumulative dose of 860 mg/m², the patient experienced LS with persistent paresthesias and hypoesthesias. Oxaliplatin was discontinued, and the PN and LS completely resolved after 4 months.

case-3

A 54-year-old woman, with a resected stage III colon adenocarcinoma, was treated with adjuvant FOLFOX4 [4]. At the eighth cycle, after an oxaliplatin cumulative dose of 680 mg/m², the patient experienced an LS and peripheral persistent paresthesias grade 1. This patient continued on oxaliplatin up to complete five cycles, when oxaliplatin was interrupted due to grade 3 peripheral neurotoxicity. The peripheral neurotoxicity and LS persisted 11 months.

LS appeared in these cases after lower oxaliplatin cumulative doses than the cases previously reported and were promptly resolved after its discontinuation in the first two cases with any other severe neurological symptoms. Nevertheless, in the third case, the continuation of oxaliplatin after the appearance of LS was associated with a posterior severe neurotoxicity and a long time to recovery. Patients did not receive other neurotoxic concomitant drugs; however, the second received PTK787 which is an antiangiogenic agent. Recently, Giantonio et al. [7] have reported a higher incidence of severe neuropathy when FOLFOX4 is combined with bevacizumab (P < 0.016) in previously treated patients. In conclusion, these case reports suggest that LS could appear at oxaliplatin cumulative doses <900 mg/m² and must be considered a severe event which could anticipate future incapacitant neurotoxicity.

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