Plantar warts, especially the mosaic types, are often very refractory to any form of treatment. Imiquimod is a imidazoquinoline compound with cytokine-inducing (including interferon) and immunomodulatory activities that has been approved for the topical treatment of genital warts. We report a 27-year-old woman with a painful plantar mosaic wart that been present for 5 years. She had been previously treated with topical salicylic acid and curettage without any success. Dermatologic examination revealed several hyperkeratotic contiguous plaques with multiple black points over their surfaces, covering her right heel. Several courses of cryotherapy in concomitant with 25% topical salicylic acid, topical 5-flurouracil, topical cantharidin (three courses), and intralesional bleomycin injections (three courses) were applied, but no evident regression was obtained with either of the treatment modality. Then, 5% imiquimod cream was prescribed, she started to use it every other night. Clinical improvement was noted starting at 2 weeks, with the complete clearance of the warts after 3 months. No adverse events were noted. During 12 months of follow-up, no recurrent lesions were observed. We suggest that topical 5% imiquimod is an effective, safe and painless modality for the treatment of recalcitrant plantar mosaic warts.