Purpose: To evaluate safety and efficacy of dexamethasone intravitreal implant in combination with direct laser photocoagulation of microaneurysms for treatment of refractory diabetic macular edema (DME). Methods: Two patients were presented with persistent DME after grid laser photocoagulation and intravitreal triamcinolone acetonide and/or intravitreal bevacizumab. Only left eye of the first patient and both eyes of the second patient were included into the study. The eyes were evaluated separately (Cases 1, 2 and 3). In a 64-year-old gentleman the intravitreal dexamethasone implant was injected 3 times at 6-month interval to the LE (Case 1). In a 61-year-old lady 1 implant was injected to the RE (Case 2) and 2 implants at 8-month interval to the LE (Case 3). Direct photocoagulation of leaking microaneurysms was started after the implant injection according to FA findings and performed several times in all 3 eyes. Results: The BCVA improved from 4/12, 4/8 and 4/8 to 4/8, 4/4 and 4/4 respectively in Case 1, 2 and 3 respectively at the last visit. The central macular thickness decreased from 525, 512 and 353 um to 175, 257 and 256 um respectively in Case 1, 2 and 3 respectively at the last visit. No edema was found in either eye at the last visit (HD-OCT). The follow-up period was 30, 15 and 9 months respectively in Case 1, 2 and 3 respectively. Conclusions: Dexamethasone intravitreal implant in combination with direct laser photocoagulation of microaneurysms seems to be safe and efficient for treatment of refractory DME.