Blood transfusion and dermatology

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SUMMARY

Blood transfusion is an accepted therapeutic procedure in all specialties of medicine. In dermatology, specialized techniques like plasmapheresis and extracorporeal photochemotherapy have provided a good treatment option in immune-mediated disorders like bullous dermatoses, collagen vascular diseases and cutaneous lymphomas. Other anecdotal and less substantiated reports point to its use in chronic disorders like atopic dermatitis and psoriasis. Untoward dermatological manifestations include mainly purpuric rash and GVHD. Since planned studies may not be possible, pertinent observations from chance situations on the effect of blood transfusion in dermatoses would add valuable information.

KEY WORDS

blood transfusion, dermatological disorders, adverse effects

Introduction

Blood transfusion (BT) is a life saving procedure. Blood letting (venesection) was widely practiced from the time of Hippocrates (circa. 430 BC) for variety of medical conditions. In 1628,William Harvey(1) published his book *Exercitatio Anatomica* de *Motu Cordis et, Sanguinis in Animalibus* which established that blood circulated through the body and could be added or subtracted from the body. In March 1656, Boyle, Wilkins and Wren discussed possibility of developing "a way to convey any liquid poison in the Mass of Blood" (2) Wren isolated the crural vein of a dog, inserted a thin syringe tube and injected a solution of opium. In 1667, Jean-Baptiste Denis, an eminent physician to King Louis XIV of France, transfused calf's blood into a manic patient thinking it would calm him down; unfortunately the madness recurred and he died. Following this, BT was not used and remained unexplored for as long as one and a half centuries. Revival coincided with improved instruments and techniques. The first person credited with human to human BT was James Blundell (3), an English obstetrician, who also insisted that only human blood had to be used. Nevertheless fatalities occurred till the procedure was rendered safer by the discovery of blood types by the Austrian pathologist Karl Landsteiner (4) in 1900.The outbreak of the Second World War stimulated work towards fractionation

of blood. Cohn (5) isolated various fractions of plasma proteins in 1940, which had a dramatic effect on lives of patients. This represented the beginning of the modern era of transfusion medicine.

BT is one of the most frequently employed procedures in medicine. Modern BT was developed during the 20th century. BT has been used in the treatment of diseases of organs as small as the eye (6) to ones as large as the liver (7). Understandably, skin diseases are no exception, and studies of the relationship of BT to skin diseases are very old (8, 9). Of late BT has been used successfully to treat many dermatoses. In this report, we wish to evaluate the current role of BT in this role. The report is divided into three main groups, the first that enumerates disorders treated by blood products using sophisticated methods which are mostly accepted procedures; a second group that lists disorders in which BT has been used as a therapeutic attempt to modify the disease; and a third group that pertains to adverse effects following BT.

Specialized methods using blood products to treat dermatological disorders

1. Therapeutic plasmapheresis (10,11). The term plasmapheresis means 'taking away plasma' and was first used by Abel (12) et al, to describe the removal of small amounts of plasma (500-650 ml) without infusing any fluid as replacement or infusing only saline. This allows for the removal of cytotoxic antibodies, immune complexes, inflammatory mediators, paraproteins, drugs and antigens. It also enhances the function of the reticuloendothelial system, removes blocking antibodies and makes lymphocytes more vulnerable to immunosuppresion. It has definite therapeutic advantage in the following conditions:

(i) Bullous disorders (13-15): pemphigus vulgaris, paraneoplastic pemphigus, bullous pemphigoid.
(ii) Collagen vascular diseases (16-22): systemic lupus erythematosus, systemic sclerosis, severe localized scleroderma, dermatomyositis, polymyositis
(iii) Miscellaneous: toxic epidermal necrolysis (23), epidermolysis bullosa equisita (24), pyoderma gangrenosum, (25) chronic idiopathic urticaria (26), porphyria cutanea tarda (27), papular mucinosis (28), severe intractable psoriasis (29), solar urticaria (30).

2. Extracorporeal phototherapy (ECP) (31-36). ECP is a procedure involving concentrated WBC, spiked with 8-Methoxypsoralen (8 MOP), exposed to a UVA source and then reinfused into the patient. ECP causes activation of macrophages against neoplastic cells (as in Cutaneous T-Cell Lymphoma CTCL) and downregulation of the activity of T cell clones in autoimmune diseases. The overall response rate for CTCL's is 55.7%. It has been successfully used in GvHD. It causes stabilization and partial remission of cutaneous findings in systemic sclerosis.
3. Platelet derived growth factor, Platelet gel (Becaplermin Gel) (37). Platelet gel is a mix of concentrated platelets and cryoprecipitate activated by batroxobin in the presence of calcium chloride. It has been used for topical therapy on the lower extremities, neuropathic, diabetic and full thickness chronic pressure ulcers.

Dermatological conditions modified by blood transfusion

Here BT has been given to cure or mitigate the illness. They can be categorized as follows:

1. Through *restoration of some component of blood.* If the condition has resulted from a deficiency of some blood component then there is no better alternative to BT. Skin rash accompanied by fever and arthralgia results from a hereditary deficiency of C3, and disappears after BT (38).
2. *Autohemotherapy.* The procedure was widely used in the preantibiotic era to foster the immunologic response such as in the treatment of furunculosis. This is based on the principle that autologous blood therapy has immunomodulating effects that elicit a beneficial response. It has been used mainly in atopic dermatitis in some European countries and promoted on internet sites. In a double-blind placebo-controlled trial, 31 patients were given an intramuscular injection of 1 ml of their own venous blood into the thigh. The data suggested some relief but this was not corroborated by patient rated assessments (39). This form of therapy has also been tried in chronic urticaria, a condition related to atopic dermatitis, and the authors reported a subsidence of pruritus, a decrease in weal formation and an increased interval between two episodes (40). It has been suggested that the effect on immune parameters such as IL10, and the activation of macrophages and T-cell subpopulations are involved (41-42).
3. *Modification of the Immune System.* It has long been the subject of debate whether a transient immunosuppression results from BT (43), and this intended consequence has led to its use in psoriasis, a T-cell mediated autoimmune disease. However, results have fallen short of proving its usefulness (45).
4. *Miscellaneous.* BT has been used in other dermatoses like Pautrier's lipmelanotic reticulosis (45) but the exact effect is unclear.

Dermatological adverse effects of blood transfusion

The changes caused by BT are complex, not clearly known and need to be elucidated by well-planned studies. Many mechanisms may play a role in giving rise to adverse effects. They include the adoptive transfer of immunity to the recipient, autoimmune phenomena, Koebner's phenomenon and microchimerism, which refers to a condition in which a person has circulating non-self cells (46). The most important adverse reaction to BT is graft-versus-host disease (GVHD). Transfusion of blood products that contain viable T lymphocytes can lead to GVHD in patients with deficient cell-mediated immunity (47). Clinically, transfusion associated GVHD occurs 2-30 days after BT and presents as a fever followed by a rapidly spreading exanthem and systemic manifestations.

Post-transfusion pupura (48) has a history of being a reported hazard of BT, which occurs mainly in women with a latent period of 2-7 days .

BT has also been implicated in erythroderma following cardiac surgery (49) cutaneous necrosis in cold agglutinin disease (50) and self-limited periocular reaction (51). BT was said to have resulted in a purpuric phototherapy-induced eruption in six neonates. Blood levels of both coproporphyrin and protoporphyrins were elevated. Hepatic cholestasis, poor hepatic metabolism or release of porphyrins by hemolysis of erythrocyte precursors were thought to be the source of the porphyrins (52). In some cases skin lesions were associated with systemic symptoms like purpura with hypertension and convulsions (53), or with other disorders like vitiligo seen along with Sjogren syndrome (54).

Conclusion

There is no consistent pattern to the progress or relief of skin diseases following BT since most of the reports are anecdotal. A controlled study in a large group may not be possible due to ethical and medical limitations. It may however be possible to make pertinent observations on patients with skin diseases when they are required to undergo BT for other reasons.

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