

“NON NEUROLOGICAL MANIFESTATIONS OF VITAMIN B12 DEFICIENCY”

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ABSTRACT

Background: Vitamin B12 deficiency may present with a variety of non specific, non neurological manifestations like the involvement of, skin, hair, mucous membrane and hematological systems, which may antedate the neurological symptoms by years! There are few reported cases in literature about the same.

Aims: The present study aimed to evaluate and analyse the various nonneurological manifestations in patients of vitamin B12 deficiency presenting with various neurological manifestations.

Material & Method: Forty patients presenting clinically with evidence of neuropathy, myelopathy, optic neuropathy, dementia, neuropsychiatric manifestations, and cerebellar ataxia, either alone or in combination with serum vitamin B12 level <200 pg/ml or a megaloblastic bone marrow or both were included. The non neurological manifestations were then critically analysed

Results: Anaemia was the commonest manifestation seen in 60%, followed by premature graying of hair with hair fall in 45%, glossitis in 15%, jaundice in 10% and hyperpigmentation, vitiligo & retinal haemorrhage seen in 5% each. A significant correlation was seen ($p < .05$) with a disease duration of >2 years for premature graying of hair with hair fall, hyperpigmentation, vitiligo & retinal haemorrhage. Except vitiligo, there was a complete resolution of all symptoms within 3-4 months of injectable B12 therapy.

Conclusions: This study highlights the importance of various non neurological manifestation of B12 deficiency which may precede the neurological diagnosis by years. As these manifestations are not specific for B12 deficiency a high index of suspicion is required so that a potentially treatable cause may not be missed!

KEYWORDS: Vitamin B12 Deficiency and Non Neurological Manifestations, Vitamin B12 and Mucocutaneous manifestations, Vitamin B12 and Hyperpigmentation, Vitiligo

INTRODUCTION

Vitamin B12 deficiency may be asymptomatic or present with a wide spectrum, of neuropsychiatric, hematologic, skin, hair or mucous membrane affection.(1,2).The brunt of the damage in B12 deficiency is believed to fall on three tissues primarily: namely the hematological, neurological and skin hair and mucous membrane. The hematological manifestations are because of anaemia which is usually of the megaloblastic type. Skin manifestations include diffuse or patchy brownish pigmentation particularly seen in knuckles (3). There may be vitiligo as an autoimmune phenomenon associated with pernicious anaemia(4) Premature graying of hair, abnormal hair fall glossitis stomatitis, and recurrent mouth ulceration are the other manifestations which may occur. Pigmentation and graying of hair is usually reversible

after treatment(4) These mucocutaneous manifestations though not specific for vitamin B12 deficiency , may antedate the neurological symptoms by months to years when the diagnosis may be overlooked. There are few reported cases where the dermatological manifestations antedate the neurological manifestations. Present study aimed to evaluate and analyze the non neurological manifestations of vitamin B12 deficiency in patients presenting with any neurological symptoms and or signs.

MATERIAL AND METHOD

Patients attending the neurology out patient department & or admitted in the neurology wards were enrolled after a proper informed consent. Forty patients presenting clinically with evidence of neuropathy, myelopathy, optic neuropathy, dementia, neuropsychiatric manifestations, and cerebellar ataxia, either alone or in combination with serum vitamin B12 level <200 pg/ml or a megaloblastic bone marrow or both were included. Patients were subjected general and neurological examination with particular emphasis to the skin, hair and mucous membrane. Non Neurological manifestations of these patients were critically analyzed. Fisher's exact probability test was used to calculate the p value.

RESULTS

Age of presentation varied between 23 to 71 years , mean \pm SD (43.2 \pm 11 years). There were 16 female patients (40%) and 24 male patients(60%) with the M:F being 1.5:1. Duration of presentation ranged 20.45 months \pm 14.75. Eighteen patients (45%) were pure vegetarians and 22 patients(55%) were taking a non vegetarian meal <5 times /month .

Details of the neurological presentation are given in table I and of the non neurological manifestations in table 2:

Anaemia was the commonest manifestation seen in 60% of patients with no correlation with the neurological manifestations and with the presence of megaloblastic changes in the bone marrow and low vitamin B12 levels. Premature greying of hair 45%, with graying +abnormal hair loss in 40% was the next commonest feature seen(image 2). These manifestations were present 2-10 years prior to the neurological manifestations. Premature graying of hair with abnormal hair fall showed a significant correlation with the disease duration >2 years and no correlation was seen presence of megaloblastic changes in the BM, MCV >98 FL and low vitamin B12 levels. There was a marked improvement in hair loss and greying of hair in all patients within 2-3 months. Hyperpigmentation and vitiligo were present 5-6 years prior to the neurological manifestations seen in 5% of patients.

Hyperpigmentation, vitiligo (image 1) and retinal hemorrhage showed a significant correlation ($p < .05$) with increased disease duration(>2 years). Improvement was seen in the hyperpigmentation within 3-4 months, with no improvement in vitiligo. 15% patients had glossitis with all having anaemia. There was improvement in all with symptomatic treatment. Two patients with dementia and neuropsychiatric manifestations & ataxia had retinal haemorrhage, but without any visual symptoms. They also had severe anaemia. Jaundice with predominantly unconjugated hyperbilirubinemia was seen in 4 patients. One patient with the above symptom presented with recurrent attacks of jaundice followed by ataxia with neuropsychiatric manifestations. There was a complete amelioration of symptoms following injectable B12 treatment within 3-4 months.

DISCUSSIONS

Although few reports of different dermatological and hematological manifestations have been described

previously in literature (3, 45, 6), ours is the first large series of patients from India. Also we found some interesting findings. One particular young vegetarian male had presented with attacks of recurrent dementia and ataxia always preceded by jaundice with an unconjugated bilirubinemia of 7.7mg%, was found to have severe B12 deficiency and improved dramatically with injectable B12 therapy(7)

Anaemia was the commonest manifestation (60%) but there was no correlation with the neurological manifestation or disease duration. Majority of the patients (45%) also had abnormal graying of hair with hair fall antedating the symptoms by 2-10 years with significant correlation with disease duration >2 years, while hyperpigmentation and vitiligo was seen in only 5%. As this is a very common complaint even in the normal population and in a host of other disorders it is difficult to draw any conclusion. But as our patients had a good response to injectable B12 patients presenting with any skin, hair or mucous membrane changes, even in the absence of any neurological involvement, should be investigated for B12 deficiency if the symptoms are refractory to treatment and all causes have been ruled.

CONCLUSIONS

Thus vitamin B12 deficiency can cause a wide variety of mucocutaneous manifestations which may antedate the neurological manifestations. Diagnosis is often overlooked in the early stages as these findings are non specific. A high index of suspicion for the non resolving skin lesion should be there as it is a potentially treatable condition.

Thus this study highlights the importance of recognizing the non neurological manifestations of vitamin B12 deficiency which may antedate the neurological symptoms by several years, so that a potentially treatable cause may not be missed!

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APPENDICES

Table 1: Neurological Manifestations of B12 Deficiency

Clinical Presentation	No of pts	%
neuropathy	4	10
myeloneuropathy	14	35
myelopathy	4	10
Cerebellar ataxia	4	10
Dementia, myeopathy	2	5
dementia	2	5
Dementia, neuropathy	2	5
Dementia, cerebellar ataxia	2	5
Dementia, optic neuropathy, Cerebellar ataxia, Neuropathy	2	5
Dementia , optic neuropathy, anosmia	2	5

Table 2: Non Neurological Manifestations in Patients with B12 Deficiency

	No	%	Duration
hyperpigmentation	2	5	1-12 month
vitiligo	2	10	4-6 years
Glossitis/angular stomatitis	6	15	2-4 months
Graying of hair	18	45	2-10 years
Graying of hair & abnormal hair loss	16	40	2-10 years
jaundice	4	10	1-4 months
Retinal haemorrhage	2	5	8 months-1 year
anaemia	24	60	4-16 months

Table 3: Laboratory Parameters

	N=number 40	Percentage%
anaemia	22	60
Hypersegmented neutrophils	30	75
Macrocytosis>98fl	8	20
Indirect hyperbilirubenemia	4	10
Vit B12< 200pg/ml	26	65
Megaloblastic bone marrow	32	80
leucopenia	12	30
thrombocytopenia	2	5
Antiintrinsic factor antibody	9(30pts)	30



Figure 1



Figure 2

