CONTINUING MEDICAL EDUCATION

HAEMOGRAM IN DERMATOLOGY

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Dermatology has often been referred to as a speciality that is only skin-deep. The astute dermatologist can learn to rely on keen observation and trained palpation for effective diagnosis. Though clinical acumen may suffice in a large proportion of cases, a back-up of side-lab and other specialized investigations may be necessary in certain situations. The haemogram is an investigative tool that is often considered the prerogative of other specialities. But it could be of immense value to the dermatologist if interpreted carefully. It could tilt the tide in favour of a diagnosis, determine the course and prognosis or help to make a therapeutic decision.

The haemogram to the dermatologist has a role in two major clinical situations. The first is when a primarily haematological disorder like sickle-cell anemia presents with a cutaneous manifestation such as a leg ulcer. The second is when a cutaneous disorder like eosinophilic fasciitis reflects on the haemogram.

Haemoglobin

The normal values of haemoglobin are 15.5 ± 2.5 gm/100 ml in the adult male, and 14.0 ± 2.5 gm/100 ml in the adult female.[1] In addition, other parameters usually scanned in relation to anemia include a haematocrit and a reticulocyte count (0.2-2% in adults). Increased haemoglobin and haematocrit values are a feature of polycythemia rubra vera which may manifest to the dermatologist as plethora or generalized pruritus[2] especially after a shower.

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Anemia, a qualitative or quantitative decrease in the oxygen carrying capacity of blood manifests as pallor. The severity of anemia can reflect in the degree of pallor, pale palmar creases signify a haemoglobin of < 7 gm%.[3] Cutaneous pallor may however, be misleading as is evidenced by the pseudo-pallor seen in myxoedema[4] which is due to an increase in the thickness of skin, causing refraction of light, and a greater amount of carotene in the skin. Pallor therefore, is more reliably interpreted based on the conjunctival or mucosal findings.

Iron deficiency anemia may present as koilonychia—a spooning or scalloping of the nail resulting in a positive water drop sign.[5] Glossitis and generalized pruritus[2] may also be the presenting complaints. The cutaneous examination may reveal features suggesting the cause such as a bleeding disorder, or other deficiency manifestations like cheilitis, angular stomatitis or the flag sign.

Pernicious anemia, being an auto-immune disorder, may manifest in association with other auto-immune disorders of the skin including vitiligo and alopecia areata.[6] In addition, premature canities has been described in patients with pernicious anemia. Haemolytic anemia may be due to intracorpuscular causes as in sickle-cell anemia or due to extracorpuscular causes including drugs, paroxysmal cold haemoglobinuria or hypersplenism. Upto 75% of all cases of sickle-cell anemia have leg ulcers. Leg ulcers are also seen in thalassemia[9] and spherocytosis.[10] Haemolytic anemia may occur as a part of SLE,[11] Gunther's disease[12] or as a

complication of dapsone therapy especially in patients with a G-6PD deficiency.[13]

Anemia may be only a part of pancytopenia in Fanconi's anemia in which skeletal abnormalities coexist with a mottled hypo/hyper-pigmentation of the skin. Pancytopenia is also a manifestation of dyskeratosis congenita and Chediak-Higashi syndrome.[14]

Primary cutaneous disorders may also have anemia as a feature. In exfoliative dermatitis, as in psoriasis, upto 50 gm of scales may be shed every day.[15] The iron content of the stratum corneum is approximately 26 μg/gm. Iron loss of 2.5 mg/day from the skin alone may thus contribute to anemia in erythroderma.[16] The associated dermatogenic enteropathy may be another contributory factor.[17] Similarly, dermatitis herpetiformis is also linked with coeliac disease which can in turn lead to malabsorption and deficiency anemia, in addition to other factors such as achlorhydria. Progressive systemic sclerosis may manifest as a multifactorial anemia.[18] Diverticulosis and atony result in bacterial proliferation as in a blind loop syndrome. This can interfere with vitamin B_{12} and folate absorption. Iron deficiency may also be a consequence of GI bleed. Micro-angiopathic haemolytic anemia occurs due to fibrin deposition and finally a hypoproliferative anemia is a feature of any chronic inflammatory disease. All or any of the above factors could contribute to the anemia in scleroderma.[19] Anemia has been documented in leprosy patients[20] and the relative contribution of undernutrition, chronic disease and drugs are the subject of debate.

Leukocytes

The normal total leukocyte count generally ranges from 4,500-11,000/cu mm, and neutrophils (40-60%), lymphocytes (20-40%), eosinophils (1-3%), basophils (0-1%) and monocytes (4-8%) form the components.[1] Leukopenia may occur as a part of pancytopenia in conditions enumerated earlier and in the end-stage marrow infiltration. Leukopenia is a criterion for the diagnosis of AIDS-related complex (ARC) and AIDS.[21] In addition, drugs and SLE[11] may cause a significant depression in the number of circulating leukocytes. Neutropenia is a feature of viral infections including measles and rubella. Granulocytopenia is considered to be a poor prognostic indicator in toxic epidermal necrolysis.[22]

Leukemia may manifest as leukemia cutis in the form of nodules or ulcerated plaques. Erthroderma, erythema muitiforme, erythema nodosum, pyoderma gangrenosum and Sweet's syndrome could be the presentation of an underlying leukemic process.[23] Acute myeloblastic leukemia may present with a characteristic chloroma, while upto 34% of the patients with acute monocytic leukemia may show gum hypertrophy.[24] A blood picture alone may mislead the unwary in a leukemoid reaction as has been reported with acne fulminans.[25]

Neutrophilia is a feature of Sweet's syndrome and was initially considered an essential diagnostic criterion.[26] A count of 10,000-20,000 white cells/cu mm is common. Acute generalized pustular psoriasis of von Zumbush,[27] dapsone syndrome,[13] and high dose corticosteroid therapy may also manifest with neutrophilia.

Basophils are found in an absolute count of 40 ± 3.2/cu mm of peripheral blood and > 50/cu mm is considered to represent basophilia[1] which is an initial step in the dermatological disorders mediated by cutaneous basophil hypersensitivity or the Jones-Mot reaction.

Eosinophilia is an ubiquitous phenomenon seen in conditions ranging from chronic urticaria, worm infestation and cat-scratch disease to bullous pemphigoid and incontinentia pigmenti.[29] The diagnostic significance in the above conditions is not absolute but some skin disorders are consistently characterized by eosinophilia (Table I).

Table I. | Skin disorders characterized by eosinophilia.

Disease	Eosinophil counts	Skin features
Hypereosinophilic syndrome[30]	1500/cu mm diagnostic criterion	Urticaria, angioedema, pruritic rash.
Eosinophilic fasciitis (Shulman's syndrome[31])	4—49%	Follows heavy exercise, indurated swelling and pain.
Eosinophilic cellulitis (Well's syndrome[32])	13—14%	Urticarial rash, annular erythema, resembles cellulitis but with a sharp edge.
Angiolymphoid hyperplasia (Kimura's disease[33])	++	Acute onset, flesh-coloured nodules on head and neck.
Eosinophilic pustular folliculitis (Ofuji's disease[34])	5—40%	Mildly pruritic, follicular polycyclic array on face/arms, marker of AIDS.

Platelets

The normal platelet count varies between 150,000 and 400-000/L. A count of <100,000 is considered to denote thromlocytopenia, <40,000 leads to bleeding following minor trauma, and <10,000 results in spontaneous bleeds.[1] Idiopathic thrombocytopenic purpura may thus manifest as a positive Hess test and petechial haemorrhages. Immune thrombocytopenia is drawing renewed interest as a manifestation of AIDS.[35] The Kassabach-Merritt syndrome due to sequestration of platelets (in addition to other factors) can complicate a cavernous haemangioma.[36,37] Drugs such as rifampicin can cause thrombocytopenia per se, or as a part of pancytopenia.[13] The Wiskott-Aldrich syndrome[38] is characterized by thrombocytopenia, recurrent infections and eczema.

Though patients of Henochs-Schonlein purpura may present with lesions of palpable purpura, the condition is essentially a vasculitis and the platelet count is normal.

Peripheral smear

The red blood cells may show anisocytosis (variation in size), poikilocytosis (variation in shape) or hypochromia. Characteristic cells such as the sickle cell or the spherocyte may give a clue to the specific diagnosis. Polychromasia and basophilic stippling are both indications of a compensated haemolysis.[1] The Heinz bodies seen on supravital staining are suggestive of haemolytic anemia due to G-6PD deficiency which may be of relevance to dapsone therapy.[13]

The leukocytes may show findings ranging from the hypersegmented neutrophils of B_{12} deficiency[1] to Sezary cells. The Dorfman-Chanarin syndrome[40] is characterized by congenital ichthyosis with systemic features including mental retardation, and vacuolated leukocytes in blood smears which are better seen with special lipid stains.

Erythrocyte sedimentation rate (ESR)

ESR is a relatively non-specific parameter and no diagnosis is based on this single investigation. It may be raised in a variety of dermatological disorders which include tuberculosis, collagen vascular disease, Behcet's syndrome, Reiter's syndrome, psoriatic arthropathy and erythema elevatum diutinum among others. A raised ESR has recently been mentioned as a relatively consistent finding in urticarial vasculitis.[41]

Role in dermatology

A. Diagnosis

The haemogram may help to decide the diagnosis in the following conditions :

(1) SLE : The 1982 revised ARA criteria[11] for the diagnosis of systemic lupus erythema-

tosus mention haematological parameters such as haemolytic anemia, or leukopenia <4000/cu mm, or lymphopenia <1500/cu mm, or thrombocytopenia <100,000/cu mm.

(2) The absolute eosinophil count (>1,500/cu mm) is diagnostic in the hypereosinophilic syndrome.[29]

(3) Vacuolated leukocytes in the Dorfman-Chanarin syndrome.[40]

(4) The CDC definition[21] of the AIDS related complex requires two clinical and two laboratory parameters, of which anemia, leukopenia and thrombocytopenia can form a part.

B. Prognosis :

The haemogram is useful as a predictive marker in :

(1) Toxic epidermal necrolysis : Granulocytopenia has been noted as a poor prognostic indicator in TEN and the failure of granulocytopenia to improve in 5-7 days was correlated with a grave prognosis.[22]

(2) Cutaneous T-cell lymphoma : Schechter[42] has noted that 10% of cells with convoluted nuclei are seen in 100% of mycosis fungoides patients in the erythrodermic phase and in 42% in the plaque or tumour stage. The TNMB staging[43] of mycosis fungoides includes :

B_0 < 5%/no atypical cells

B_1 > 5% (to count 100 lymphocytes)

Peripheral blood may be an independent prognostic variable and is therefore not incorporated in the routine staging classification.[43]

C. Therapeutic decisions :

Drugs used in dermatology can show significant haematologic effects. Razoxane[44] which was earlier used in psoriasis was withdrawn due to the significant neutropenia and acute myelomonocytic leukemia associated with the drug. Certain situations in which the haemogram is used to monitor the therapy include :

(1) Leprosy[13]

Anemia is common in leprosy. Dapsone at 50 mg/day causes some degree of haemolysis. At 150 mg/day, there is a drop in haemoglobin by upto 2 gm%. In patients with G-6PD deficiency, this haemolysis is exaggerated resulting in significant anemia. Eosinophilia and leukocytosis may be features of the dapsone syndrome, while agranulocytosis is fortunately a rare complication of dapsone. Rifampicin is known to cause thrombocytopenia.

(2) Methotrexate in psoriasis[44,46]

According to the revised guidelines for methotrexate therapy in psoriasis, the premethotrexate evaluation should include a haemoglobin, a total and differential leukocyte count and a platelet count. The follow-up evaluation should include a platelet and leukocyte count at 1-4 week intervals. Leukopenia of a significant nature beyond 1 week may necessitate temporary discontinuation of methotrexate. Methotrexate should be avoided in patients with a haemoglobin of less than 10 gm%.

(3) Miscellaneous

Drugs may cause anemia due to decreased absorption of various blood-forming factors, due to bone marrow suppression or haemolysis. In porphyria cutanea tarda,[12] phlebotomy is a mode of treatment and the end-point aimed for is a haemoglobin of 10 gm% or a serum iron level of 50-60 mg/100 ml.

References

1. Krupp MA, Tierney LM, Jawetz E et al : Physician's Handbook, 21st ed, Lange Medical Publications, California, 1982; p 146.
2. Denman ST : A review of pruritus, J Amer Acad Dermatol, 1986; 14 : 375-391.
3. Bunn HF : Anemia, in : Harrison's Principles of Internal Medicine 1, 11th ed, Editors, Braunwald E, Isselbacher KJ, Petersdorf, RG et al : Mc-Graw Hill Book Company, New York, 1987; p 262-266.

4. Feingold KR and Elias PM : Endocrine-skin interaction, J Amer Acad Dermatol, 1987; 17 : 921-940.
5. Hogan GW and Jones B : The relationship of koilonychia and iron deficiency in infants, J Pediat, 1970; 77 : 1054-1057.
6. Howitz J and Schwartz M : Vitiligo, achlorhydria and pernicious anemia, Lancet, 1971; 1 : 1331-1332.
7. Dawber RPR : Premature greying and pernicious anemia, Brit J Dermatol, 1970; 82 : 221-222.
8. Serjeant GR : Leg ulceration in sickle cell anemia, Arch Int Med, 1974; 133 : 690-694.
9. Kinatender J : Leg ulcers in beta-thalassemia, Hautarzt, 1980; 31 : 273-275.
10. Beinhauer LG and Gruhn JG : Dermatologic aspects of congenital spherocytic anemia, Arch Dermatol, 1957; 75 : 642-646.
11. Tan EM, Cohen AS, Fries JF et al : The 1982 revised criteria for the classification of systemic lupus erythematosus, arthritis and rheumatism, 1982; 25 : 1271-1277.
12. Eubanks SW, Patterson JW, May DL et al : The porphyrias, Internat J Dermatol, 1983; 22 : 337-347.
13. Jopling WH : Side-effects of antileprosy drugs in common use, Leprosy Rev, 1983; 54 : 261-270.
14. Blume RS and Wolff SM : The Chediak Higashi syndrome, Medicine (Baltimore), 1972; 51 : 247-249.
15. Shuster S and Brown JB : Gynaecomastia and urinary estrogens in patients with generalized skin disease, Lancet, 1962; 2 : 1358-1359.
16. Molin L and Reizenstein P : Haematological changes in psoriasis, Acta Dermato-Venereol (Stockh), 1974; 54 : 465-469.
17. Touraine R : Study of folate in psoriasis : Blood levels, intestinal absorption and cutaneous loss, Brit J Dermatol, 1973; 89 : 335-336.
18. O'Donoghue DP : Gastric lesions in dermatitis herpetiformis, Gut, 1976; 17 : 185-188.
19. Gilliland BC : Progressive systemic sclerosis, in : Harrison's Principles of Internal Medicine 1, 11th ed, Editors, Braunwald E, Isselbacker KJ, Petersdorf RG et al : Mc-Graw Hill Book Company, New York, 1987; p 1430.
20. Jopling WH : The disease, in : Handbook of Leprosy, Third ed : Heinermann, New York, 1983; p 17.
21. Killen J : AIDS-related complex : A definition, AIDS Memorandum, 1984; 1 : 4.
22. Westhy ED and Eschsler HL : Toxic epidermal necrolysis : Granulocytic leukopenia as a prognostic indicator, Arch Dermatol, 1984; 120 : 721-726.
23. Braverman IM : Leukemia and allied disorders, in : Skin Signs of Systemic Diseases, 2nd ed, WB Saunders, Philadelphia, 1981; p 179.
24. Boggs DR : The acute leukemias : Analysis of 322 cases and review of the literature, Medicine (Baltimore), 1962; 41 : 163-164.
25. Statham BN : Leukemoid reaction in acne fulminans, Clin Exp Dermatol, 1983; 8 : 401-403.
26. Sweet RD : Further observations in acute febrile neutrophilic dermatosis, Brit J Dermatol, 1968; 80 : 800-805.
27. Lyons JH : Generalized pustular psoriasis, Internat J Dermatol, 1987; 26 : 409-418.
28. Johnson RB and Lazarus CS : Pulse therapy, Arch Dermatol, 1982; 118 : 76-84.
29. Pincus SH and Wolff SM : Dermatologic diseases associated with eosinophilia, in : Dermatology in General Medicine Update, Fitzpatrick TB : 1986; p 13.
30. Chusid MJ : The hypereosinophilic syndrome : Analysis of 14 cases with a review of literature, Medicine (Baltimore), 1975; 54 : 1-27.
31. Moore TL and Zuckner J : Eosinophilic fasciitis, Semin Arthritis Rheum, 1980; 9 : 228-234.
32. Wells GC and Smith N : Eosinophilic cellulitis, Brit J Dermatol, 1979; 100 : 101-110.
33. Wells GC and Whimster IW : Subcutaneous angiolymphoid hyperplasia with eosinophilia, Brit J Dermatol, 1969; 81 : 1-15.
34. Ofuji S : Eosinophilic pustular folliculitis, Acta Dermato-Venereol (Stockh), 1970; 50 : 195-203.
35. Walsh CM, Nardi MA and Karpatkins K : On the mechanism of thrombocytopenic purpura in sexually active homosexual men, New Eng J Med, 1984; 311 : 635-636.
36. Esterley NB : Kasabach-Merritt syndrome, J Amer Acad Dermatol, 1983; 8 : 504-506.
37. Kasabach HH and Merritt KK : Platelet sequestration in cavernous haemangioma, Amer J Dis Child, 1940; 59 : 1063-1064.
38. Spitler LE : Wiskott Aldrich syndrome, Amer J Med, 1979; 67 : 59-61.

39. Bianchini G : Henoch's-Schonlein purpura, Internat J Dermatol, 1983; 22 : 103-104.

40. Williams ML and Elias PM : Genetically transmitted, generalized disorders of cornification, in : Genodermatoses, Dermatology Clinics, 1987; p 166.

41. Soter NA : Urticarial vasculitis, in : Urticarias, Editors, Champion RH, Greaves MW, Black AK et al : Churchill Livingstone, New York, 1985; p 61.

42. Schechter GP : Blood and lymph node T lymphocytes in cutaneous T cell lymphoma : Evaluation by light microscopy, Cancer Treat Rep, 1979; 63 : 571-574.

43. Bunn PA and Lamberg SI : Report of the committee on staging and classification of T-cell lymphomas (Mycosis fungoides and Sezary syndrome), Cancer Treat Rep, 1979; 63 : 725-728.

44. Kaur S and Kaur I : Treatment of psoriasis, Ind J Dermatol Venereol Leprol, 1987; 53 : 9-18.

45. Roenigk HH, Anuerbach R, Maibach H et al : Methotrexate guidelines-revised, J Amer Acad Dermatol, 1982; 6 : 145-156.

46. Roenigk HH, Anuerbach R, Maibach H et al : Methotrexate in psoriasis : Revised guidelines, J Amer Acad Dermatol, 1988; 19 : 145-156.