Thalidomide induced impotence in male hematology patients: a common but ignored complication?

Thalidomide has become an important agent in the treatment of myeloma. However, thalidomide induced erectile dysfunction is a serious complication which has received very little attention. In our hematology department, 6 out of 11 male patients developed erectile dysfunction (grade 3 in 5/6) within 4 weeks of starting thalidomide. Our results suggest that thalidomide induced impotence is a common complication in male hematology patients.

Haematologica 2007; 92:1440. DOI: 10.3324/haematol.11095

In recent years, thalidomide, either singly or in combination, has become an important therapeutic agent in a number of medical disorders. In particular, thalidomide has become a popular treatment for myeloma, initially in relapsed or refractory cases, but also as first line therapy and as maintenance.[1] In addition to the risk of birth defects, common side effects such as somnolence, constipation, rash, venous thromboembolic disease and peripheral neuropathy are well recognized.[2] Impotence is also a complication of thalidomide in myeloma,[3] although there are no published data on the incidence and outcome of this complication in hematology patients.

To assess the frequency of this complication, all male patients (14 patients with myeloma, one case of angioimmunoblastic lymphadenopathy, and one patient with massive inoperable intra-abdominal hemangioma) attending our hematology department who were taking or had taken thalidomide were asked about erectile dysfunction. Five cases (median age 74, range 59-79) were impotent (grade 3 erectile dysfunction, using the National Cancer Institute Common Toxicity Criteria, revised version 2) prior to a diagnosis of myeloma and to commencement of thalidomide. A further 5 patients with myeloma (median age 63, range 39-70) did not complain of erectile dysfunction during thalidomide therapy. Of these, 3 relapsed myeloma cases received up to 100 mg thalidomide daily in combination with intermittent high dose corticosteroids for periods of between 2 months and 21 months, and the other 2 patients received single agent thalidomide 50 mg daily as maintenance therapy post-autologous peripheral stem cell transplant (PSCT) for 1 month and 18 months, respectively. Four of these 5 cases developed grade 1 peripheral neuropathy after a median duration of thalidomide therapy of 5 months (range 1-15 months).

All 6 remaining patients developed erectile dysfunction (grade 3 in 5 cases) within 4 weeks of starting thalidomide. The 4 patients with myeloma in this group of 6 were diagnosed a median of 13 months (range 4 months-6 years) prior to commencement of thalidomide therapy. Only 2 of the 6 cases had mentioned this side effect prior to direct questioning about this complication. All 6 cases also developed thalidomide induced grade 1 peripheral neuropathy, after a median duration of therapy of 7 months (range 1-24 months). Of the 2 patients developing erectile dysfunction while taking single agent thalidomide 50 mg daily as maintenance post-PSCT, 1 patient (aged 44) developed grade 1 erectile dysfunction which has resolved following drug discontinuation after 14 months of therapy, while the second patient (aged 51), who discontinued thalidomide after 15 months, remains impotent. Two other patients (aged 58 and 64), who had received a combination of thalidomide (maximum dose of 200 mg in both cases) and intermittent high dose corticosteroids for 3 months and 24 months respectively, remain impotent despite discontinuation of thalidomide for 12 months and 23 months, respectively. The final 2 patients with thalidomide-induced impotence remain on this medication. One of these (aged 55) with massive intra-abdominal hemangioma has had a marginal clinical improvement since starting thalidomide 100 mg daily 6 months ago, while a patient (aged 63) with relapsed myeloma is responding to a combination of thalidomide (maximum dose 150 mg daily) and intermittent high dose corticosteroids, started 2 months ago. The 64-year old patient with myeloma with ongoing grade 3 erectile dysfunction, despite discontinuation of thalidomide, has responded satisfactorily to sildenafil 100 mg as required. However, the 55-year old patient, who continues on thalidomide for massive hemangioma, has failed to respond to sildenafil at a similar dosage.

The results from our small number of patients suggest that erectile dysfunction is an extremely common side effect of thalidomide in male hematology patients. It should be of some concern to the hematology community that this complication, which might be regarded as quite important by some patients and their sexual partners, should be largely ignored in the medical literature. It is likely that embarrassing questions about erectile dysfunction are not routinely asked at the hematology review of these patients, who are equally unlikely to volunteer such information, especially if they are having a favorable clinical response to thalidomide. With large numbers of male myeloma patients likely to receive thalidomide in the foreseeable future, it is essential that hematologists specializing in this area should treat this complication seriously and produce reliable data, from studies of larger numbers of patients, on such issues as its incidence, its relationship to patient age and to thalidomide dose and the likelihood of recovery on drug discontinuation. In particular, accurate recording of this complication should be mandatory in all future clinical trials of thalidomide therapy in myeloma. Although the favorable response of 1 of the 2 patients given a trial of sildenafil is encouraging, further assessment of the role of sildenafil and similar agents will clearly be required as part of any attempt to adequately manage this complication.

Philip T. Murphy, John Rory O'Donnell

Department of Haematology, Beaumont Hospital, Dublin, Ireland

Key words: myeloma, thalidomide, erectile dysfunction.

Correspondence: Philip T. Murphy, Department of Haematology, Beaumont Hospital, Dublin 9, Ireland. Phone: international +353.1.8092622; Fax: international +353.1.8093319. E-mail: philipmurphy@beaumont.ie

References

1. Raje N, Hideshima T, Anderson KC. Therapeutic use of immunomodulatory drugs in the treatment of multiple myeloma. Expert Rev Anticancer Ther 2006;6:1239-47.
2. Glasmacher A, Hahn C, Hoffmann F, Naumann R, Goldschmidt H, von Lilienfeld-Toal M, et al. A systematic review of phase-II trials of thalidomide monotherapy in patients with relapsed or refractory myeloma. Br J Haematol 2005;132:584-93.
3. Kyle Ra, Rajkumar SV. Multiple myeloma. N Engl J Med 2004;351:1860-73.