## Folate deficiency and knuckle pad hyper-pigmentation

Dear editor,

A 45-year-old male initially presented in hematology with generalized weakness and loss of appetite for 1 month. Laboratory evaluation showed white blood cells (WBCs) of  $3.4 \times 10^9/L$ , hemoglobin (Hb) of 5.7 g/dl, MCV of 90 fl, and platelets of  $29 \times 10^9$ /l. The auto-immune profile was negative. The serum levels of folate and B12 were 2.50 ng/ml (ref: >5.38) and 1512 pg/ml (180–940), respectively. Clinical examination showed a pale appearance and knuckle pad hyper-pigmentation. [Panel A] The bone marrow examination showed megaloblastic erythroid maturation and 3+ iron stores. The diagnosis of folate deficiency was made. The patient has been given Tab folate 5 mg once a day for 1 month. After 1 month of treatment, his counts became normal, showing WBCs of  $6.4 \times 10^9$ /L, Hb of 12.7 g/dl, MCV of 90 fl, and platelets of  $213 \times 10^9$ /l. On clinical examination, paleness disappeared and knuckle pad hyper-pigmentation decreased. [Panel B] Folate deficiency is mainly because of the poor intake of folate in the population, malabsorption, and increased utilization. Other causes of folate deficiency include excess urinary loss in heart failure, liver cirrhosis, dialysis, and alcoholism. In the present case, the cause of folate deficiency was nutritional. The daily requirement of folate is 150 ug, which



Panel A: A pale appearance and knuckle pad hyperpigmentation Before treatment

may increase up to 600 ug in pregnancy. The normal body stores of folate are 10–12 mg, which are enough for 3 to 4 months, so folate deficiency occurs very fast. [1] Folate is required in the form of methyl tetrahydrate folate (Methyl TH4) as a one-carbon unit transfer in DNA synthesis. This defective DNA synthesis leads to activation of micro-ophthalmia-associated transcription factor (MITF), subsequently up-regulates both tyrosinase and tyrosinase-related proteins, and increases melanin synthesis. [2] This leads to hyper-pigmentation of the skin, which is reversible with the correction of folate. Primary care physicians should be aware that folate deficiency can present with knuckle pad hyper-pigmentation.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

Nil.

### **Conflicts of interest**

There are no conflicts of interest.



Panel B: Paleness disappeared and knuckle pad hyperpigmentation decreased after treatment

## Santosh Govind Rathod, Ayeshah Jalid

Department of Clinical Hematology, SKIMS, Srinagar, Jammu, and Kashmir, India

Address for correspondence: Dr. Santosh Govind Rathod, Department of Clinical Hematology, SKIMS, Srinagar, Jammu Kashmir - 190 011, India. E-mail: Drsgrathod2007@gmail.com

### References

- 1. Devalia V, Hamilton M, Molloy A. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. Br J Hematol 2014;166:496-513.
- Speeckaert R, Gele MV, Seeckaert MM, Lambert JL, van Geel N. The biology of hyperpigmention syndromes. Pigment Cell Melanoma Res 2014;27:512-24.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**Received:** 30-04-2022 **Accepted:** 14-07-2022

**Published:** 16-12-2022

# Access this article online Quick Response Code: Website: www.jfmpc.com DOI: 10.4103/jfmpc.jfmpc\_958\_22

How to cite this article: Rathod SG, Jalid A. Folate deficiency and knuckle pad hyperpigmentation. J Family Med Prim Care 2022;11:7506-7. © 2022 Journal of Family Medicine and Primary Care | Published by Wolters Kluwer - Medknow

Volume 11: Issue 11: November 2022