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CASE REPORTS

Methotrexate in Resistant ENL[1]

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ABSTRACT

This is a report of a case of steroid resistant severeType 2 reaction that was managed with methotrexate and prednisolone. Synergistic action of both the drugs in severe Type 2 reaction make them one of the preferred combinations in the absence of other agents such as thalidomide.

RÉSUMÉ

Cet article rapport un cas de réaction sévère de type 2, résistante aux corticostéroïdes, qui fut contrôlée par du méthotrexate et de la prednisolone. L 'action synergique de ces deux médicaments dans les réactions sévères de type 2 en fait une des combinaisons préférées en l'absence d'autres composés tels que la thalidomide.

RESUMEN

Este es el reporte de un caso de reacción leprosa tipo 2 resistente a esteroides que fue tratado con metotrexato y prednisolona. La actividad sinér gica de estas dos drogas en el tratamiento de la reacción tipo 2 severa, hacen que esta combinación sea la preferida cuando no se cuenta con otros agentes como la talidomida.

Corticosteroids will continue to dominate the drug list for management of reactions in leprosy until an ideal substitute is found. The aim of all those dealing with leprosy and its complications is always to minimize steroid-induced side effects. Methotrexate, being the most widely used antimetabolite by dermatologists the world over, is a particularly important candidate since it is well established.

CASE HISTORY

A 60-yr-old man was referred to Karigiri hospital with fever and multiple skin nodules of 20 days duration. The patient was a diagnosed case of multibacillary (MB) Hansen's disease and was released from treatment 4 months before upon completion of 12-month MB Multi-drug Therapy (MDT). He had no complaints of such attacks during treatment. He also complained of multiple joint pains along with pain along the medial border of left hand. On examination, the patient had multiple subcutaneous nodules of which a few had ulcerated over the back, face, and forearms. No skin patch was visible but there was diffuse skin infiltration with some areas of sparing. Both the ulnar nerves were thickened and the right ulnar had developed an abscess. Patient also had bilateral weakness of hands assessed by motor testing. The peripheral sensations were relatively preserved. On investigating, he had neutrophilia with toxic granules, slit skin smear was positive with a Bacillary Index (BI) of 3.75+ and Morphological Index of –0. Liver function tests and renal function tests were all within normal limits. ELISA for HIV was negative. Chest X-Ray was normal. No focus of infection could be found. Patient was diagnosed as a case of completely treated borderline lepromatous (BL) leprosy with severe Type 2 reaction and was started on systemic prednisolone

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40 mg/day. The abscess in the right ulnar nerve was managed with decompression and splinting. Erythema nodosum leprosum (ENL), as well as the features of toxicity, started subsiding within 4 days of initiation of steroid therapy, when the patient developed another crop of nodules along with fever. The dose of Presdnisolone was increased to 50 mg/day. The patient was still developing a number of new lesions of ENL even at that dose. After 2 weeks, methotrexate was added to the regimen, as he was not responding to steroid monotherapy satisfactorily and thalidomide was not available. It was given at a dose of 5 mg 12 hourly for 3 doses every week as the gastric upset was supposed to be less compared to a single dose regimen. After 2 weeks, the dose of methotrexate was tapered by 2.5 mg/week and at present he is receiving a dose of 7.5 mg every week in a divided manner along with a daily dose of 20 mg of Presdnisolone. The patient did not have any new ENL lesions after starting the additional methotrexate treatment.

DISCUSSION

Reactions are immune mediated complications seen in leprosy patients before, during, or after treatment with MDT. Pfaltzgraff, *et al*. ([1]) reported that almost half of the lepromatous cases and one quarter of borderline lepromatous cases experience ENL reaction. By definition, ENL is recurrent and self-limiting in the majority of cases. But some patients behave differently and are resistant to all modalities. Depending upon the severity of the ENL, various drugs are used ranging from non-steroidal anti-inflammatory agents in mild cases to corticosteroids and thalidomide ([2]) in severe cases. Thalidomide acts as a wonder drug in severe ENL ([3]) but it has its own limitations. Non-availability and high cost are the two major issues concerned with the routine use of the drug. The drug has to be given under supervision and is contraindicated in women of childbearing age in most of the countries. So practically speaking, corticosteroids are the main stay in management of the condition. The WHO recommended dose is 40 mg/day ([4]) and majority respond to this regime. Prednisolone ([2]) acts by suppression of cell mediated immunity, inhibition of release of lysosomal enzymes and cytokines, decrease of fluid leakage at the site of inflammation, decrease in the response of neutrophils to chemotaxis, and inhibition of prostaglandin synthesis, etc. The drug has to be tapered over 4 months, though in some patients the dose has to be individualized. This is likely to lead to a lot of complications ([5]). So the use of this drug should be judicious and the search is always on to find an ideal steroid-sparing agent. Methotrexate is being used for the treatment of psoriasis since late 1950s ([6]) and remains one of the most commonly used antimetabolites in dermatology practice. Dermatologists have been using this drug routinely since then and the safety record is so far impressive though hepatic and bone marrow side effects are the major concerns ([7]). Low doses of methotrexate suppress division of mononuclear cells and inhibit their response to interleukin 2, suppress neutrophil and monocyte chemotaxis *in vitro* and *in vivo,* and depress Langerhans cell activity and leukotriene B4 synthesis by neutrophils ([8, 9, 10, 11, 12, 13, 14]), which also contribute to the manifestations of ENL. So a synergistic action of methotrexate to corticosteroids is expected in ENL cases; in other words, it would act like a steroid-sparing agent in those who are likely to be put on a high dose of prednisolone for a prolonged period. Taking into consideration the side effects of methotrexate, the risk benefit ratio should be carefully calculated and individualized while combining it with prednisolone for the steroid resistant cases. Double blind controlled trials are welcome in the near future.

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