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Original Article

Early diagnosis of granulomatosis with polyangiitis: An introduction to the newly designed Iran criteria

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ABSTRACT

Backgrounds: In the absence of practical diagnostic criteria for diagnosis of granulomatosis with polyangiitis (GPA), a new diagnostic criteria for GPA is proposed based on literature review for characteristic manifestations of GPA and expert opinion. The sensitivity of the new criteria, Iran criteria for GPA, is assessed in comparison with 1990 American College of Rheumatology (ACR) criteria for Wegener's granulomatosis (WG).

Methods: Evaluation of three organs (ear, nose and throat (ENT); lung; kidney) and two laboratory findings (anti-neutrophil cytoplasmic antibody; biopsy), abbreviated mnemonically as ELKAB, is suggested in our criteria. A retrospective sensitivity analysis was performed based on medical records of 35 patients. Clinical diagnosis of GPA by a single rheumatologist was used as the gold standard.

Results: Records of a total of 15 male and 20 female patients with a mean follow-up duration of 21.26 ± 4.13 months were considered. Mean age at diagnosis and mean disease duration were 32.37 ± 2.33 years and 19.06 ± 5.41 months, respectively. The sensitivity for Iran criteria for GPA and 1990 ACR classification criteria for WG were calculated as 100% and 80%, respectively.

Conclusions: Iran criteria for GPA is a highly sensitive instrument for detecting GPA patients in comparison with 1990 ACR classification criteria for WG.

1. Introduction

Granulomatosis with polyangiitis (GPA), previously named as Wegener's granulomatosis (WG), is a rare anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis affecting small and medium sized vessels.[1] GPA is a multi-organ disease mainly involving ear, nose and throat (ENT), lung and kidneys. Because of the high toxicity of available therapies, a

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precise and definite diagnosis of the disease is of great importance, further early diagnosis and treatment can significantly improve outcomes.[2–4] There are few pathognomic presentations and no definite laboratory finding for diagnosing GPA; as a result, GPA is suspected based on a collection of clinical manifestations, laboratory tests and histological findings. The 1990 American College of Rheumatology (ACR) criteria for WG classification consider nasal/oral inflammation, abnormal chest X-ray, abnormal urinary sediment and granulomatous inflammation on biopsy (Table 1).[5] Though, ACR criteria are classification criteria rather than a diagnostic one, and have low sensitivity for diagnosis. They are primarily intended to generate homogenous sets of patients for research purposes.[5] Besides, the ACR criteria cannot distinguish between GPA and microscopic polyangiitis (MPA) or non-vasculitis systemic diseases that mimic GPA. However, it is widely used as diagnostic criteria in clinical practice due to lack of proper criteria for accurate diagnosis of GPA. The primary purpose of diagnostic criteria is to diagnose the condition in an individual patient and to distinguish one type of disease from another which poses a diagnostic challenge even to experienced clinicians.[3]

In the present article, we propose Iran criteria for GPA as an experience-based set of criteria for GPA diagnosis by using our experiences during 14 years of clinical practice in rheumatology[6,7] and assess its sensitivity in comparison with 1990 ACR criteria for WG.

2. Methods

The study protocol was approved by the Medical Ethics Committee of Tehran University of Medical Sciences. The medical records of the patients with a definite diagnosis of GPA, made by a single expert rheumatologist (ISA) at the outpatient Rheumatology Clinic or Rheumatology Clinic of Amir-Álam Hospital (a general hospital with a tertiary otolaryngology referral center in Tehran, Iran) between 2001 and 2011 were reviewed. Infectious disease specialists and ENT specialists helped in ruling out other suspected diagnoses when necessary. The patients with overlap disease, suspected as MPA, on treatment of GPA before referral to the clinic, follow-up for less than 1 month, and the patients with incomplete medical records were excluded.

Demographic and clinical information including gender, age at diagnosis, disease duration and follow-up duration were extracted. The findings of imagings (chest or sinus X-rays, CT-scan of sinuses and HRCT of lungs) were interpreted by both an experienced rheumatologist and a radiologist. Serum ANCA was done by indirect immunofluorescence assay or were analyzed for specific antibodies directed against PR3 or MPO by enzyme-linked immunosorbent assay (ELISA). The data on each criterion of Iran criteria for GPA (Table 2) and 1990 ACR criteria for Wegener's granulomatosis were extracted and the patients with definite diagnosis of GPA according to each set of criteria were recognized. Iran criteria for the diagnosis of GPA suggests evaluation of three organs and two laboratory findings (ANCA and biopsy), abbreviated as ELKAB, after ruling out other prominent diagnoses by history and physical examination (Table 2).

The definition of persistent otitis media which is generally accepted in the literature is persistence of the disease during antimicrobial therapy of symptoms and signs of infection (treatment failure) and/or relapse of the disease within 1 month of completion of antibiotic therapy. Recurrent disease is defined as recurrence of the disease for at least 3 episodes in 6 months or 4 episodes in 12 months. Recurrent sinusitis was defined as more than 3 episodes of the disease in a season and chronicity as unresponsiveness to more than three weeks of antibiotic therapy. The appropriate approach toward a correct diagnosis for a patient suspected as suffering from GPA is outlined in Table 3, Amir-Álam Hospital approach towards diagnosis of GPA.

Considering the clinical diagnosis of GPA by a rheumatologist as the gold standard, sensitivity of the two sets of criteria was measured using the following formula: Sensitivity = (number of the patients classified as GPA by the criteria)/(number of the patients diagnosed as GPA by a rheumatologist). Statistical analysis was conducted using SPSS software version 16.00 (SPSS Inc., Chicago, IL). Continuous and categorical variables are expressed as mean ± standard error of the mean (SEM) and number (%), respectively.

Table 1 – The 1990 American College of Rheumatology criteria for Wegener's granulomatosis classification.

Nasal or oral inflammation
• Painful or painless oral ulcers *or*
• Purulent or bloody nasal discharge
Abnormal chest radiograph showing
• Nodules *or*
• Fixed infiltrates *or*
• Cavities
Abnormal urinary sediment with
• Microscopic hematuria with *or* without red cell casts
Granulomatous inflammation on biopsy
• Within the arterial wall *or*
• In the perivascular area

The presence of 2 or more of these 4 criteria is associated with a sensitivity of 88.2% and a specificity of 92.0%.

3. Results

The medical records of 35 patients with a mean follow-up duration of 21.26 ± 4.13 months were reviewed. The mean age at the diagnosis was 32.37 ± 2.33. Frequencies of the findings for each criterion of GP criteria for GPA are expressed in Table 4. A total of 17 patients were diagnosed as limited and 18 as systemic GPA. The 1990 ACR classification criteria for GPA were 80% sensitive in diagnosing GPA among our study sample; however, 100% of the patients fulfilled Iran criteria for GPA.

4. Discussion

In the absence of practical diagnostic criteria for diagnosis of GPA, the authors introduce a diagnostic set of criteria for GPA after doing a literature review and using expert opinion.