Successful treatment of scleromyxedema with dexamethasone cyclophosphamide pulse therapy

Sir,

Scleromyxedema is an uncommon disorder of mucin deposition associated with paraproteinemia, especially IgG gammopathy.[1] Its pathogenesis is still uncertain, but there are various hypotheses, one of which suggests that some circulating factor, not the paraprotein, might be stimulating fibroblast activity.[2] Scleromyxedema shows little tendency for spontaneous remission. Its treatment is frequently disappointing and the evidence of therapeutic efficacy is largely anecdotal.[3] We would like to share our experience of using dexamethasone-cyclophosphamide pulse (DCP) therapy in a patient of scleromyxedema. We chose DCP therapy because of its successful use in auto-immune disorders like pemphigus, scleroderma and SLE.[4,5]

A 45-year-old male presented to us with gradually progressive asymptomatic hyperpigmentation and tightening of skin for three years. There was no history of Raynaud's phenomenon. He was enjoying good general health otherwise. Personal and family history excluded silicosis, collagen vascular disease, thyroid disorder, neoplasm or drug reaction.

Cutaneous examination revealed firm, closely set, lichenoid papules and plaques over the face, neck, buttocks and both extremities. The underlying skin showed generalized thickening and sclerosis. The skin of the forehead showed vertical furrows. Systemic examination was unremarkable.

Routine hematological investigations revealed mild iron deficiency anemia and raised ESR (60 mm/1st hr). Serum biochemistry was normal. A chest X-ray and USG of the abdomen were normal. ANA test and thyroid function tests were normal. Serum electrophoresis did not reveal paraproteinemia. Histopathology of lesional skin revealed epidermal atrophy, and diffuse deposition of mucin in the papillary dermis that stained with Alcian blue. There was fibroblast proliferation, thickening and homogenization of collagen bundles with mild perivascular mononuclear infiltration.

He was treated with dexamethasone-cyclophosphamide pulse therapy which consisted of 100 mg dexamethasone dissolved in 500 ml of 5% dextrose intravenous infusion given for 3 consecutive days along with cyclophosphamide 500 mg intravenously on day 2 every month. Therapy was well tolerated. Initial clinical improvement was noticed after the third pulse and a near total softening of skin was achieved after 24 DCP pulses.

The mechanism through which DCP worked in our case is uncertain but it is likely that DCP either directly inhibits fibroblast proliferation or a circulating factor responsible for fibroblast proliferation. DCP seems to offer promise in this disorder that is difficult to treat.

C. M. Kuldeep, A. K. Mittal, L. K. Gupta, V. K. Paliwal, P. Sharma, A. Garg
Departments of Dermatology, Venereology and Leprosy, RNT Medical College, Udaipur, India.

Address for correspondence: Dr. C. M. Kuldeep, Professor and Head, Departments of Dermatology, Venereology and Leprosy RNT Medical College, Udaipur - 313001, Rajasthan, India.
Email: asit_mittal@yahoo.com

REFERENCES

1. Dinneen AM, Dicken CH. Scleromyxedema. J Am Acad Dermatol 1995;33:37-43.
2. Harper RA, Rispler J. Lichen myxedematous serum stimulates human skin fibroblast proliferation. Science 1978;199:545-7.
3. Lister RK, Jolles S, Whitteker S, Black C, Forgacs I, Cramp M, et al. Scleromyxedema: Response to high dose intravenous immunoglobulin (hdIVIG). J Am Acad Dermatol 2000;43:403-8.
4. Pasricha JS, Thanzama J, Khan UK, Intermittent high dose dexamethasone cyclopospamide therapy for pemphigus. Br J Dermatol 1988;119:73-7.
5. Pai BS, Srinivas CR, Sabitha L. Efficacy of dexamethasone pulse

therapy in progressive systemic sclerosis. Int J Dermatol 1995;34:726-8.

Generalized hypopigmentation due to imatinib: A fairness boon?

Sir,

Imatinib (STI571, Glivec©) is a new selective tyrosine kinase inhibitor that is very useful in the treatment of chronic myelogenous leukemia (CML) and gastrointestinal stromal tumors (GIST). More side effects are being reported with its increasing use. We report generalized hypopigmentation with the use of this drug.

The majority of CML and GIST patients on imatinib mesylate experience some undesirable side effects that involve many organ systems in the body, including the skin. The most common dermatological side effects are periorbital edema and dermatitis. Facial edema, pruritus, erythema, dry skin, alopecia, night sweats and photosensitivity reaction are infrequently reported.[1]

Over 120 patients of CML or GIST are being treated with imatinib at our institute since 2001. For the last one year, during routine outdoor visits, many patients have been reporting that their skin was becoming fairer while on imatinib. We interviewed 26 patients regarding this side effect; 22 of the patients and their relatives confirmed this experience at varying durations of treatment (median 2 months; range 2 to 8 months). Three patients in whom the drug had to be discontinued because of different reasons reported that their skin complexion had reverted to the original one.

Skin biopsies were performed on seven of these 'fair' patients. On H and E staining, even though melanin pigment was seen in all of these biopsy specimens, low melanin content was observed in two of them. In the absence of a pretreatment biopsy, quantification of the melanin pigmentation was not possible. Currently, we are doing electron microscopy and tyramine based tyrosinase assay on the skin biopsies performed pre- and post-imatinib treatment for quantification of the melanin deposition in melanosomes.

The exact mechanism for this generalized hypopigmentation with imatinib is not known. Apart from inhibiting a tyrosine kinase, the BCR-ABL oncoprotein, imatinib also inhibits platelet-derived growth factor receptors (PDGFRs) and c-KIT receptor tyrosine kinases.[2] The latter two kinases have important roles in normal pigmentation.[3] Certain hypopigmentary disorders like piebaldism and vitiligo are associated with mutations in the c-KIT gene causing alteration in the respective tyrosine kinases.[4] Tsao et al recently reported a similar finding.[5] However, we found hypopigmentation to be much more common than they did, possibly because it is more apparent in Blacks or Indians because of their otherwise dark skin complexion. Based on our observation, we hypothesize that inhibition of melanocyte c-KIT receptor tyrosine kinase by imatinib leads to generalized hypopigmentation. The long-term implications of this observation need to be studied. Meanwhile, it will be interesting to see whether topical use of imatinib is possible in the future.

Atul Sharma, Amish Vora, Manisha Bhutani
Department of Medical Oncology, Institute Rotary Cancer Hospital, All India Institute of Medical sciences, New Delhi, India.

Address for correspondence: Dr. Atul Sharma, Assistant Professor of Medical Oncology, Department of Medical Oncology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi - 110029, India. E-mail: atul1@hotmail.com

REFERENCES

1. Glivec® (imatinib) Summary of Product Characteristics. Basel, Switzerland: Novartis Pharma AG; 2001.
2. Buchdunger E, Cioffi CL, Law N, Stover D, Ohno Jones S, Druker BJ, et al. Abl protein-tyrosine kinase inhibitor STI 571 inhibits in vitro signal transduction mediated by c-kit and platelet-derived growth factor receptors. J Pharmacol Exp Ther 2000;295:139-45.
3. Luo D, Chen H, Searles G, Jimbow K. Coordinated mRNA expression of c-Kit with tyrosinase and TRP-1 in melanin pigmentation of normal and malignant human melanocytes and transient activation of tyrosinase by Kit/ SCF-R. Melanoma Res 1995;5:303-9.
4. Dippel E, Haas N, Grabbe J, Schadendorf D, Hamann K, Czarnetzki BM. Expression of the c-Kit receptor in hypomelanosis: A comparative study between piebaldism, nevus depigmentosus and vitiligo. Br J Dermatol 1995;132:182-9.
5. Tsao AS, Kantarjian H, Cortes J, O'Brien S, Talpaz M. Imatinib mesylate causes hypopigmentation in the skin. Cancer