Journal of Advances in Medical and Pharmaceutical Sciences
6(2): 1-6, 2016, Article no.JAMPS.22595
ISSN: 2394-1111

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Association of Butterfly Rash and Antinuclear Antibody Positivity with Inflammatory Bowel Disease

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2016/22595
Editor(s):
(1) Franciszek Burdan, Experimental Teratology Unit, Human Anatomy Department, Medical University of Lublin, Poland.
(2) Hamdy A. Sliem, Internal Medicine, Suez Canal University, Egypt and College of Dentistry, Qassim University and EL-Jouf University, Saudi Arabia.
Reviewers:
(1) Kamenarska Zornitsa, Medical University, Sofia, Bulgaria.
(2) Anonymous, Hospital Quiron Teknon, Barcelona, Spain.
(3) Safak Sahin, Gaziosmanpasa University, Turkey.
(4) Simon Francis Thomsen, University of Copenhagen, Denmark.
Complete Peer review History: http://sciencedomain.org/review-history/12912

Case Report

Received 13th October 2015
Accepted 21st December 2015
Published 6th January 2016

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.

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Conclusion: We conclude that, clinical and laboratory features mimicking SLE like butterfly rash, positive antinuclear antibody can occur in inflammatory bowel disease 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 inflammatory bowel disease.

Keywords: ANA- Antinuclear Antibody; IBD- Inflammatory Bowel Disease; CD- Crohn's Disease; butterfly rash.

1. 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 inflammatory bowel disease 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 [2]. The diseases may have gastrointestinal (GI) manifestations, laboratory results and radiographic findings that appear similar, consequently differentiating between gastrointestinal involvement in crohn's disease and in SLE may be difficult. We present the case of crohn's disease presenting with clinical and laboratory features mimicking that of SLE.

2. 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-15.26 kg/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 negative. There was no evidence of haemolysis (Both Direct and Indirect Coombs test were negative), C-reactive protein and Rheumatoid factor were negative. Complete blood picture showed microcytic hypochromic anaemia, iron profile was normal. Liver function tests were normal except for hypoproteinemia and hypoalbuminemia (5.4 gm% and 2.5 gm% respectively). Renal function tests, serum electrolytes, blood sugar level, urine analysis – were normal. Blood group- AB positive. Found to have hypothyroidism (Free T3 -2.53 pg/ml, Free T4 - 1.32 ng/dl, TSH -13 uIU/ml). HBsAg and HIV were non-reactive. HCV RNA – negative.

Ascitic fluid analysis showed exudative nature with 800 cells (80% lymphocytes, 20% mesothelial cells, no malignant cells) and protein - 4.7 gm/dl, sugar – 85 mg/dl. It did not show growth of any organisms and also negative for

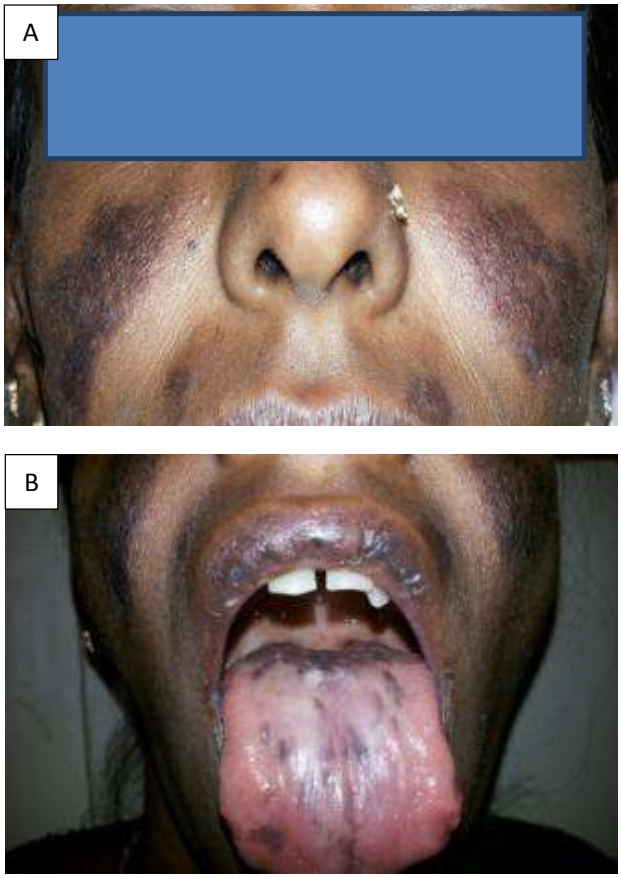
acid fast bacilli staining. Adenosine deaminase level was significantly increased (51.5 IU/L).

Cardiac evaluation was normal.

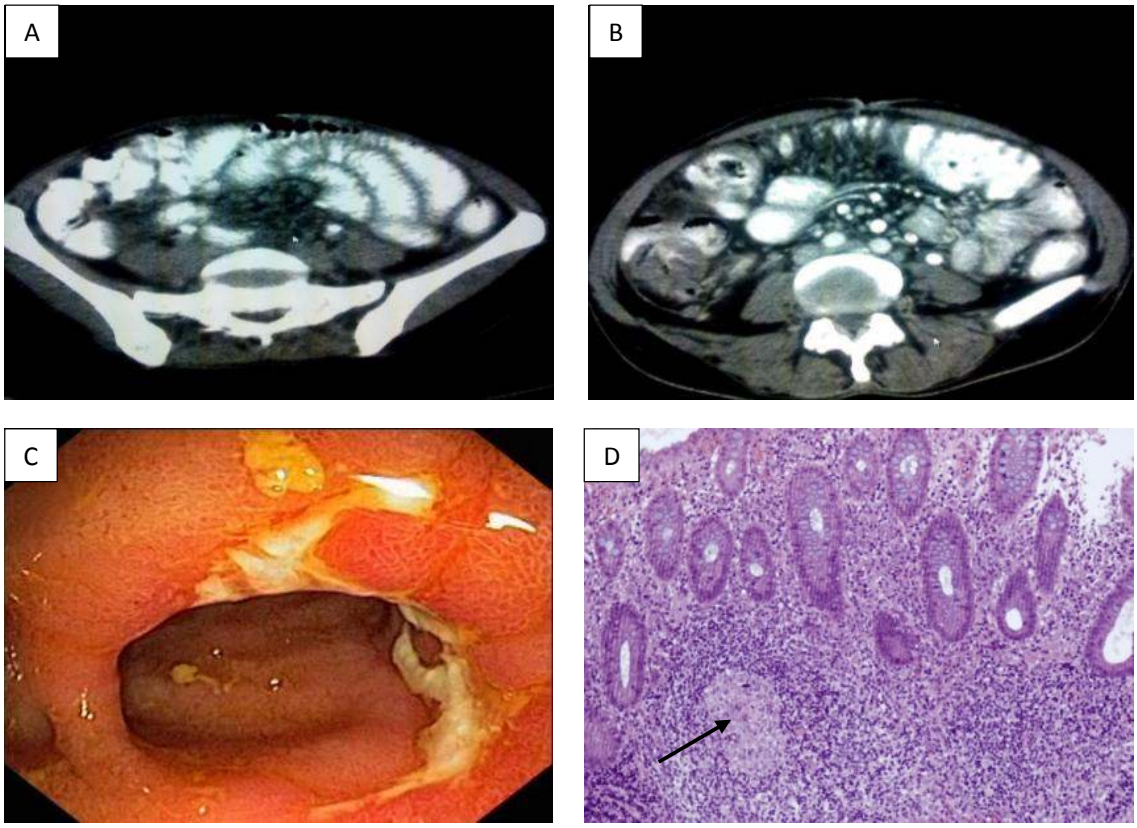
With these features she was not fitting into definite SLE according to 2012 SLICC SLE criteria. So we proceeded with other non-invasive methods of investigations.

Radiological investigations revealed lesion at terminal ileum and ileocecal junction. Ultrasonography of abdomen and pelvis showed thickened small bowel wall with minimal ascites. Contrast enhanced computed tomography of abdomen and pelvis showed irregular mural thickening of terminal ileum and ileocecal junction- maximum thickness of wall being 10 mm extending over length of 3 cm (Fig. 2A), with pre and para aortic lymph node enlargement (Fig. 2B). Then we suspected inflammatory pathology involving the small bowel, so proceeded with colonoscopy. Colonoscopy showed irregular ulcerative lesion at terminal ileum (Fig. 2C). Biopsy was taken from same site and subjected for histopathological examination. Histopathological examination showed- noncaseating granuloma with no evidence of vasculitis consistent with inflammatory bowel disease – crohn's Disease (Fig. 2D). So we made the diagnosis of crohn's Disease. She was treated with Inj. Methylprednisolone 1 gm/day for initial 5 days, followed by oral prednisolone 1 mg/kg/day and tapering started after 6 weeks. She responded well. We with-holded the treatment with anti-TNF alpha inhibitors 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 3 years 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.



Figs. 1A. Malar rash, B. Atrophic tongue



Figs. 2A. CECT abdomen showing irregular mural thickening of terminal ileum and ileocecal junction, B. CECT abdomen showing enlarged pre and para aortic lymph node enlargement, C. Colonoscopy showing ulcerative lesions at terminal ileum, D. Histopathological examination of biopsy taken from ulcerative lesion at terminal ileum showed- noncaseating granuloma with no evidence of vasculitis. (Features suggestive of crohn's disease)

3. DISCUSSION

The peak age of onset of ulcerative colitis and crohn's disease is between 15-30 yrs. A second peak occurs between 60–80 yrs [3]. Crohn's disease can affect any part of the gastrointestinal tract from mouth to the anus. In 75% of the patients with small intestine disease, terminal ileum is involved in 90% [3]. In crohn's disease involving Ileocecal region, severe inflammation of the ileocecal region may lead to localised thinning of wall with micro perforation - responsible for exudative ascitic fluid [3]. In our case terminal ileum and ileocecal junction was involved, with exudative ascites. Erythema nodosum (EN) occurs in up to 15% of crohn's disease and 10% of ulcerative colitis patients [2].

The rate of thyroid disorders is reported to be increased in patients with inflammatory disease than normal population. Mustafa Yakut et al. [4] study showed thyroid gland disease in 14/146(9.5%) inflammatory bowel disease patients. Hashimoto thyroiditis has been found in 4(2.7%) inflammatory bowel disease patients, in that one patient was hypothyroid. 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 crohn's disease 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 crohn's disease was confirmed by histopathological examination.

Table 1. Comparison of reported patients with SLE complicating crohn's disease

Patient	Age/sex	SLE disease duration	Immunological findings	Symptoms	ESR (mm/hr)	Colonoscopy findings	Result of biopsy	Treatment	References
1	28M	7 yrs	ANA 1280x Anti-DNA 160x	Diarrhoea Pyoderma gangrenosum	89	Deep linear ulceration, Psuedopolyps, Skip lesions	Acute and chronic inflammation	mPSL 40 mg/day iv	[5]
2	15F	3 yrs	ANA 1280x Anti-DsDNA 50x	Abdominal pain diarrhoea Blood stained stool	68	Multiple ulcers with linear ulcer, Skip lesion, Psuedopolyps	CD	Salazosulphapyridine	[6]
3	55F	12 yrs	ANA 80x Anti-DsDNA 80x	Intermittent hematochezia, Tenesmus and loose bowel movements	35	Multiple ulcers with linear ulcer, diffuse apthous ulcers	CD	Prednisolone	[7]
4	25F	She developed SLE 4 yrs 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 3 gm/day	[8]
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 1 gm/day-5 day Followed by oral prednisolone 1 mg/kg/day	The present case

mPSL – Methyl prednisolone

One case report by Nishida Y et al. [8] diagnosed with crohn's disease 4 years prior to SLE, that patient did not have malar rash and positive antinuclear antibody titre at the time of diagnosis of crohn's disease. That patient was put on treatment with sulfasalazine for crohn's disease and during follow up developed SLE.

Nitzan O et al. [2] 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 crohn's disease was based on histopathological examination. She has strongly positive antinuclear antibody titre (++++) 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.

4. CONCLUSION

The clinical and laboratory features mimicking SLE can occur in crohn's disease even in absence of SLE, making them difficult to diagnose correctly. It is important to consider the possibility of crohn's disease in patients who have clinical and laboratory features of SLE like butterfly rash, positive antinuclear antibody 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 inflammatory bowel disease.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/12912