TREATMENT OF PSORIASIS WITH DIALYSIS


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Summary

Five patients with psoriasis were treated with haemodialysis. Dialysis therapy was initiated for subsequent development of uraemia in three cases. All of these had successful renal transplants without recurrence of psoriasis while being maintained on post-transplant anti-rejection regimens. Two other cases were haemodialysed, not for uraemia but primarily for psoriasis. One case had moderate improvement of psoriasis after twice-weekly dialysis for two months while the second had no objective improvement up to one month after a single haemodialysis treatment.

Introduction

Psoriasis, a disease of unknown aetiology, affects between one and three percent of the population [1]. Current treatments with topical steroids, tar, tar and light combinations with ultraviolet light of B wavelength or psoralens in combination with ultraviolet light of A wavelength may be ineffective in some cases [2,3]. Antimetabolites are effective but have deleterious side effects [4].

Some patients who had recalcitrant psoriasis and who later contracted severe renal disease have had long-term remissions after dialytic therapy both by haemo and peritoneal dialysis techniques [5-7]. Although remissions were prolonged, some recurrences were noted [7]. Other psoriatics who did not develop uraemia were treated with peritoneal dialysis with variable degrees of success [8]. To those reports, we now add our personal experience with five patients.

Case Reports

Case No.1 A 51-year old female had uraemia secondary to polycystic kidney disease. She had a sixteen year history of psoriasis involving the face, scalp, neck, buttock, abdomen, knees and nails. Attempts at control of her skin
problems with various shampoos, fluorinated topical steroids, and keratolytic agents were unsuccessful. Haemodialysis was begun on June 2, 1977 for six hour periods three times per week. After five dialyses all skin lesions cleared and she was able to discontinue her topical therapy. Dialysis was continued on the same schedule until October 6, 1977 when she received a renal transplant. Currently, six months post-transplant, she has normal renal function with a creatinine of 0.7 mg% and no other known laboratory abnormalities. Her post-transplant medications include prednisone 20 mg daily, azathioprine 125 mg daily, and sulfisoxazole 1 gram 4 times daily. Psoriasis has not recurred.

Case No. 2 A 37-year old male had renal failure secondary to chronic glomerulonephritis. Psoriasis had persisted for twenty years involving scalp, elbows, face, knuckles, hands, and buttocks. Attempts at control of his skin problems with various shampoos, fluorinated topical steroids, and tar preparations were only moderately successful. Haemodialysis was begun January 3, 1970 for six hour periods, two to three times weekly. Psoriasis cleared after fifteen days and he was able to discontinue all topical therapy. He received a renal transplant on August 1, 1973. Now, four and a half years post-transplant, he has a creatinine of 1.6 mg% with BUN of 20 mg%. Psoriasis has not recurred. His current post-transplant medication regimen includes prednisone 22.5 mg daily, azathioprine 100 mg daily, sulfisoxazole 1 gram 4 times daily, spironolactone 25 mg 3 times daily and hydrochlorothiazide 50 mg 3 times weekly.

Case No. 3 A 55-year old male had renal failure secondary to chronic pyelonephritis. His history of psoriasis spanned 38 years with involvement of the hands, elbows, scalp, knees, buttocks and nails. Despite the application of topical medications, shampoos and keratolytic agents the psoriasis continued. Haemodialysis was begun July 30, 1972 for six hour periods two to three times per week. Skin lesions began to clear at two weeks and were totally gone by one month after institution of the dialysis therapy. He discontinued all topical therapy and received a transplant on September 15, 1972. Currently, five and a half years post-transplant, he has a creatinine of 1.2 and psoriasis has not recurred. Post-transplant medications include prednisone 10 mg twice daily, azathioprine 50 mg twice daily, sulfisoxazole 500 mg 4 times daily, and coumadin 10 mg daily.

Case No. 4 A 74-year old lady had psoriasis and was without any renal abnormalities. Her psoriasis was extensive involving the face, scalp, neck, chest, trunk, arms, legs, hands, feet, and nails. The psoriasis did not respond satisfactorily to topical steroids, tars in combination with ultraviolet B light or psoralen in combination with ultraviolet A wavelength light. She did have a response to methotrexate but it was discontinued because of minor elevations of liver enzymes and the possibility of further hepatic damage. During a course of psoralen and ultraviolet A wavelength light therapy she became photosensitive. Thus, dialysis was initiated on February 23, 1978 on a six hour, twice weekly schedule. She experienced improvement of her psoriasis within the first two weeks and now continues to show slow resolution of the various psoriatic lesions two months after haemodialysis has been initiated.
Case No. 5 A 27-year old male without renal disease had psoriasis of 21 years duration. It involved the face, the scalp, chest, trunk, extremities, buttocks and pubis. Attempts at therapy with topical steroids, various shampoos, and tars in combination with ultraviolet B light were at times successful but during recent years became less effective. Thus he was given one haemodialysis on April 1, 1978. This dialysis was done for eight hours against a two square metre Lundia major dialyser with blood flows of 400 ml per minute and systemic heparinisation. Although there was no objective improvement in his psoriasis, he felt that there was an initial subjective improvement. His mother died ten days after therapy was initiated and his psoriasis flared.

The first five cases were dialysed against a one square metre Lundia Nova dialyser. The first three were heparinised regionally while Cases No.3 and No.4 received systemic and constant regional heparinisation.

Comment

It is apparent that dialysis does have a beneficial effect on some psoriatics but that this effect may not be permanent or totally curative. Although successful therapy of non-uraemics with peritoneal dialysis has been reported [8], our non-uraemics have not, as yet, demonstrated dramatic improvement. It should be noted, however, that one patient received only one haemodialysis treatment.

It is interesting to speculate on the mechanism of the dialytic effect on psoriasis, a disease characterised by rapid epidermal turnover and intense inflammation. These phenomena are probably interrelated, since psoriatic scales contain substances which are chemotactic and chemokinetic for neutrophils [9]. It is likely that the inflammatory infiltrates may in some way modulate the lesion in psoriasis. It is also possible that leucocyte-elaborated products such as lymphokines or 'monokines', as well as enzymes released by degenerating cells may influence epidermal proliferation and growth control substances [10].

Furthermore, serum contains growth factors which affect a wide variety of tissues and cell types, including epidermal cells and fibroblasts [11]. Epidermis, exposed to serum, whether due to injury as in the case of a wound or to inflammation as in the case of psoriasis, is bathed in a nutrient-rich and growth factor-rich medium which may facilitate proliferation of these cells. Control of proliferation then may be dependent upon integrity of the dermal vasculature and the absence or presence of an inhibitory inflammatory cell infiltrate.

Initially one might have postulated removal or infusion of substances through the dialysis membrane. However, a psoriatic has recently been seen to clear after cardiopulmonary bypass oxygenation for open heart surgery (case report in preparation). Thus one might favour an immune mechanism related to the exposure of a constantly exchanging portion of blood through the extracorporeal unit or medications used in association with that unit. Immunological mechanisms seem attractive because chemotaxis which is depressed in uraemia, appears to be further depressed by dialysis treatment [12]. During dialysis, complement is activated and large amounts of C5a are
produced. Polymorphonuclear cells are apparently initially activated by the C5a (increased chemotaxis, increased metabolic activity) and by this mechanism eventually deactivated through exhaustion of their enzyme or energy systems [13]. The early activation may account for the leucopenia and increased neutrophil adherence (and accumulation) in the lungs already documented to occur early in the dialysis procedure [14]. The question is whether or not these cells recover their normal function with time. Preliminary studies regarding this point are being carried out but are not conclusive at the time of this publication.

Other mechanisms of relevance may be the depressed folate levels which can occur in dialysis and might interfere with DNA synthesis, analogous to the beneficial effect on psoriasis of the inhibition of transformation of dihydrofolate to tetrahydrofolate by methotrexate [4]. Glucose-6-phosphate dehydrogenase may be abnormal in dialysis [15] and this enzyme is essential to the Krebs’ cycle, the glucose monophosphate shunt, and to the energy generation system within the cell. Further, the dialysis-induced leucopenia may relate in some way to the remission of psoriasis with hydroxyurea-induced leucopenia although the mechanism by which a short-term dialysis-induced leucopenia could affect the long-term course of psoriasis is speculative at the very least. There is also increased heparin-precipitable cryofibrinogen in psoriasis [16,17]. Thus changes in this substance may be significant especially in view of the use of heparin during the procedure. Finally, prostaglandins and intracellular cyclic nucleotides may be of importance in the explanation of the pathophysiology of psoriasis. While the theory that depressed levels of cyclic AMP cause increased epidermal proliferation may now have become outmoded, there is a growing body of evidence suggesting that cyclic AMP formation is less than optimally stimulated by physiological levels of naturally occurring prostaglandins in psoriasis. This may be due to either a qualitative or quantitative defect of these substances or their intermediates [18]. The actual defect may be secondary to inhibition of prostaglandin synthesis [19], or, insensitivity of adenylate cyclase receptor sites to prostaglandin stimulation [20] secondary to a structurally abnormal membrane-bound enzyme complex [19–23]. Newer ideas indicate that short-lived prostaglandin endoperoxide intermediates are involved in cyclic GMP metabolism [24]. These substances have not yet been measured in epidermis, but may be important in light of recent studies showing that cyclic GMP rather than cyclic AMP may be more influential on cellular proliferation in many tissues, including epidermis [25–27]. Basal cell proliferative rates, then, may be controlled directly or indirectly by intracellular cyclic nucleotide systems and their modulators.

Conclusion

It is apparent that dialysis and possibly exposure of an extracorporeal segment of the blood to cardiopulmonary bypass oxygenation machinery may advantageously affect the course of psoriasis. The procedure is not always effective and remissions achieved may be short-lived with relapses occurring either spon-
taneously or after withdrawal of antirejection medications. The procedure may not produce early remission and there is at least preliminary evidence that one dialysis may not be effective. While the mechanism of action is unknown, we favour immunologically-mediated effects.

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Open Discussion

GURLAND (Munich) We recently treated a 39-year old man with acute renal failure who had been suffering from severe psoriasis for approximately 20 years. We dialysed him eight times over a period of two weeks. At the end of dialysis there was no further evidence of any psoriasis and he remained free of the condition for one month. Five weeks after the termination of dialysis, however, his psoriasis had returned to the same severe degree we had seen prior to dialysis.

BUS ELMEIER There are some failures I certainly agree. The question is why?
DOWZENKO (Warsaw) We have a patient with psoriasis and uraemia. The psoriasis disappeared with haemodialysis. We treated psoriasis without kidney disease with peritoneal dialysis. In one patient this was successful and two improved. The dialysis fluid contained very many leucocytes.

BRUNNER (Basel) We have experience of two patients with psoriasis who were dialysed. One got relief from his psoriasis, the other did not. The one who got relief was later transplanted, and a few months after transplantation he developed the same frequency and the same intensity of psoriatic flare-ups. So it might be wise to warn psoriatic uraemics on dialysis whose skin problem is cured that they might develop a recurrence of psoriasis after successful transplantation.

BUSELMEIER It is interesting to note that the uraemic patients seem to respond better than non-uraemic patients to dialysis therapy. Both MacIlroy's case and one of the most recent cases reported in the British Medical Journal did have recurrence of their psoriasis after withdrawal of anti-rejection medicine which was given during their post-transplant period of six months to a year, but did not have recurrence of their psoriasis during their non-uraemic state with the transplant and the anti-rejection medicine.

BEHROOZ BROUMAND (Tehran) I would like to speculate that in psoriatic patients there is some material which is retained in the blood which can be removed by dialysis, but in the normal kidney is reabsorbed in the tubules after glomerular filtration. Have you tried to find any unusual substances in the blood of psoriasis patients?

BUSELMEIER No I haven't. One will have to look further at the effect of cardiopulmonary bypass oxygenation. This might dispel your theory. I am sure that people will now look at more patients who are having heart surgery and will see in these cases, where nothing is removed from the blood, whether or not psoriasis is cleared.

PECCHINI (Cremona) Have you experience in the treatment of porphyria with different dialysis membranes?

BUSELMEIER No experience whatsoever. I would be interested in yours.

KLINKMANN (Chairman) Well, you know there was a short discussion about the influence of different dialysis membranes on psoriasis as well as on schizophrenia, and I am quite happy that no one around here is giving a paper on schizophrenia today, to add to the confusion.

FARR (Hull) Psoriasis is a very common disease which waxes and wanes and dialysis is a very expensive form of treatment. I would just like to mention that we have two patients, both of whom have psoriasis. One patient has been on dialysis for about eight years and his psoriasis waxes and wanes as he gets upset or he has a little domestic problem. And so his psoriasis occurs again. And when the problem settles down, his psoriasis settles. Now he is on regular haemodialysis and dialysis has not really helped him much. We have a second patient who has been on dialysis for six months, and his psoriasis remains much the same.
BUSELMEIER I think that is an important observation. We have one case who gets worse each haemodialysis and that may mean, if one listens to the peritoneal dialysers, that maybe he should be tried on peritoneal dialysis to clear skin disease as well as his uraemia. Can I just ask one more thing? Everybody here has had some experiences with dialysis and psoriasis, and I would be happy to correspond with anyone to put together all of our different experiences; for instance, which membrane, how much heparin, which type of dialysis, what different techniques were used, in order to study the specific effect which may cause this alleviation of the skin disease. Thank you.

KLINKMANN Thank you very much, Ted, for this offer. Just to add a little bit more to the confusion, we had a patient who was cured of psoriasis before entering the dialysis programme, and after being on dialysis for one year, re-developed very severe psoriasis. So let’s all write to Ted.