Am J Digest Dis 2016;3(1):21-23
www.ajdd.us /ISSN:2329-6992/AJDD0033487

Editorial
Rare diseases of the digestive system

Henry T Lynch[1], Hengjun Gao[2], Claus Hellerbrand[3], Dongfeng Tan[4], Hanlin L Wang[5], Chengfeng Yang[6], Xianzhong Ding[7], Lanjing Zhang[8,9]

[1]Creighton University School of Medicine, Omaha, NE, USA; [2]Tongji University School of Medicine Shanghai, China; [3]University Hospital Regensburg, Regensburg, Germany; [4]University of Texas MD Anderson Cancer Center Houston, TX, USA; [5]David Geffen School of Medicine University of California, Los Angeles, CA, USA; [6]Department of Physiology, Michigan State University, East Lansing, MI, USA; [7]Department of Pathology, Loyola University Medical Center, Maywood, IL, USA; [8]University Medical Center of Princeton at Plainsboro, and [9]Rutgers University, New Brunswick, NJ, USA

Received March 31, 2016; Accepted April 3, 2016; Epub June 25, 2016; Published June 30, 2016

In 1932, Crohn et al. described a new disease, named "regional ileitis" in the JAMA as a case report [1]. The disease now is known as Crohn disease (CD). It carries a 2.6-4.5 fold increased risk for colorectal cancer, compared with the general population [2]. Regular surveillance is recommended for the patients with a history of CD for more than 8-10 years [2, 3]. Recognizing CD is critical for the associated mortality, treatment plans and comorbidities. CD involves approximately 0.5% of the population in the developed countries, with an estimated prevalence ranging from 0.6 to 322 per 100,000 persons in Europe, 16.7 to 318.5 in North America, and 0.88 to 67.9 in Asia and the Middle East [4]. According to the definition of rare diseases by the European Union (no more than 5 in 10,000 persons) [5], CD may not qualify for the designation of a rare disease in Europe and North America , but it may in Asia and Middle East. Nevertheless, CD has been included in the databases of the OrphaNet [6] and National Organization for Rare Disorders [7]. Its rarity has indeed been an ongoing challenge to conducting clinical trials [8].

Similar phenomena hold true in oncology research and practice. For example, Lynch syndrome was first described when studying two families of hereditary colorectal cancer in 1962 [9], which had been the research interest of late Professor Warthin at University of Michigan [10]. Nowadays, more than 100 cancer-prone syndromes and many genetic and molecular mechanisms have been discovered [11]. A whole body of clinical and scientific evidence supports regular screening and surveillance for Lynch syndrome [12]. Several "classics in oncology" also started from case reports or small case-series, including Kaposi sarcoma [13], post-mastectomy lymphangiosarcoma [14], lymphoepithelial tumor [15] and pheochromocytoma [16]. Undoubtedly, case reports played an important role in promoting the clinical practice and scientific research in oncology.

It appears clear to the editors that rare diseases involving the digestive system may have significant impact on the individual patients, public health, medical education and scientific advancement. There are currently 7,000 rare diseases identified [5, 17]. CD and Lynch syndrome are just two examples where case reports eventually led to critical scientific and clinical research findings, and benefited numerous patients. Many rare diseases, however, are poorly studied. Their etiopathogenesis, clinical presentation, diagnosis, management and prognosis are poorly defined. We therefore believe that there is an under-recognized need for more reports and studies on rare or uncommon diseases. A decision of accepting case reports in *American Journal of Digestive Disease* is thus made to meet such a need. While many journals have started eliminating the category of case report, we hope that this journal will offer a platform for publication of rare, yet interesting, cases with exceptional

educational values. We are particularly interested in publishing cases with unique clinical, pathological and molecular features, ideally exceedingly rare yet clinically important. It is our hope that the publications will increase the awareness of rare diseases and thus strengthen the world-wide efforts in combating these diseases [5, 18].

In line with our thoughts, oncologists have already started paying more attention to rare diseases (rare tumors in their specialty), in part because there is a lack of clinical practice guidelines and personal experience. Reimbursement is also an issue associated with rare tumors [19]. Collaborative efforts are being made in accumulating experience on managing rare pediatric tumors [20]. Expanding clinical trials of novel therapeutics for rare diseases based on similar molecular mechanisms is also under way [17]. It is clear that an orchestrated effort involving policy-making, social support, patient education, physician education and research is needed to achieve the goal of better diagnosis and treatment of rare diseases [5, 18, 21]. We hope our decision of publishing case reports will contribute to the effort.

Address correspondence to: Dr. Lanjing Zhang, Department of Pathology, University Medical Center of Princeton at Plainsboro, Plainsboro, NJ 08536, USA. E-mail: lanjing.zhang@rutgers.edu; ljzhang@hotmail.com

References

[1] Crohn BB, Ginzburg L and Oppenheimer GD. Landmark article Oct 15, 1932. Regional ileitis. A pathological and clinical entity. By Burril B. Crohn, Leon Ginzburg, and Gordon D. Oppenheimer. JAMA 1984; 251: 73-79.

[2] Farraye FA, Odze RD, Eaden J, Itzkowitz SH, McCabe RP, Dassopoulos T, Lewis JD, Ullman TA, James T 3rd, McLeod R, Burgart LJ, Allen J, Brill JV; AGA Institute Medical Position Panel on Diagnosis and Management of Colorectal Neoplasia in Inflammatory Bowel Disease. AGA medical position statement on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology 2010; 138: 738-745.

[3] Baumgart DC and Sandborn WJ. Crohn's disease. Lancet 2012; 380: 1590-1605.

[4] Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, Benchimol EI, Panaccione R, Ghosh S, Barkema HW and Kaplan GG. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology 2012; 142: 46-54 e42; quiz e30.

[5] Rodwell C and Ayme S. Rare disease policies to improve care for patients in Europe. Biochim Biophys Acta 2015; 1852: 2329-2335.

[6] Orphanet/INSERM US14 Rare Disease Platform. Crohn disease: ORPHA206. web page: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=206 Last updated: Jan. 2013, accessed on Dec. 29, 2015.

[7] National Organization for Rare Disorders (NORD). Crohn's Disease. web page: https://rarediseases.org/rare-diseases/crohns-disease/accessed on Dec. 29, 2015.

[8] D'Haens G, Feagan B, Colombel JF, Sandborn WJ, Reinisch W, Rutgeerts P, Carbonnel F, Mary JY, Danese S, Fedorak RN, Hanauer S, Lémann M; International Organization for Inflammatory Bowel Diseases (IOIBD) and the Clinical Trial Committee Clincom of the European Crohn's and Colitis Organisation (ECCO). Challenges to the design, execution, and analysis of randomized controlled trials for inflammatory bowel disease. Gastroenterology 2012; 143: 1461-1469.

[9] Lynch HT, Shaw MW, Magnuson CW, Larsen AL and Krush AJ. Hereditary factors in cancer. Study of two large midwestern kindreds. Arch Intern Med 1966; 117: 206-212.

[10] Classics in oncology. Heredity with reference to carcinoma as shown by the study of the cases examined in the pathological laboratory of the University of Michigan, 1895-1913. By Aldred Scott Warthin. 1913. CA Cancer J Clin 1985; 35: 348-359.

[11] Lynch HT, Snyder CL, Shaw TG, Heinen CD and Hitchins MP. Milestones of Lynch syndrome: 1895-2015. Nat Rev Cancer 2015; 15: 181-194.

[12] Rubenstein JH, Enns R, Heidelbaugh J and Barkun A. American Gastroenterological Association Institute Guideline on the Diagnosis and Management of Lynch Syndrome. Gastroenterology 2015; 149: 777-782; quiz e716-777.

[13] Braun M. Classics in Oncology. Idiopathic multiple pigmented sarcoma of the skin by Kaposi. CA Cancer J Clin 1982; 32: 340-347.

[14] Stewart FW and Treves N. Classics in oncology: lymphangiosarcoma in postmastectomy lymphedema: a report of six cases in elephantiasis chirurgica. CA Cancer J Clin 1981; 31: 284-299.

[15] Classics in oncology. On lymphoepithelial tumors: Alexander Schmincke. 1921. CA Cancer J Clin 1983; 33: 172-179.

[16] Classics in oncology. A case of bilateral completely latent adrenal tumor and concurrent nephritis with changes in the circulatory system and retinitis: Felix Frankel, 1886. CA Cancer J Clin 1984; 34: 93-106.
[17] Brooks PJ, Tagle DA and Groft S. Expanding rare disease drug trials based on shared molecular etiology. Nat Biotechnol 2014; 32: 515-518.
[18] Svenstrup D, Jorgensen HL and Winther O. Rare disease diagnosis: A review of web search, social media and large-scale data-mining approaches. Rare Dis 2015; 3: e1083145.
[19] Shin DW, Cho J, Yang HK, Kim SY, Lee SH, Suh B, Shin HY, Lee HJ, Kim DG and Park JH. Oncologist Perspectives on Rare Cancer Care: A Nationwide Survey. Cancer Res Treat 2015; 47: 591-599.
[20] Pappo AS, Furman WL, Schultz KA, Ferrari A, Helman L and Krailo MD. Rare Tumors in Children: Progress Through Collaboration. J Clin Oncol 2015; 33: 3047-3054.
[21] Ayme S and Rodwell C. The European Union Committee of Experts on Rare Diseases: three productive years at the service of the rare disease community. Orphanet J Rare Dis 2014; 9: 30.