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THALIDOMIDE INDUCED PERIPHERAL NEUROPATHY IN LUPUS: DRUG PLASMA LEVELS AND INCIDENCE

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BACKGROUND

Thalidomide is very effective for treatment of cutaneous involvement of systemic lupus erythematosus (SLE) and cutaneous lupus erythematosus (CLE). Its main adverse effect is thalidomide-induced peripheral neuropathy (TiPN). There are scarce prospective studies in CLE/SLE regarding TiPN incidence/reversibility, and the majority has not excluded confounding causes. In addition, none monitored thalidomide plasma levels or coasting effect using nerve conduction (NCS). The objective of this work was to assess TiPN incidence through NCS and its correlation with thalidomide plasma levels in CLE/SLE.

METHODS

Prospective study lasting up to 12 months of thalidomide treatment in 20 CLE/SLE patients without other PN risk factors and with normal NCS. Exclusion criteria were: other autoimmune diseases; previous/ current alcoholism; diabetes mellitus; history of PN; previous use of thalidomide, leflunomide, TNF-alpha inhibitors, chemotherapy; history of cancer or thrombosis; current renal or nervous system activities, hemolytic anemia, and/or thrombocytopenia < 50,000. Nerve conduction was performed at 0, 6 and 12 months. Thalidomide initial dose was 100 mg/day for 3 months and reduced at any time depending on the therapeutic response and adverse effects until completing 12 months. This drug was discontinued if any PN symptoms and/or altered NCS. Thalidomide plasma levels were determined by liquid chromatography of high efficiency and tandem mass spectrometry.

RESULTS

The mean age was 44.8 ± 7.6 years. The median thalidomide use was 9 (1–12) months and its average cumulative dose was 20.7 ± 13.5 g. Twelve patients (60%) developed TiPN: 4/12 (33.3%) were symptomatic (one with normal NCS, one had not performed NCS, and two with altered NCS), and 8/12 (66.6%) were asymptomatic with altered NCS. Half of this final group (4/8 [50%]) developed TiPN symptoms 1–3 months after drug withdrawal (coasting effect). Multivariate regression analysis showed that the main predictive factor for TiPN was duration of thalidomide treatment ($p = 0.006$), especially ≥ 6 months ($p = 0.025$). Plasma thalidomide levels were not different between patients with/without TiPN ($p = 0.464$). After drug withdrawal (6.0 ± 1.6 months), 2/8 (25%) symptomatic TiPN patients persisted symptomatic (including those with coasting effect), 6/8 (75%) improved their symptoms, and 4/12 (33.3%) persisted asymptomatic. Seven of 12 (58.3%) TiPN patients underwent a supplementary NCS after drug removal. Three (3/7, 42.8%) of them worsened NCS, 1 (1/7, 14.2%) was stable, and 3 (3/7, 42.8%) had improved NCS.

CONCLUSION

Our study provides novel evidence of coasting effect in 50% of asymptomatic TiPN patients. The irreversible aspect of this lesion in one-fourth of TiPN patients supports the importance of NCS monitoring.

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