

Association of Butterfly rash and ANA positivity with IBD.

ABSTRACT:

A 30 year old female presented with diarrhoea and gastrointestinal bleeding, along with photosensitive rash over malar region of face. Clinically she had features of essential nutrients deficiency, extra intestinal manifestations of inflammatory bowel disease and malar rash typical of systemic lupus erythematosus (SLE). On evaluation she found to have hypothyroidism and features consistent with inflammatory bowel disease, with significantly high titres of antinuclear antibody (++++). According to 2012 SLICC SLE criteria she did not have any other features consistent with SLE. Inflammatory bowel disease was confirmed by histopathological examination showing non-caseating granuloma with no evidence of vasculitis. Patient was started on treatment with systemic corticosteroids and thyroxine supplementation. Patient responded well. No flare up of symptoms or appearance of any new symptoms during her regular follow up.

CONCLUSION: We conclude that, clinical and laboratory features mimicking SLE like butterfly rash, positive ANA can occur in IBD even in absence of SLE making them difficult to diagnose. But either of the patients should be regularly followed up to look for the development of the other disease. Not only graves, association of hypothyroidism following hashimotos thyroiditis is also seen with IBD.

Abbreviations: ANA- antinuclear antibody, IBD- inflammatory bowel disease, CD- crohn's disease.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic recurrent disease characterized by intestinal mucosal inflammation, includes ulcerative colitis (UC) and crohn's disease (CD). Almost one fourth of IBD patients suffer from extra-intestinal manifestations, including oligoarticular or polyarticular non-deforming peripheral arthritis, spondylitis or sacroilitis, episcleritis or uveitis, erythema nodosum, pyoderma gangrenosum, sclerosing cholangitis and thromboembolic

events. On the other hand, systemic lupus erythematosus (SLE) is an autoimmune disorder occurring predominantly in women during reproductive years. It is a multisystem disease with numerous clinical manifestations such as skin rashes, photosensitivity, oral ulcers, arthritis, serositis, renal, neurologic and hematologic disorders. The characteristic immunologic findings include the presence of antinuclear antibodies (ANAs), anti-dsDNA, anti-Smith and antiphospholipid antibodies.⁽¹⁾

Systemic lupus erythematosus(SLE) and crohn's disease(CD) are multisystem diseases characterised by wide spread tissue damage.⁽⁸⁾ The diseases may have gastrointestinal(GI) manifestations, laboratory results and radiographic findings that appear similar, consequently differentiating between GI involvement in CD and in SLE may be difficult. We present the case of CD presenting with clinical and laboratory features mimicking that of SLE.

CASE REPORT

Informed written consent was taken from patient.

A 30 year old female presented with 3 months history of moderate grade fever, hyper pigmented skin lesions over the face- which are photosensitive, with significant weight loss; For photosensitive rash she has consulted family doctor, there was no improvement with topical emollients and sunscreen. With 2 weeks history of diffuse colicky pain abdomen which used to relieve following defecation and she also had associated diarrhoea. History of 2 episodes of passage of blood in stool in last two days, with no history of other bleeding manifestations. Urine output was good. Menstrual cycles were regular. Non smoker. Past and family history was unremarkable.

She was poorly nourished with BMI-15.26kg/m², anaemic, has got malar rash (Fig.1A) typically looking like as seen in SLE, atrophic tongue(Fig.1B), knuckle pigmentation, erythema nodosum like skin lesions over anteromedial aspect of leg were seen. Fundus examination of eye was- normal. She had tender abdomen with mild ascites.

In view of multisystem involvement, we proceeded with investigations for autoimmune diseases. ESR was raised- 45 mm at the end of 1st hour, antinuclear antibody was strongly positive (++++), Anti-dsDNA, Anti smith antibody, smooth muscle antibody and other components of ANA profile were

68 negative. There was no evidence of haemolysis (Both Direct and Indirect
69 Coombs test were negative), C-reactive protein and RA factor were negative.
70 Complete blood picture showed microcytic hypochromic anaemia, iron profile
71 was normal. Liver function tests were normal except for hypoproteinemia and
72 hypoalbuminemia (5.4gm% and 2.5gm% respectively). Renal function tests,
73 serum electrolytes, blood sugar level, urine analysis – were normal. Blood
74 group- AB positive. Found to have hypothyroidism (Free T3 -2.53pg/ml, Free
75 T4 - 1.32ng/dl, TSH -13uIU/ml). HBsAg and HIV were non-reactive. HCV RNA –
76 negative.

77 Ascitic fluid analysis showed exudative nature with 800 cells (80%
78 lymphocytes, 20% mesothelial cells, no malignant cells) and protein - 4.7gm/dl,
79 sugar – 85mg/dl. It did not show growth of any organisms and also negative for
80 acid fast bacilli staining. Adenosine deaminase level was significantly increased
81 (51.5 IU/L).

82 Cardiac evaluation was normal.

83 With these features she was not fitting into definite SLE according to 2012
84 SLICC SLE criteria. So we proceeded with other non-invasive methods of
85 investigations.

86 Radiological investigations revealed lesion at terminal ileum and ileocecal
87 junction. Ultrasonography of abdomen and pelvis showed thickened small
88 bowel wall with minimal ascites. Contrast enhanced computed tomography of
89 abdomen and pelvis showed irregular mural thickening of terminal ileum and
90 ileocecal junction- maximum thickness of wall being 10mm extending over
91 length of 3cm(Fig.2A), with pre and para aortic lymph node enlargement –
92 largest one measuring – 1.5*0.6cm(Fig.2B). Then we suspected inflammatory
93 pathology involving the small bowel, so proceeded with colonoscopy.
94 Colonoscopy showed irregular ulcerative lesion at terminal ileum (Fig.2C).
95 Biopsy was taken from same site and subjected for histopathological
96 examination. Histopathological examination showed- noncaseating granuloma
97 with no evidence of vasculitis consistent with inflammatory bowel disease –
98 crohn's Disease (Fig.2D). So we made the diagnosis of crohn's Disease. She
99 was treated with Inj. Methylprednisolone 1gm/day for initial 5 days, followed
100 by oral prednisolone 1mg/kg/day and tapering started after 6 weeks. She
101 responded well. We with-held the treatment with anti-TNF alpha inhibitors
102 because of risk of development of drug induced lupus. She is on regular follow

up. No flare ups or appearance of new symptoms from last 3years and no new laboratory features suggestive for other autoimmune disease development.

We have counselled the patient regarding – possibility of development of SLE symptoms at later stage, available treatment options and its side effects. Side effects of systemic corticosteroids explained and advised for regular follow up.

DISCUSSION:

The peak age of onset of UC and CD is between 15- 30yrs. A second peak occurs between 60 – 80yrs.⁽⁷⁾ CD can affect any part of the GI tract from mouth to the anus. In 75% of the patients with small intestine disease , terminal ileum is involved in 90%.⁽⁷⁾ In CD involving ileocecal region, severe inflammation of the ileocecal region may lead to localised thinning of wall with micro perforation - responsible for exudative ascitic fluid⁽⁷⁾) In our case terminal ileum and ileocecal junction was involved, with exudative ascites. Erythema nodosum (EN) occurs in up to 15% of CD and 10% of UC patients⁽⁸⁾

The rate of thyroid disorders is reported to be increased in patients with IBD than normal population. Mustafa Yakut *et al.* study showed thyroid gland disease in 14/146(9.5%) IBD patients. Hashimoto thyroiditis has been found in 4(2.7%) IBD patients, in that one patient was hypothyroid.⁽⁶⁾ Our patient had hypothyroidism.

Table 1- shows comparison of reported patients with SLE complicating crohn's disease.

In most cases, SLE was diagnosed prior to the CD and all the patients had anti-dsDNA positive, there was tendency towards anaemia and thrombocytopenia. In all those patients SLE was diagnosed based on clinical features and ANA profile study. No tissue diagnoses was used. Few patients had malar rash at the time of diagnosis of SLE. In the later stage during the follow-up they developed gastrointestinal manifestations and diagnosis of CD was confirmed by histopathological examination.

One case report by Nishida Y⁵ *et al.* diagnosed with CD 4 years prior to SLE, that patient did not have malar rash and positive ANA titre at the time of diagnosis of CD. That patient was put on treatment with sulfasalazine for CD and during follow up developed SLE.

Nitzan O⁸ *et al.* study showed most of cases of SLE were associated with ulcerative colitis. They found patients with both diseases tend to have less photosensitivity, less arthritis and less serositis than patients with SLE alone.

In our patient diagnosis of CD was based on histopathological examination. She has strongly positive ANA (+++++) and anti-dsDNA was negative, malar rash typical of that of SLE at the time of presentation, but According to 2012 SLICC SLE criteria she did not have other features for SLE.

CONCLUSION:

The clinical and laboratory features mimicking SLE can occur in CD even in absence of SLE, making them difficult to diagnose correctly. It is important to consider the possibility of CD in patients who have clinical and laboratory features of SLE like butterfly rash, positive ANA with Gastrointestinal manifestations. Either of the patients should be followed up regularly to look for the development of the other disease. Not only graves, association of hypothyroidism following hashimotos thyroiditis is also seen with IBD.

REFERENCES:

1. Konstantinos H.Katsanos, Paraskevi V.Voulgari, Epameinondas V.Tsianos: Inflammatory bowel disease and lupus: A systematic review of the literature. Journal of Crohn's and Colitis (2012) 6, 735-742.

2. Johnson DA, Diehl AM, Finkelman FD et al: Crohn's disease and systemic lupus erythematosus. Am J Gastroenterol 1985, 11:869-70.

3. Nagata M, Ogawa Y, Hisano S et al: Crohn's disease in systemic lupus erythematosus: a case report. Eur J Pediatr 1989, 148:525-6.

4. Buchman AL, Wilcox CM: Crohn's disease masquerading as systemic lupus erythematosus. South Med J 1995, 88:1081-3.

5. Nishida Y, Murase K, Ashida R et al: Familial Crohn's disease with systemic lupus erythematosus. Am J Gastroenterol 1998, 93:2599-601.

6. Mustafa Yakut, Yusuf Üstün, Gökhan Kabacan et al: Thyroid Disorders in Patients with Inflammatory Bowel Diseases. *International Journal of Clinical Medicine*, 2011, 2, 89-92.

7. *Harrison's principles of Internal Medicine 18th ed.* Inflammatory bowel disease (295), 2477-2495.

8. Nitzan O, Elias M, Saliba WR: Systemic lupus erythematosus and inflammatory bowel disease. *Eur J Intern Med* 2006, 17:313-8.

Fig 1: A. Malar rash
B. Atrophic tongue

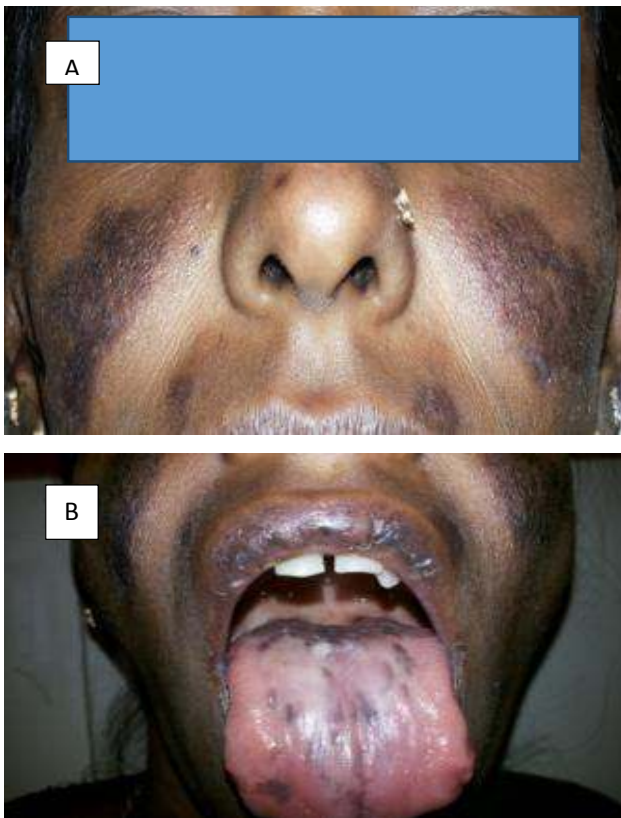
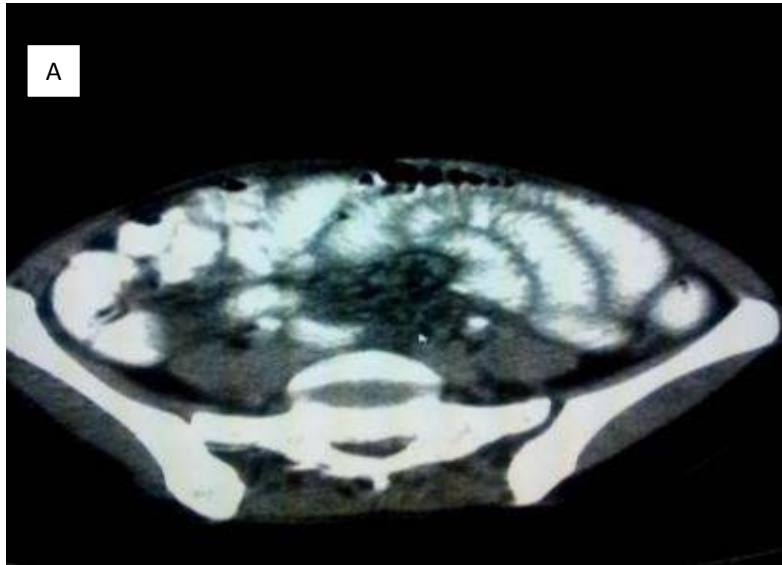


Fig 2: A. CECT abdomen showing irregular mural thickening of terminal ileum and ileocecal junction.

187 B. CECT abdomen showing enlarged pre and para aortic lymph node enlargement.
188 C. Colonoscopy showing ulcerative lesions at terminal ileum.
189 D. Histopathological examination of biopsy taken from ulcerative lesion at terminal ileum
190 showed- noncaseating granuloma with no evidence of vasculitis. (Features suggestive of crohn's
191 disease).
192
193



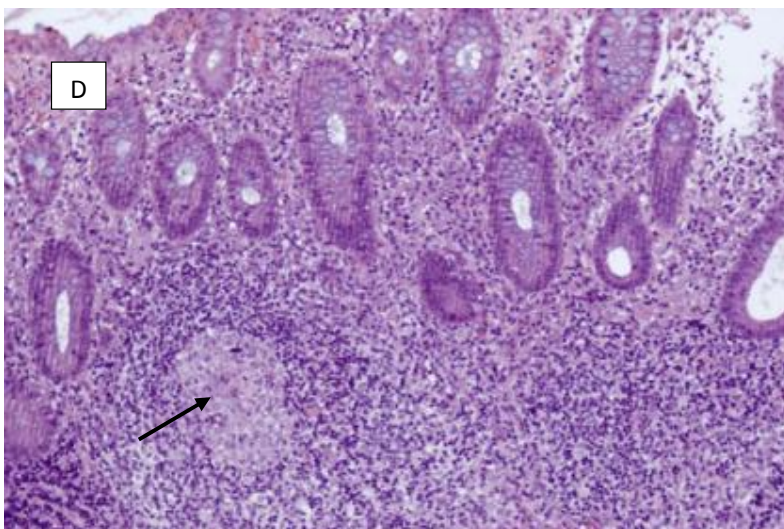


201

202



203



204

205 Table 1: Comparison of reported patients with SLE complicating crohn’s disease

206

Patient	Age/sex	SLE disease duration	Immunological findings	Symptoms	ESR (mm/hr)	Colonoscopy findings	Result of biopsy	Treatment	Reference
1	28M	7yrs	ANA 1280x Anti-DNA 160x	Diarrhoea Pyoderma gangrenosum	89	Deep linear ulceration, Psuedopolyps, Skip lesions	Acute and chronic inflammation	mPSL 40mg/day iv	(2)
2	15F	3yrs	ANA 1280x Anti-DsDNA 50x	Abdominal pain diarrhoea Blood stained stool	68	Multiple ulcers with linear ulcer, Skip lesion, Psuedopolyps	CD	Salazosulphapyridine	(3)
3	55F	12yrs	ANA 80x Anti-DsDNA 80x	Intermittent hematochezia, Tenesmus and loose bowel movements	35	Multiple ulcers with linear ulcer, diffuse aphthous ulcers	CD	Prednisolone	(4)

4	25F	She developed SLE 4yrs after developing crohn's disease	ANA 160x Anti-DsDNA 800IU/ml pANCA positive	Watery diarrhoea, Lower Abdominal pain, Perianal abscess	N/A	Longitudinal ulcers and mucosal erosions	CD	Salazosulphapyridine 3gm/day	(5)
5	30F	No history of SLE	Positive result of ANA Anti-dsDNA-Negative	diarrhoea Abdominal pain Malar rash	45	Ulcers at terminal ileum	CD	mPSL 1gm/day-5 day Followed by oral prednisolone 1mg/kg/day	The present case

207 mPSL – Methyl prednisolone

208

209