Autoimmunity Reviews 13 (2014) 467–471

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Diagnosis and classification of Crohn's disease

Martin W. Laass [a], Dirk Roggenbuck [b,c], Karsten Conrad [d,*]

[a] Department of Paediatrics, Medical Faculty of the Technical University of Dresden, Dresden, Germany
[b] Faculty of Science, Brandenburg Technical University Cottbus-Senftenberg, Senftenberg, Germany
[c] GA Generic Assays GmbH, Dahlewitz, Germany
[d] Institute of Immunology, Medical Faculty of the Technical University of Dresden, Germany

ARTICLE INFO

Article history:
Accepted 13 November 2013
Available online 11 January 2014

Keywords:
Inflammatory bowel diseases
Crohn's disease
Ulcerative colitis
Diagnostic criteria
Autoantibody

ABSTRACT

Crohn's disease (CrD) is a chronic relapsing inflammatory bowel disease (IBD) potentially affecting any portion of the gastrointestinal tract from the mouth to the anus. CrD usually manifests between 15 and 30 years of age and presents typically with abdominal pain, fever, bloody or non-bloody diarrhoea, and weight loss. Paediatric patients may show failure to thrive, growth impairment, and delayed puberty additionally. Extraintestinal manifestations like arthritis, uveitis, and erythema nodosum are diagnosed in almost half of the patients. CrD is characterized by a discontinuous and ulcerous transmural inflammation often involving the ileocaecal region and leading to a stricturing or even fistulising phenotype in up to 50% of patients finally. Incidence and prevalence of CrD have been rising worldwide over the past decades. Although many details of the pathophysiology of CrD have been elucidated, no common aetiopathogenic model exists for all forms of CrD, presenting more an umbrella term for a phenotypically and genotypically heterogeneous clinical condition. In CrD, we see an inappropriate response of the innate and/or adaptive immune system to the intestinal microbiota in genetically predisposed individuals. The diagnosis of CrD is based mainly on patient's history and clinical examination and supported by serologic, radiologic, endoscopic, and histologic findings. Antibodies to *Saccharomyces cerevisiae* and autoantigenic targets such as glycoprotein 2 may aid in differentiating CrD from UC. Their single use, however, is limited by low sensitivity requiring antibody profiling for an appropriate serologic diagnosis. This review focuses on diagnostic and classification criteria of CrD.

Contents

1. Introduction . . . 467
2. Epidemiology . . . 468
3. Aetiopathogenesis . . . 468
4. Diagnostic criteria . . . 469
   4.1. Medical history and clinical manifestations . . . 469
   4.2. Radiologic and endoscopic diagnostics . . . 469
   4.3. Laboratory and serologic markers . . . 470
   4.4. Classification . . . 470
   4.5. Disease activity and activity indices . . . 471
5. Medical management . . . 471
References . . . 471

1. Introduction

Crohn's disease (CrD) is a lifelong and chronic relapsing inflammatory bowel disease (IBD) potentially affecting any portion of the gastrointestinal tract from the mouth to the anus. Similar to ulcerative colitis (UC), the other main IBD (see chapter "Diagnosis and classification of Ulcerative Colitis" in this issue), CrD manifests most often in the second

* Corresponding author at: Institute of Immunology, Medical Faculty of the Technical University of Dresden, Fetscherstrasse 74, 01307 Dresden, Germany. Tel.: +49 351 458 6540; fax: +49 351 458 6308.
E-mail address: k_conrad@mail.zih.tu-dresden.de (K. Conrad).

1568-9972/$ – see front matter © 2014 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.autrev.2014.01.029

and third decade but disease onset can occur at any age. In 25% of all IBD patients, disease starts before the age of 18 years.

2. Epidemiology

CrD and UC are the most frequently diagnosed IBDs. In a recent systematic review, the highest annual incidence of CrD has been determined at 12.7 per 100,000 person-years in Europe, 5.0 person-years in Asia and the Middle East, and 20.2 per 100,000 person-years in North America [1]. The highest prevalence for CrD has been obtained for Europe (322 per 100,000 persons) and North America (319 per 100,000 persons). The somewhat increased risk for colorectal and small bowel cancer is one of the reasons for the slightly reduced life expectancy of patients with CrD.

3. Aetiopathogenesis

Although the precise aetiopathogenesis of CrD is unknown, several immunological, genetic and environmental factors contributing to the disease have been identified. The current discourse refers to an imbalance between tolerance to commensal microbiota or food derived antigens and immune responses to pathogens. Thus, mucosal inflammation observed in CrD is triggered in genetically predisposed individuals by dysregulated innate and adaptive immune responses [2–4]. In a meta-analysis of CrD genome-wide association studies, 71 distinct loci associated with CrD were identified [5]. Recently, the number of risk loci for IBD was extended to 163; of which 110 are associated with both CrD and UC [6]. Among the most important susceptibility genes for CrD are the intracellular pathogen-recognition receptor *NOD2*, the autophagy genes *ATG16L1* and *IRGM* and the transcription factor *XBP1*

Table 1
Diagnostic features of Crohn's disease.

	Features
Medical history (symptoms should be present for 4–6 weeks)	Diarrhoea with blood and/or mucus
	Nocturnal diarrhoea
	Gross or occult rectal bleeding
	Abdominal pain
	Weight loss
	Delayed puberty, growth impairment (in children and adolescents)
	Family history of inflammatory bowel disease
	Symptoms suspicious of extraintestinal manifestations (joints, eyes, skin)
Physical examination	Abdominal tenderness
	Abdominal mass (suggestive of ileocaecal infiltration or abscess)
	Perianal disease (fissures, fistulae, perirectal abscesses, skin tags)
	Aphthous stomatitis
	Orofacial granulomatosis
	Signs of extraintestinal disease (joint pain, swelling, redness or stiffness, erythema nodosum, redness of the eye)
Laboratory findings	Elevated C-reactive protein
	Elevated erythrocyte sedimentation rate
	Anaemia
	Iron deficiency (low ferritin)
	Vitamin B12 deficiency
	Thrombocytosis
	Hypoalbuminemia
	Elevated faecal calprotectin
	Antibodies against mannan of *Saccharomyces cerevisiae* (ASCA)
	Pancreatic autoantibodies (PAB), anti-glycoprotein-2 antibodies
Microbial studies	Exclusion of intestinal infection (see Table 3)
Imaging (Transabdominal ultrasound and MR enterography) [21]	Enteric findings
	Wall thickening and oedema
	Small bowel involvement
	Deep ulcerations (early and superficial ulcerations are not well detectable by MR enterography)
	Strictures
	Entero-colic or entero-enteric fistulae
	Fatty infiltration of the bowel wall
	Extraenteric findings
	Enterocutaneous fistulae
	Mesenteric fat hypertrophy/fat wrapping
	Abscesses
	Mesenteric lymphadenitis
Endoscopic features	Discontinuous pattern of inflammation (“skip lesions”)
	Small aphthous, fissural, and longitudinal ulcers
	Cobblestone pattern (non-ulcerated mucosa, separated by ulcers)
	Strictures
Histologic features [36] (at least two biopsies from at least five colonic segments each including the ileum)	Focal (discontinuous) chronic inflammation
	Focal crypt architectural irregularity
	Transmural inflammation
	Granulomas (not related to crypt injury)
	Increased intraepithelial lymphocytes
	Pyloric gland metaplasia