CORRESPONDENCE

CYCLOSPORINE THERAPY FOR REFRACTORY LANGERHANS CELL HISTIOCYTOSIS

To the Editor:

Mahmoud et al. reported partial responses to cyclosporine in three children with advanced Langerhans cell histiocytosis (LCH). All patients, newly diagnosed and previously untreated, had complete resolution of organ dysfunction and regression of the majority of lesions. Complete responses were then attained by adding steroid and/or vinblastine.

We report one case of LCH in whom progressive disease after conventional antiblastic chemotherapy was successfully treated with cyclosporine.

The girl presented at 5 months with systemic disease including organ dysfunction (liver and bone marrow). After front-line treatment with etoposide she developed a poor response and then progressive disease: fever, skin rash, severe anemia, diabetes insipidus, lung infiltration, skull bone lesions, and adjacent soft tissue swelling with severe exoftalmus. Vinblastine and oral prednisone (2 mg/kg/d) were substituted for etoposide. No result was obtained and therapy was changed into combined treatment with oral prednisone (2 mg/kg/d) and cyclosporine (two oral doses, 6 mg/kg/dose). There was immediate constitutional improvement, evidenced by resolution of fever and skin rash, weight gain, increase in hemoglobin level, and disappearance of exoftalmus and lung infiltration. Steroid could be withdrawn by 4 months, while cyclosporine was continued at the same dosage. This child remains in complete remission 9 months after starting treatment. She had no relevant toxicity and diabetes insipidus is controlled under oral 1-desamino-8-D-arginine Vasopressin (DDAVP).

Young children with systemic LCH are at high risk to develop progressive disease, refractory to conventional treatment including antiblastic agents such as vinblastin and etoposide. Use of etoposide in LCH as in other nonmalignant disorders is to be carefully considered after the report of therapy-related myeloid neoplasia in children who had received etoposide. Thus, satisfactory treatment regimen for high-risk LCH patients was not yet achieved. Reports of response to treatment with cyclosporine are urgently needed to evaluate the role of this relatively nontoxic agent, both in untreated or refractory patients. A pilot study for use of cyclosporine in LCH children with organ dysfunction could be hypothesizable within some cooperative group, such as the international “Histiocyte Society,” to assess one treatment protocol for refractory patients. If preliminary favorable results will be confirmed, early front-line treatment with cyclosporine for high-risk patients could be considered.

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REFERENCES

RESPONSE

Dr Arico’s findings of response of a refractory case to cyclosporine (CSA) confirms our results that CSA is of potential benefit in treating children with Langerhans cell histiocytosis (LCH) and this needs to be verified in a larger multicenter randomized trial. Of interest, complete remission in Dr Arico’s patient was also obtained with CSA and prednisone therapy.

Again, the risk of developing therapy-related secondary neoplasia in patients with LCH has been documented by Greenberger et al in seven (11%) of their treated surviving patients. Thus, the addition of etoposide to treatment protocols in these patients is a considerable risk for developing therapy-related malignancy.

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REFERENCE
Cyclosporine therapy for refractory Langerhans cell histiocytosis [letter; comment]

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