Masked presentation of giant-cell arteritis[1]

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The charts of 48 patients with biopsy-proved giant-cell arteritis evaluated at the Cleveland Clinic from 1975 through 1980 were analyzed to determine the frequency of masked presentation, correlating two sets of criteria together with the initial diagnosis. One or more classical criteria were lacking in nine cases (18%) and 25 (52%) were initially misdiagnosed. However, if published criteria for polymyalgia rheumatica were applied, that diagnosis should have been considered at presentation in all cases.

Index terms: Polymyalgia rheumatica • Temporal arteritis

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Diagnosis of giant-cell arteritis (GCA) is not difficult when the clinical presentation is typical: this includes bitemporal headaches, scalp tenderness, abnormalities of the superficial temporal artery, and claudication of the jaw with or without the proximal muscle pain and stiffness of polymyalgia rheumatica (PMR). Prompt diagnosis is important, since proper treatment is necessary to avert serious arterial occlusion with the possible development of blindness or stroke.[1] Unfortunately, not all patients present with typical signs and symptoms: some may have a nonspecific or misleading clinical picture ("masked presentation") which can delay diagnosis and increase the risk of serious sequelae. Because estimates of the incidence of the masked presentation vary (*Table 1*),[2–8] we conducted a retrospective study of the clinical records of patients with biopsy-proved GCA at our institution. The clinical material was analyzed based on (*a*) the classical criteria for GCA,[9] (*b*)

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Table 1. Masked or atypical presentation: summary of the literature

Year of Publication	Authors	No. of cases	No. of atypical cases
1958	Wagener and Hollenhorst[8]	122	2 (1.6%)
1962	Simmons and Cogan[4]	32	5 (15.6%)
1966	Meadows[5]	80	2 (2.5%)
1967	Cullen[3]	19	17 (89.5%)
1971	Hamilton et al[6]	25	1 (4%)
1972	Fauchald et al[18]	94	5 (5.3%)
1980	Healey and Wilske[2]	74	30 (40.5%)
1981	Bengtsson and Malmvall[7]	126	10 (7.9%)

the criteria derived by Bird et al[10] for PMR, and (*c*) the initial diagnosis made at our institution.

Materials and methods

Clinical records of all patients with histological evidence of GCA evaluated at the Cleveland Clinic from 1975 through 1980 were reviewed. Histopathological changes considered necessary for a diagnosis of GCA included fragmentation of the internal elastic lamina, intimal proliferation, and infiltration of the media by mononuclear cells with or without giant-cell formation.

Clinical and laboratory data taken from the charts were analyzed for two sets of criteria. Classical criteria were adapted from a recent review of vasculitis[9] and included (*a*) patient older than 50, (*b*) headaches of recent onset, (*c*) a significantly elevated erythrocyte sedimentation rate (ESR), and (*d*) proximal muscle pain and/or temporal artery tenderness. Significant elevation of the ESR was defined as either Westergren sedimentation rate $\geq$ 40 mm/hr,[9] uncorrected Wintrobe sedimentation rate $\geq$ 40 mm/hr,[11,12] a zeta value $\geq$ 60%,[13] or Rourke-Ernstene sedimentation rate $\geq$ 1.0 mm/min.[14] If all of these criteria were noted, the presentation was described as "classical." The second set of criteria, published by Bird et al,[10] included (*a*) bilateral shoulder pain and/or stiffness, (*b*) onset over a period of $\leq$ two weeks, (*c*) initial Westergren sedimentation rate $\geq$ 40 mm/hr, (*d*) morning stiffness lasting $\leq$ 1 hr, (*e*) age >65, (*f*) depression and/or weight loss, and (*g*) tenderness in both upper arms. Patients with three or more of these criteria, or one of them combined with palpable abnormality of the superficial temporal artery, have been shown to have a high likelihood of PMR,[10] and such cases may be called "probable PMR." We also sought other data which might suggest GCA, including claudication of the jaw and visual symptoms, as well as signs and symptoms which might suggest other diagnoses, *e.g.*, anemia (hemoglobin < 11 g/dL), anorexia, malaise, fatigue, fever, autoantibodies, or elevated tissue enzymes. Finally, the initial impression of the first examining physician was recorded in each case.

Results

During the years 1975–1980, histological changes in the superficial temporal arteries consistent with GCA were observed in 53 patients. Five were excluded, leaving a total of 48; 2 were receiving corticosteroids at the time of the initial evaluation, and 3 had insufficient data. Our study population consisted of 34 women and 14 men with a mean age of 70.19 years (range, 53–82). Of these, 38 fulfilled the classical criteria for GCA as outlined earlier. Of the 10 remaining patients (*Table 2*), one (Case 1) was considered atypical because the Wintrobe sedimentation rate was only 36 mm/hr, compatible with low values reported in other inflammatory diseases.[15] Fibrinogen and glycoproteins were significantly elevated; however, in all other respects the clinical course was consistent with GCA, and this patient was included in the "classical" group for statistical purposes. The other 9 patients had a confusing clinical picture corresponding to loosely defined diagnostic subsets which we have identified as vascular occlusive (4 patients), febrile (3 patients), malignant (1 patient), and general symptoms (1 patient). Seven patients did not have headaches, 6 lacked proximal myalgias, and 6 had no temporary artery abnormalities. Analysis of the entire patient population for masked GCA based on the absence of one or more classical symptoms resulted in an estimate of 9 in 48 or 18.75%. If the initial diagnosis was the only criterion for a masked presentation, 25 patients would fall into

Table 2. Classical features insufficient for diagnosis of giant-cell arteritis (N = 9/48 or 18.7%)

Case	Age (yr)	Sex	Proximal Myalgia	Headaches	Clinically Abnormal Temporal Artery	ESR/WSR* (mm/hr)	Visual Symptoms or Blindness	Other Signs and Symptoms	Temporal Artery Abnormality	Type of Masked Presentation
1	64	F	Yes	Yes	No	Wintrobe 36 FIB 510	No	A.M. gel depression	No	None
2	65	F	No	Yes	No	Zeta 69%	No	Fever (101–102° F)	No	Fever of unknown origin
3	73	M	No	No	No	Wintrobe 47 FIB 1,030	No	Fever (103° F)	No	Fever of unknown origin
4	73	F	Yes	No	No	Wintrobe 64 115	No	Low-grade fever; hemoglobin, 9.7 g/dL	No	Anemia versus fever of unknown origin
5	75	M	No	No	Yes	110	Yes (bilateral)	None	Yes	Occlusive
6	77	M	No	No	No	77	Yes (left)	30-lb weight loss	No	Occlusive
7	68	F	No	No	Yes	Wintrobe 52	Yes (right)	Anorexia, 8-lb weight loss	Yes	Occlusive (?)
8	81	F	No	No	Yes	Wintrobe 51	Yes (left)	Claudication of the jaw	Yes	Occlusive (?)
9	81	F	No	Yes	No	56	No	Anorexia, 12-lb weight loss	No	Malignant
10	62	F	Yes	No	No	Wintrobe 50 FIB 560	No	Malaise; morning gel	No	Fibrositis

ESR = erythrocyte sedimentation rate, and *WSR* = Wintrobe sedimentation rate.

this category. Initial diagnoses included depression and/or fibrositis (6 patients), fever of undetermined origin (5 patients), occult malignancy (5 patients), no diagnosis (5 patients), lumbosacral osteoarthritis (2 patients), cervical osteoarthritis (1 patient) and transient ischemic attacks or a cerebral vascular accident (1 patient). Four of these patients were among the 9 previously designated as having masked GCA, while the other 21 were included in the "classical" group (*Table 3*).

When signs and symptoms were analyzed using Bird's criteria, all patients were found to have at least minimal criteria (mean, 3.85), allowing classification as probable PMR (*Figure*). Only 1 patient, a 64-year-old woman, had as few as 2; however, she also had bilateral superficial temporal artery tenderness, allowing a designation of probable PMR. Altogether, 32 patients (66.6%) had abnormalities involving the superficial temporal arteries.

Three of our 48 patients were found to have significant titers of antinuclear factors, totalling 1:160 in 2 and 1:80 in 1. None of these patients

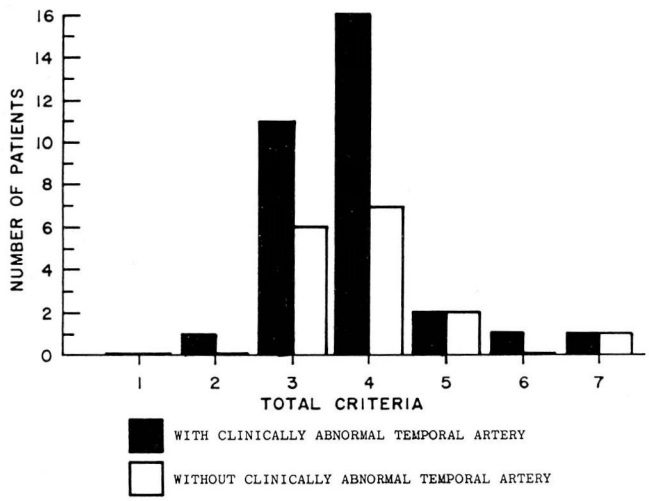

Fig. Number of criteria suggested by Bird et al[10] for diagnosis of polymyalgia rheumatica in 48 patients.

was on medication known to cause drug-induced lupus erythematosus, nor did any of them have signs or symptoms of systemic lupus erythematosus (SLE).

Discussion

The lower incidence of masked or occult disease in this series is difficult to reconcile with previous reports. The earliest of these were written before the relationship between PMR and GCA was fully appreciated. Paulley and Hughes described this relationship in 1960,[16] and both Alestig and Barr[17] and Fauchald et al[18] subsequently demonstrated histological evidence of GCA in patients who had symptoms of PMR alone. Many reports of atypical, masked, or occult GCA note that the typical signs and symptoms, though present, were overshadowed by more dramatic and atypical symptoms including fever, weight loss, and/or anemia.[2,19–21] The purpose of our study was twofold: to emphasize the importance of considering all signs and symptoms at the initial presentation and to caution clinicians against misinterpreting one or two prominent symptoms. Using the initial diagnosis as the criterion of "masked GCA," 25 of our 48 patients would have been so diagnosed; in retrospect, however, classical symptoms were present in fully 21 of these 25 patients.

In order to label a disease "masked" or "atypical," there must be an understanding of what constitutes "typical" disease. Present criteria of GCA have been arrived at based on the consensus of the literature. Unlike some diseases, including rheumatoid arthritis and SLE,[22,23] we know of no attempt until recently to define statistically relevant criteria based on patients with the disease, in contrast to groups with similar but different diseases. Bird et al[10] arrived at a better clinical definition of PMR by contrasting signs and symptoms in 236 patients with the disease versus 253 patients with diseases which may mimic PMR. Percent sensitivity and specificity were calculated

Table 3. Misdiagnosed cases (N = 25/48 or 53%)

Patients with Classical Criteria (21/39 Misdiagnosed)		
Initial Diagnosis	No. of Patients	No. of criteria of Bird et al[10] + = abnormal temporal artery – = normal temporal artery ( ) = number of patients
No diagnosis referable to symptoms	5	3 + (1), 4 + (4)
Fever of unknown origin	4	4 + (4)
Occult neoplasm	4	3 + (2), 5 – (2)
Depression/fibrositis	4	2 + (1), 3 + (1), 4 + (1), 7 – (1)
Osteoarthritis of the lumbosacral spine	2	4 – (1), 7 + (1)
Transient ischemic attacks/cerebrovascular accident	1	4 + (1)
Osteoarthritis of the cervical spine	1	4 – (1)
Patients without Classical Criteria (4/9 Misdiagnosed)		
Initial Diagnosis	No. of Patients	No. of criteria of Bird et al[10] + = abnormal temporal artery – = normal temporal artery ( ) = number of patients
Depression/fibrositis	2	4 – (2)
Occult neoplasm	1	3 – (1)
Fever of unknown origin	1	3 – (1)

for a variety of clinical and laboratory features which have been thought to define PMR, and seven characteristics which best discriminated PMR from other diseases were listed. Further statistical analysis demonstrated that three or more of these criteria (or one or more plus palpable abnormalities of the superficial temporal artery) had a high discriminative value. When we applied these criteria to our cases, we found that all of them could be classified as probable PMR, from which it is a short and logical step to consideration of GCA as a diagnosis.

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