OPEN ACCESS Freely available online

Journl of Hepatology and Gastrointestinal Disorders Research

Case Report

Erythema Annulare Centrifugum and Celiac Disease- Case Report and Review of Literature

Virtut Velmishi[1],Gentiana Cekodhima[2], Anila Godo[3], Paskal Cullufe[1]

[1]Department of Pediatric Gastroenterology, Mother Teresa Hospital, Tirana, Albania; [2]Department of histopathology, Mother Teresa Hospital Tirana, Albania; [3]Department of pediatric hematology, Mother Teresa Hospital, Tirana, Albania

ABSTRACT

Celiac disease (CD) is an autoimmune gluten-dependent enteropathy characterized by atrophy of intestinal villi that improves after gluten-free diet (GFD). CD is often associated with extra-intestinal manifestations; among them, several skin diseases are described in CD patients. This case report presents association of celiac disease with a rare skin manifestation such as erythema annulare centrifugum in a 5 year old boy. The opportunity to evaluate the possible presence of CD in children affected by this rare form of skin disorder is discussed.

Keywords: Celiac disease (CD); Erythema annulare centrifugum (EAC); Gluten free diet (GFD)

INTRODUCTION

Celiac disease (CD) is known as a chronic immune-mediated gluten-dependent enteropathy, resulting from an inappropriate T-cell-mediated immune response, against ingested gluten in genetically predisposed people [1]. Epidemiological studies have shown that CD is very common and affects about 1 in 100 people [2]. CD is a multigenic disorder associated with HLA-DQ2 (DQA1*/DQB1*2) expressed in more than 90% of patients, or HLA-DQ8 (DQA1*0301/DQB1*0302) [3]. The expression of these molecules is necessary, but not sufficient, to develop the disease [4]. CD is characterized by intestinal malabsorption and subtotal or total atrophy of intestinal villi which improves after gluten-free diet (GFD) [5]. The classic form of CD presents several symptoms such as diarrhea, abdominal pain, weight loss and nutritional deficiencies, particularly of iron, folate, calcium, and vitamin D [6]. However, there is a large variety of clinical presentations characterized by the presence of extra-intestinal manifestations, including anemia [7], persistent hypertransaminasemia[8], osteopenia [9], neurological [10], psychiatric and affective disorders [11-13], and autoimmune diseases [5]. In the last years, growing evidence has documented the involvement of skin diseases among the extra-intestinal manifestations of CD [14]. Association with EAC is reported very rarely.

CASE PRESENTATION

Our proband is a 5- year- old- boy who is referred to appointment with gastroenterologist from our colleagues of hematology because of a refractory iron deficiency anemia . According to his mother the little boy has been under treatment with oral iron three or more times but 2 or 3 months later her boy presented again low ferritine . Last check performed by hematologist has noticed a high level of IgA antitransglutaminase . Suspecting celiac disease this boy was sent to us. He was the first child of an albanian couple . No family history of other diseases or autoimmune diseases. Pregnancy and delivery were normal. Birth weight was 3,4 kg. Breast fed for 6 months . Solid foods were introduced beetween 4 to 6 months of age. Till 2-year-old no particular history to tell. Since then he presented mild abdominal pain and sideropenic anemia. He was treated several times but without any result. Last three or four months her mother has noticed some skin manifestations on the chest and on the upper part of back [Figure 1]. It was an interesting erythema, nonscaling ,nonpruritic and annular. Her mother has taken an appointement with dermatologist who has taken a skin biopsy . Histopathology report showed lymphohistiocytic infiltrate in the middle and lower dermis more compatible with Erythema annulare centrifugum.During physical examination this boy is playful.Heart sounds were normal. Lungs partake uniformly in respiration . Abdomen was soft and palpable. His weight was 17 kg (Zscore =-0.67 ; p=25,1%) and his height was 109 cm (Zscore=-0.004; p=48.4%). We have performed again blood analyses which showed:WBC=11,4x 10^3/mm3 ;RBC=3,44x 10^6/mm3 ;Hgb=9,4g/dl ; PLT-290x 10^3/mm3;Ferritine= 4,8 ng/ml (low), IgA antitransgluataminase = 46,9 u/ml (>20 positive); IgG antitranslutaminase= 38.8 u/ml (>20 positive). Liver and kidney function were normal. Other autoimmune tests for diabet type

Correspondence to: Virtut Velmishi, Universitary Hospital Center " Mother teresa" Dibra street Nr 372 , Tirana ,Albania Mail :tutimodh@yahoo.com

Received: November 25, 2020, **Accepted:** December 10, 2020, **Published:** December 17, 2020

Citation: Velmishi V, Cekodhima G, Godo A, Cullufe P (2020), Erythema annulare centrifugum and celiac disease- Case report and review of literature, J Hepatol Gastroint Dis 7:179.

1 or Hashimoto thyroiditis were also normal. The rest of other examinations was uneventful. According the level of IgA and IgG antitransgutaminasis we decide to perform a duodenal biopsy [Figure 2] which showed typical changes of Celiac disease (Marsh 3 B). In this context we started gluten free diet. We have seen this boy three months later. He had no complains and erythema was disappeared totally. Ferritine level was also normal.

DISCUSSION

The term Erythema annulare centrifugum was first described by Darier in 1916 [15]. Most commonly, no cause is found for the erythema annulare centrifugum (EAC) [16]. However, the literature contains numerous case reports documenting association with other diseases. The most common cause of Erythema annulare centrifugum are infections by bacteria , fungi , mycobacteria viruses and parasites [17-22] .There are some case reports about drug uses and EAC [23-29]. Another group of pathologies associated with EAC are neoplasms such as leukemia, lymphoma , breast cancer etc [30-33]. Other cases found in the literature are foods such as blue cheese and tomatoes reported as cause EAC. Some surgery events such as acute appendicitis or choledocholithiasis are reported as a cause of EAC which is resolved after surgery [34,35]. Graves disease, Hypereosinophilic syndrome , Sjorgen syndrome , sarcoidosis , osteoarthritis and stress remain most known diseases which are associated with EAC [35,36].

On the other hand celiac disease is associated with a lot of dermatological manifestations. The most known is dermatitis herpetiformis described by Luis Duhring in 1983 [37]. Psoriasis and alopecia areata are the most frequent skin disorder described

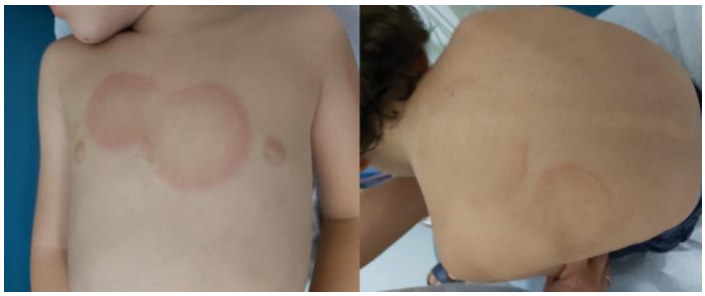

Figure 1. Erythema annulare centrifugum on the chest and back.

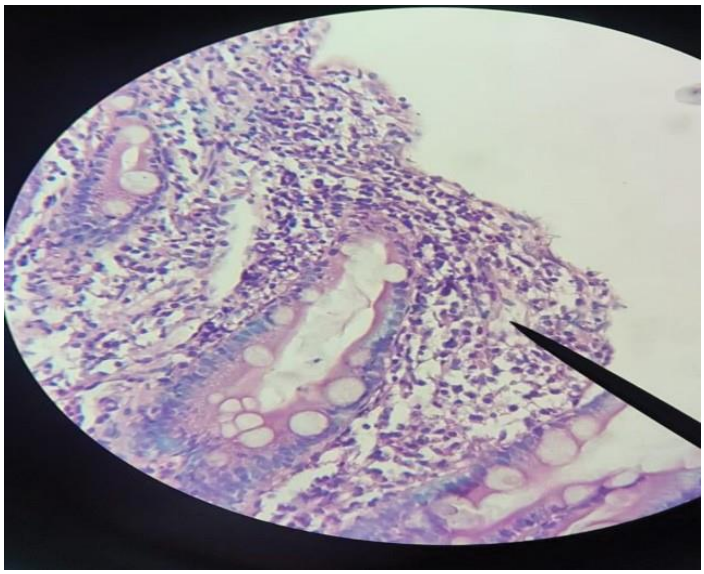

Figure 2. Microscopic image of duodenal biopsy showing CD enteropathy.

associated with celiac disease after dermatitis herpetiformis. There are a lot of case reports which showed a link between celiac disease and other skin manifestation such as chronic urticaria , hereditary angioneurotic edema , cutaneous vasculitis and atopic dermatitis. Caproni et al performed a detalied review of the literature and reported association between CD and skin conditions [38]. Although is not demonstrated a pathogenic link between the diseases are reported association with lupus erythematosus [39], dermatomyositis [40] , vitiligo [41] , Behcet disease [42] , linear IgA bullous dermatosis [43] and both skin and mucosal manifestations of lichen [44,45]. Less frequently are reported prurigo nodularis [46] , erythema nodosum [47] , necrolytic migratory erythema [48], porphyria [49], cutaneous amyloidosis [50], pityriasis rubra pilaris [51] , erythroderma [52], partial lypodistrophy [53], generalised acquired cutis laxa [54], ichtyosis [55], atypical mole syndrome and congenital giant nevus [56].

EAC is not listed above and there are few case reports which show the link between EAC and CD. Today is wellknown the relation between autoimmunity and EAC made us to believe that in our case this association is not occasionally. EAC is usually a self limiting condition and resolves with treatment of underlying disease. Initially we were doubtful if gluten free diet will work for EAC. Three months later the result was spectacular because erythema was totally disappear

CONCLUSION

CD is a frequent enteropathy associated with various extra-intestinal manifestations, involving several skin diseases. EAC is a rare skin disorder associated with variable diseases including autoimmune diseases such as CD. Autoimmunity remains the main mechanism of link between those diseases. However at present the data are scarse and most of the evidence for the association between CD and EAC is based on “case-reports”, making it difficult to draw definitive conclusions on this topic.

REFERENCES

1. Schuppan D. Current concepts of celiac disease pathogenesis. Gastroenterology 2000; 119:234–242.
2. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. Gastroenterology. 2001; 120:636–651
3. Green PH, Jabri B. Coeliac disease. Lancet. 2003; 362:383–391.
4. Greco L, Romino R, Coto I, Di Cosmo N, Percopo S, Maglio M, et al. The first large population based twin study of coeliac disease. Gut. 2002; 50:624–628.
5. Corazza GR, Gasbarrini G. Coeliac disease in adults. BaillieresClinGastroenterol. 1995; 9:329–350.
6. Capristo E, Addolorato G, Mingrone G, De Gaetano A, Greco AV, Tataranni PA, et al. Changes in body composition, substrate oxidation, and resting metabolic rate in adult celiac disease patients after a 1-y gluten-free diet treatment. Am J ClinNutr. 2000; 72:76–81.
7. Howard MR, Turnbull AJ, Morley P, Hollier P, Webb R, Clarke A. A prospective study of the prevalence of undiagnosed coeliac disease in laboratory defined iron and folate deficiency. J ClinPathol. 2002; 55:754–757.
8. Volta U, De Franceschi L, Lari F, Molinaro N, Zoli M, Bianchi FB. Coeliac disease hidden by cryptogenic hypertransaminasaemia. Lancet. 1998; 352:26–29.

9. Corazza GR, Di Sario A, Cecchetti L, Jorizzo RA, Di Stefano M, Minguzzi L, Brusco G, Bernardi M, Gasbarrini G. Influence of pattern of clinical presentation and of gluten-free diet on bone mass and metabolism in adult coeliac disease. Bone. 1996; 18:525–530.

10. Addolorato G, Di Giuda D, De Rossi G, Valenza V, Domenicali M, Caputo F, Gasbarrini A, Capristo E, Gasbarrini G. Regional cerebral hypoperfusion in patients with celiac disease. Am J Med. 2004; 116:312–317.

11. De Santis A, Addolorato G, Romito A, Caputo S, Giordano A, Gambassi G, Taranto C, Manna R, Gasbarrini G. Schizophrenic symptoms and SPECT abnormalities in a coeliac patient: regression after a gluten-free diet. J Intern Med. 1997; 242:421–423.

12. Addolorato G, Capristo E, Ghittoni G, Valeri C, Masciana R, Ancona C, et al. Anxiety but not depression decreases in coeliac patients after one-year gluten-free diet: a longitudinal study. Scand J Gastroenterol. 2001; 36:502–506

13. Addolorato G, De Lorenzi G, Abenavoli L, Leggio L, Capristo E, Gasbarrini G. Psychological support counselling improves gluten-free diet compliance in coeliac patients with affective disorders. Aliment PharmacolTher. 2004; 20:777–782.]

14. Zone JJ, Skin manifestations of celiac disease. Gastroenterol. 2005; 128:S87–S91

15. GuilletMH,DorvalJC,Larregue M, Guillet G: Darier `s erythema annulare centrifugum of neonatal onset with 15 years` follow up. Efficacy of interferon and role of cytokines.AnnDermatol Venerol.1995, 122:422-426

16. White JW Jr. Gyrate erythema. Dermatol Clin. 1985 Jan. 3(1):129-39.

17. Borbujo J, de Miguel C, Lopez A, de Lucas R, Casado M. Erythema annulare centrifugum and Escherichia coli urinary infection. Lancet. 1996 Mar 30. 347(9005):897-8.

18. Hendricks AA, Lu C, Elfenbein GJ, Hussain R. Erythema annulare centrifugum associated with ascariasis. Arch Dermatol. 1981 Sep. 117(9):582-5.

19. Bessis D, Chraibi H, Guillot B, Guilhou JJ. Erythema annulare centrifugum induced by generalized Phthirus pubis infestation. *Br J* Dermatol. 2003 Dec. 149(6):1291.

20. Hammar H. Erythema annulare centrifugum coincident with Epstein-Barr virus infection in an infant. ActaPaediatr Scand. 1974 Sep. 63(5):788-92.

21. Lee HW, Lee DK, Rhee DY, Chang SE, Choi JH, Moon KC, et al. Erythema annulare centrifugum following herpes zoster infection: Wolf's isotopic response?. Br *J* Dermatol. 2005 Dec. 153(6):1241-3.

22. González-Vela MC, González-López MA, Val-Bernal JF, Echevarría S, Arce FP, Fernández-Llaca H. Erythema annulare centrifugum in a HIV-positive patient. Int *J* Dermatol. 2006 Dec. 45(12):1423-5.

23. García-Doval I, Peteiro C, Toribio J. Amitriptyline-induced erythema annulare centrifugum. Cutis. 1999 Jan. 63(1):35-6.

24. TuranErkek E, KalayoğuBeğğk S. An Unexpected Inet Complication Associated with Azacitidine Treatment of Myelodysplastic Syndrome: Erythema AnnulareCentrifugum. Turk *J* Haematol. 2016 Mar 5. 33 (1):81-82

25. Kuroda K, Yabunami H, Hisanaga Y. Etizolam-induced superficial erythema annulare centrifugum. ClinExpDermatol. 2002 Jan. 27(1):34-6.

26. Hudson LD. Erythema annulare centrifugum: an unusual case due to hydroxychloroquine sulfate. Cutis. 1985 Aug. 36(2):129-30.

27. Gönül M, KülcüÇakmak S, Ozcan N, DenizOguz I, Ozhamam E. Erythema annulare centrifugum due to pegylated interferon-a-2a plus ribavirin combination therapy in a patient with chronic hepatitis C virus infection. *J* Cutan Med Surg. 2014 Jan-Feb. 18(1):65-8

28. Mendes-Bastos P, Coelho-Macias V, Moraes-Fontes MF, Milheiro A, Rodrigues AM, Cardoso J. Erythema annulare centrifugum during rituximab treatment for autoimmune haemolyticanaemia. *J* EurAcadDermatolVenereol. 2014 Aug. 28(8):1125-7

29. Chou WT, Tsai TF. Recurrent erythema annulare centrifugum during ustekinumab treatment in a psoriatic patient. ActaDermVenereol. 2013 Mar 27. 93(2):208-9

30. Ioannidou D, Krasagakis K, Stefanidou M, Tosca A. Erythema annulare centrifugum and osteoarthritis treated with hyaluronic acid. ClinExpDermatol. 2002 Nov. 27(8):720-2.

31. Ibrahim SF, Pryor J, Tausk FA. Stress-induced erythema annulare centrifugum. Dermatol Online *J*. 2009 Apr 15. 15(4):15.

32. Dogan G. Pregnancy as a possible etiologic factor in erythema annulare centrifugum. *Am J* ClinDermatol. 2009. 10(1):33-5

33. Ozkaya E, Atcı T, ErbudakDinc EE, Elinc Aslan MS. Erythema annulare centrifugum: remission during two pregnancies and exacerbation in between. *J* DtschDermatolGes. 2017 Nov. 15 (11):1136-1138.

34. Tsuji T, Kadoya A. Erythema annulare centrifugum associated with liver disease. Arch Dermatol. 1986 Nov. 122(11):1239-40.

35. Sack DM, Carle G, Shama SK. Recurrent acute appendicitis with erythema annulare centrifugum. Arch Intern Med. 1984 Oct. 144(10):2090-2

35. Ioannidou D, Krasagakis K, Stefanidou M, Tosca A. Erythema annulare centrifugum and osteoarthritis treated with hyaluronic acid. ClinExpDermatol. 2002 Nov. 27(8):720-2

36. Ibrahim SF, Pryor J, Tausk FA. Stress-induced erythema annulare centrifugum. Dermatol *Online J*. 2009 Apr 15. 15(4):15.

37. L.ADuhring, "Dermatitis herpetiformis" Journal of the American Medical Association , vol.250,no .2, pp .212- 216,1983

38. MarziaCapronil : "Celiac disease and dermatological manifestations: many skin clue to unfold gluten –sensitive enteropathy" Gastroenterology Research and Practise, Vol 2012

39. Latif S, Jamal A, Memon I, Yasmeen S, Tresa V, Shaikh S. Multiple autoimmune syndrome: Hashimoto's thyroiditis, Coeliac disease and systemic lupus erythematosus (SLE) Journal of the Pakistan Medical Association. 2010; 60(10):863–865

40. Song MS, Farber D, Bitton A, Jass J, Singer M, Karpati G. Dermatomyositis associated with celiac disease: response to a gluten-free diet. Canadian Journal *of* Gastroenterology. 2006; 20(6):433–435.

41. Rodríguez-García C, González-Hernández S, Pérez-Robayna N, Guimerá F, Fagundo E, Sánchez R. Repigmentation of vitiligo lesions in a child with celiac disease after a gluten-free diet. Pediatric *Dermatology*. 2011; 28(2):209–210.

42. Buderus S, Wagner N, Lentze MJ. Concurrence of celiac disease and juvenile dermatomyositis: result of a specific immunogenetic susceptibility? Journal of Pediatric Gastroenterology and Nutrition. 1997; 25(1):101–103.

43. Daoud W, El Euch D, Mokni M. Linear IgA dermatosis of adults associated with celiac disease. *Annales de Dermatologie et de Venereologie*. 2006; 133(6-7):588–589.

44. De D, Kanwar A. Eruptive lichen planus in a child with celiac disease. Indian Journal of Dermatology, Venereology and Leprology. 2008; 74(2):164–165.

45. Ruiz Villaverde R, Blasco Melguizo J, Menendez Garcia Estrada A, Díez García F. Erosive mucosal lichen associated to hyper IgE syndrome and coeliac disease. *Anales de Pediatria*. 2004; 60(3):281–282

46. Stefanini GF, Resta F, Marsigli L, et al. Prurigo nodularis (Hyde's

prurigo) disclosing celiac disease. *Hepato-Gastroenterology*. 1999; 46(28):2281–2284.

47. Bartyik K, Varkonyi A, Kirschner A, Endreffy E, Turi S, Karg E. Erythema nodosum in association with celiac disease. *Pediatric Dermatology*. 2004; 21(3):227–230.

48. Thorisdottir K, Camisa C, Tomecki KJ, Bergfeld WF. Necrolytic migratory erythema: a report of three cases. Journal of the American Academy of Dermatology. 1994; 30(2):324–329.

49. Dal Sacco D, Parodi A, Cozzani E, Biolcati G, Griso D, Rebora A. A case of variegate porphyria with coeliac disease and beta-thalassaemia minor. Dermatology. 2004; 209(2):161–162

50. Katsikas GA, Maragou M, Rontogianni D, Gouma P, Koutsouvelis I, Kappou-Rigatou I. Secondary cutaneous nodular aa amyloidosis in a patient with primary sjögren syndrome and celiac disease. Journal of Clinical Rheumatology. 2008; 14(1):27–29

51. Randle HW, Winkelmann RK. Pityriasis rubra pilaris and celiac sprue with malabsorption. *Cutis*. 1980; 25(6):626–627.

52. Thelander HE. Leiner's disease followed by the celiac syndrome. A case report. The Journal of Pediatrics. 1946; 28(1):101–102

53. O'Mahony D, O'Mahony S, Whelton MJ, McKiernan J. Partial lipodystrophy in coeliac disease. Gut. 1990; 31(6):717–718.

54. García-Patos V, Pujol RM, Barnadas MA. Generalized acquired cutis laxa associated with coeliac disease: evidence of immunoglobulin A deposits on the dermal elastic fibres. British Journal of Dermatology. 1996; 135(1):130–134.

55. Nenna R, D'Eufemia P, Celli M. Celiac disease and lamellar ichthyosis. Case study analysis and review of the literature. *Acta Dermatovenerologica Croatica*. 2011;19(4):268–270.

56. Montalto M, Diociaiuti A, Alvaro G, Manna R, Amerio PL, Gasbarrini G. Atypical mole syndrome and congenital giant naevus in a patient with celiac disease. *Panminerva Medica*. 2003; 45(3):219–221.