Aschoff Bodies *At Necropsy* in Valvular Heart Disease

Evidence from an Analysis of 543 Patients Over 14 Years of Age that Rheumatic Heart Disease, At Least Anatomically, Is a Disease of the Mitral Valve

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SUMMARY **Among 543 necropsy patients over age 14 years with severe chronic valvular heart disease, Aschoff bodies were found in 11 patients (2%). The ages of the 11 patients ranged from 18 to 68 years (avg 38), and nine had had a history of acute rheumatic fever earlier in life. Clinically, nine of the 11 patients had mitral stenosis with or without dysfunction of one or more other cardiac valves, one had isolated aortic regurgitation, and one had both mitral and aortic regurgitation. All 11 patients had diffuse fibrous thickening of the mitral valve leaflets, and all but one had diffuse anatomic lesions of at least one other cardiac valve. No patient with anatomic lesions limited to the aortic valve had Aschoff bodies. Thus, among patients with chronic valvular heart disease, Aschoff bodies, the only anatomic lesion pathognomonic of rheumatic heart disease, indicate diffuse anatomic lesions of the mitral leaflets and usually also anatomic lesions of one or more other cardiac valves. The functional mitral lesion is usually stenosis.**

SINCE ASCHOFF[1] first described in 1904 lesions in the heart which have subsequently become known as *Aschoff bodies,* these lesions have been sought at necropsy in patients with valvular heart disease. Of 518 necropsy patients with valvular heart disease reported from 1934 to 1961 (table 1), the percent with Aschoff bodies varied enormously (from 9 to 84% [avg 42]).[2-12] These 11 previous studies (table 1)[2-12] were based on variable and often unclear criteria for defining Aschoff bodies. Because of this marked variation in reported frequency of Aschoff bodies in necropsy patients and because of a previous study by us on the frequency of Aschoff bodies in operatively excised atrial appendage and papillary muscle,[13] it appeared worthwhile to examine a large number of necropsy patients with chronic valvular heart disease to determine the frequency and clinical significance of Aschoff bodies.

Patients Studied and Methods

All patients with chronic valvular heart disease in whom necropsy was performed at the Clinical Center of the National Institutues of Health and all necropsy patients with valvular heart disease in whom the heart was submitted to the Pathology Branch of the National Heart, Lung, and Blood Institute between 1953 and 1972 were included in this analysis. A total of 543 necropsy patients with severe (functional class III or IV, New York Heart Association classification) chronic valvular heart disease was analyzed (table 2). Each of the 543 hearts was examined grossly and histologically by one of us (WCR) and the cases were classified according to the functional valve lesion detected clinically (table 2). Tricuspid regurgitation, however, was not included in the functional classification. In over 90% of the 543 patients, the functional valve lesions had been confirmed by, or diagnosed by, cardiac catheterization with or without angiography. In addition to classifying the patients by their functional valve lesions, each was also classified anatomically. Some patients with clinically isolated mitral stenosis, for example, at necropsy also had diffuse anatomic lesions of the aortic valve. Therefore, these patients were classified anatomically as mitral plus aortic but clinically only as mitral stenosis (table 2). Also, for a valve to be considered abnormal anatomically there must have been *diffuse* thickening of all portions of each valve cusp or thickening of the *margins* around the entire valve circumference (fig. 1). Focal leaflet thickening, i.e., sparing at least some marginal areas, was not considered indicative of anatomic abnormality.

Of the 543 patients, their ages at death ranged from 15 to 88 years (avg 45); 64% were men and 36%, women. A cardiac operation (valve commissurotomy, anuloplasty or replacement) had been performed in 372 (69%) of the 543 patients.

At least one section of wall of each cardiac chamber was cut, processed, stained (hematoxylin-eosin) and examined histologically. Each section included the through-and-through thickness of wall from endocardium to epicardium. Each section for histologic study was at least 2 cm in maximal dimension. At least four histologic sections were examined from each patient, an average of seven per patient. The criteria used for recognizing Aschoff bodies are those proposed by Saphir[14] and summarized in table 3.

Results

Aschoff bodies were found in the heart in 11 (2%) of the 543 patients (table 2). The frequency of the Aschoff bodies in these 11 patients were *numerous* in six, *many* in one, and *rare* in four. The patients with either numerous or many Aschoff bodies had these structures in the walls of at least three of the four cardiac chambers and multiple ones were observed in the sections. In contrast, the patients with rare Aschoff bodies had these structures in the walls of only one or two chambers: in two patients, only in left ventricle, and in the other two, both left ventricle and left atrium. In the four patients with rare Aschoff bodies, only three to six of these structures were observed per patient in all the sections

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TABLE 1. *Reported Frequency of Aschoff Bodies At Necropsy in Valvular Heart Disease*

First author	Year (Ref. No.)	No. of patients	No. (%) with Aschoff Bodies	No. (%) pts. with MS
Rothschild	1934 (2)	161	95 (59)	—
McKeown	1945 (3)	18	15 (84)	12 (67)
Pinniger	1951 (4)	19	6 (31)	19 (100)
Waaler	1952 (5)	16	5 (31)	16 (100)
McKeown	1953 (6)	92	22 (25)	92 (100)
Decker	1953 (7)	22	6 (27)	22 (100)
Thomas	1953 (8)	40	29 (72)	40 (100)
Luse	1954 (9)	28	3 (11)	28 (100)
Tedeschi	1955 (10)	22	2 (9)	22 (100)
Lannigan	1959 (11)	76	27 (35)	76 (100)
Ruebner	1961 (12)	24	8 (33)	24 (100)
Totals		518	218 (42)	343/358 (96)

MS = mitral stenosis.

examined. In two patients, Aschoff bodies also were observed in epicardium and each of these patients had numerous Aschoff bodies. In all 11 patients Aschoff bodies were observed in both mural endocardium and in myocardium. Aschoff bodies were not observed in valvular endocardium in any patient but sections of valve were not examined in all patients. The number of histologic sections of heart examined in each of the 11 patients with Aschoff bodies ranged from 6 to 16 (avg 10).

The *functional* and *anatomic* valvular lesions in the 11 patients with Aschoff bodies are summarized in table 4. Of the 11 patients, nine had mitral stenosis with or without functional lesions of other cardiac valves, one had pure aortic regurgitation and one had both aortic and mitral regurgitation. Although only 18 functional valve lesions (excluding tricuspid regurgitation) were observed in the 11 patients with Aschoff bodies, 26 anatomic valve lesions were present in these patients. All 11 patients had anatomic lesions of the mitral valve (fig. 1), ten had anatomic involvement of the aortic valve, four also of the tricuspid valve, and one also of the pulmonic valve. Thus, of the 11 patients, only one had anatomic lesions limited to only one valve (mitral), and the other ten had anatomic lesions of two or more valves.

Certain clinical features in the 11 necropsy patients with Aschoff bodies are summarized in table 5 and these observations are compared to those in our previous study[14] of 45 surgical patients with Aschoff bodies in operatively excised atrial appendage or papillary muscle.

Comments

The last reported study describing the frequency of Aschoff bodies *at necropsy* in patients with valvular heart disease appeared in 1961 and concerned only 24 patients.[12] The largest previous study on this subject appeared in 1934 and concerned 161 patients.[2] Although several studies on the frequency of Aschoff bodies at necropsy appeared between 1934 and 1961, none provided much clinical information regarding the patients with Aschoff bodies, few described the relative frequency of distribution of the Aschoff bodies in the heart, and none described the number(s) of cardiac valves involved anatomically or functionally other than mitral

TABLE 2. *Functional Classification of Valvular Heart Disease. Data in 543 Necropsy Patients > Age 14 Years*

Functional valve lesion	Patients No. (%)	Age range in years (Avg)	Non-rheumatic etiology No. (%)	Rheumatic etiology No. (%)	Rheumatics with hx ARF or Chorea No. (%)	Total with hx ARF or Chorea No. (%)	Anatomic valve lesion(s): No. (%) AV	MV	MV + AV	MV + TV	MV + AV + TV	No. (%) with Aschoff bodies
Aortic stenosis (AS)	182 (34)	16-90 (48)	159 (87)	23 (13)	14 (61)	22 (12)	158 (87)	0	23 (12.5)	0	1 (.5)	0
Mitral stenosis (MS)	94 (17)	21-85 (46)	0	94 (100)	61 (65)	61 (65)	0	53 (57)	23 (24)	7 (7)	11 (12)	3 (3)
AS + MS	66 (12)	28-81 (50)	0	66 (100)	51 (77)	51 (77)	0	0	52 (79)	0	14 (21)	5 (8)
Aortic regurgitation (AR)	60 (11)	15-69 (41)	50 (83)	10 (17)	9 (90)	12 (20)	50 (83)	0	9 (15)	0	1 (2)	1 (2)
Mitral regurgitation (MR)	55 (10)	15-78 (40)	25 (45)	30 (55)	20 (67)	20 (36)	0	44 (80)	7 (13)	1 (2)	3 (5)	0
MS + AR	34 (6)	23-71 (44)	0	34 (100)	27 (80)	27 (80)	0	0	25 (74)	0	9 (26)	1 (3)
MR + AR	24 (5)	20-65 (38)	5 (21)	19 (79)	17 (71)	17 (71)	0	0	20 (83)	0	4 (17)	1 (4)
MR + AS	16 (3)	25-80 (51)	0	16 (100)	11 (69)	11 (69)	0	0	15 (94)	0	1 (6)	0
Tricuspid stenosis + MS ± AS	12 (2)	31-52 (39)	0	12 (100)	9 (75)	9 (75)	0	0	0	1 (8)	11 (92)	0
Totals	543	15-90 (45)	240 (44)	303 (56)	219 (72)	231 (43)	208 (38)	97 (18)	174 (32)	9 (2)	55 (10)	11 (2)

Abbreviations: ARF = acute rheumatic fever; AV = aortic valve; Hx = history of; MV = mitral valve; TV = tricuspid valve.

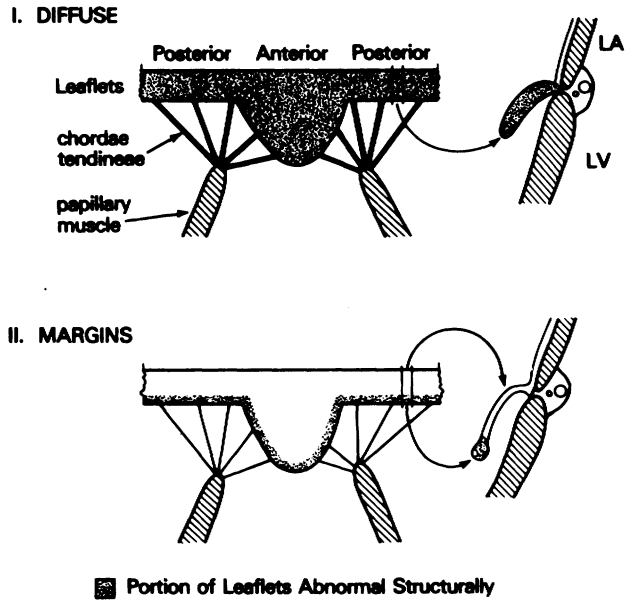


FIGURE 1. *Diagram showing the two types of anatomic involvement of the mitral valve in rheumatic heart disease.*

stenosis. In the present study a larger group of patients, 543, were examined than in all the previous studies combined. Furthermore, the types of functional and anatomic valvular lesions in our 543 patients were classified by reexamination of all 543 hearts by the same examiner and a relatively large number of histologic sections were examined from each heart. Despite this extensive search, the frequency of Aschoff bodies in our patients who died between 1953 and 1971 was surprisingly low, only 2%. The large difference in the low frequency (11 of 543) of Aschoff bodies in our patients with chronic valvular heart disease compared to the high frequency (218 [42%] of 518) in the reported patients dying between the 1920s and 1961 (table 1)[2-12] is uncertain. Presumably, differences in histologic criteria used to diagnose Aschoff bodies explains some of the difference. Also, the more frequent use of penicillin in our patients also may have prevented repeated attacks of acute rheumatic fever.[15] Although the ages of the reported necropsy patients were available in only two previous studies,[6,12] it is likely that our patients were on the average older than those described

TABLE 3. *The Aschoff Nodule: Histologic Features*

1. Round or oval shape
2. Located only in endocardium or perivascular regions.
3. Consists of a variety of cells arranged more or less in several parallel rows.
   - A. *Cardiac histocyte* (also called Antischkow cell or myocyte, Aschoff cell, and myocardial reticulocyte)—its cytoplasm is slightly basophilic (on hematoxylin-eosin stain) and its nucleus is clearly outlined, vesicular and oval. Its chromatin is arranged in bars and appears spiderlike. The area around the chromatin is clear. On cross section, the chromatin appears as a dark spot surrounded by clear area. These cells may have 2 or 3 centrally placed and overlapping nuclei.
   - B. *Lymphocytes*—few
   - C. *Polymorphonuclear leukocytes*—occasional
   - D. *Mast cell*—rare
4. Foci of fibrinoid degeneration or necrosis or both are present between and adjacent to the cells.

[Modified from Saphir O: The Aschoff nodule. Am J Clin Pathol 31:534, 1959].

in the previous reports (table 1). Our study, for example, excluded patients under 15 years of age. The composition of our 543 patients, most of whom were studied at one institution, probably differed considerably from that of the previously reported 518 patients from multiple institutions. Almost surely the frequency of isolated aortic stenosis was greater in our study patients (182 of the 543) and none of them had Aschoff bodies at necropsy. Aschoff bodies, to our knowledge, have never been described in a patient with isolated aortic valve lesions. In contrast, of the 357 previously reported patients in whom the functional valve lesion was mentioned, 343 (96%) had mitral stenosis. Among our 543 patients, 206 had mitral stenosis, with or without a functional lesion involving other cardiac valves, and only 9 (4%) of them had Aschoff bodies. Thus, it is likely that the incidence of Aschoff bodies is dropping in patients with chronic valvular heart disease just as is the incidence of acute rheumatic fever itself.[15]

Although the presence of Aschoff bodies nearly always indicates the presence of mitral stenosis (table 1), there are exceptions. Of our 11 patients with Aschoff bodies, nine had mitral stenosis but the other two had purely regurgitant lesions — purely aortic in one, and combined aortic and mitral in the other. Although mitral stenosis is not quite uni-

TABLE 4. *Aschoff Bodies at Necropsy (in 543 Patients > Age 14 Years)*

Patient	Age	Sex	Hx ARF	Valve(s) Scarred	Functional Valve Lesion(s)	Frequency Aschoff Bodies	Rhythm
1	56	M	+	MV	MS	Numerous	AF
2	39	F	+	MV–AV	MS	Rare	AF
3	40	M	+	MV–AV	MS–AS	Rare	AF
4	30	F	+	MV–AV	MR–AR	Numerous	Sinus
5	47	F	+	MV–AV	MS–AS	Rare	Sinus
6	68	M	+	MV–AV	MS–AS	Numerous	Sinus
7	33	F	0	MV–AV	MS–AS	Rare	AF
8	39	F	+	MV–AV–TV	MS–AS	Numerous	AF
9	18	F	0	MV–AV–TV	MS	Numerous	AF
10	19	M	+	MV–AV–TV	AR	Numerous	Sinus
11	31	M		MV–AV–TV–PV	MS–AR	Many	AF

Abbreviations: AF = atrial fibrillation; ARF = acute rheumatic fever; AS = aortic stenosis; AR = aortic regurgitation; AV = aortic valve; Hx = history; MS = mitral stenosis; MV = mitral valve; PV = pulmonic valve, and TV = tricuspid valve.

TABLE 5. *Clinical Observations in Patients with Aschoff Bodies At Necropsy (11 Patients) or At Operation (45 Patients)**

	11 necropsy patients	45 surgical patients*
Ages at operation or necropsy	18-68 (avg 38)	10-54 Years (avg 32)
Males:Females	5:6	20:25
White:Black:Other	All white	37:3:5
Mitral stenosis	9	44
Pure mitral regurgitation	1**	1
History of ARF	9 (82%)	26 (58%)
Age at 1st ARF	9-68 (avg 25)	4-26 (avg 13)
ASO Titer normal	—	100% (26/26)
Streptococci in throat culture	—	0 (0/13)
Sinus rhythm	4 (36%)	38 (84%)
Atrial fibrillation	7 (64%)	7 (16%)
PA systolic pressure >50 mm Hg	4 (36%)	20 (43%)

*Data from reference 13.
**Patient also had pure aortic regurgitation. An additional patient had isolated pure aortic regurgitation.
Abbreviations: ARF = acute rheumatic fever; ASO = antistreptolysin O titer; PA = pulmonary artery.

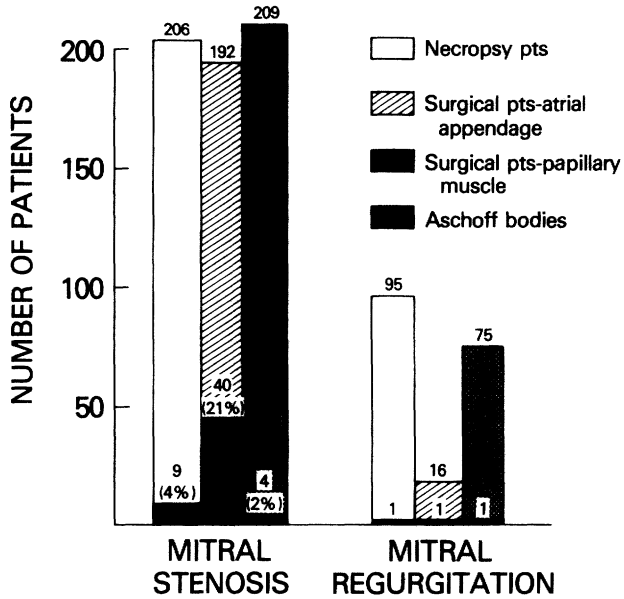


FIGURE 2. *Frequency of Aschoff bodies in necropsy and surgical patients with either mitral stenosis or pure mitral regurgitation with or without dysfunction of one or more other cardiac valves.*

versal in patients with Aschoff bodies, the presence of diffuse or marginal anatomic lesions (fig. 1) of the mitral valve does appear to be universal among the patients with Aschoff bodies. Mitral stenosis, obviously, always indicates diffuse anatomic lesions of the mitral leaflets. In each of our two patients without mitral stenosis but with Aschoff bodies, both, nevertheless, had diffuse anatomic lesions of the mitral leaflets, in one causing no mitral valve dysfunction and in the second causing pure mitral regurgitation. Among the 45 surgical patients in whom Aschoff bodies were observed by us in either atrial appendage or papillary muscle or both, 44 had mitral stenosis, and the remaining one, a 10-year-old boy, had pure mitral regurgitation.[14] Thus, all 45 had diffuse anatomic lesions of the mitral valve. Accordingly, we define rheumatic heart disease as a disease *at least anatomically* of the mitral valve (fig. 1). Other valves also may be involved either anatomically or functionally or both, but always the mitral valve is involved anatomically, either diffusely or at their margins, and, with rare exception, the functional mitral lesion is stenosis, with or without regurgitation, and rarely, pure regurgitation.

The frequency of Aschoff bodies in our 543 *necropsy* patients is significantly ($P < 0.01$) different from the frequency in our 481 *surgical* patients (previously described[14]) in whom the left atrial appendage or left ventricular papillary muscle or both were examined histologically. The frequency of Aschoff bodies in the necropsy patients was 2% and in the surgical patients, 9%. This comparison, however, has deficiencies because the necropsy patients include a large number, namely 182, with disease only of the aortic valve, whereas the surgical group excludes patients with aortic valve disease. Thus, among the 301 *necropsy* patients with only mitral valve disease, either stenosis or pure mitral regurgitation or both, with or without involvement of other cardiac valves, Aschoff bodies were found in 10 (3%); in contrast, among the 481 *surgical* patients with mitral valve disease, 45 (9%) had Aschoff bodies ($P < 0.01$).

Because Aschoff bodies are observed most frequently in patients with mitral stenosis, comparison of the necropsy and surgical patients with this particular lesion is more

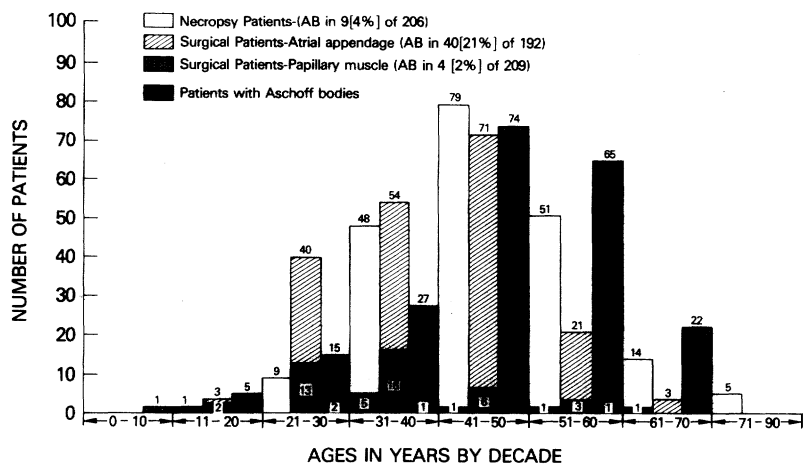
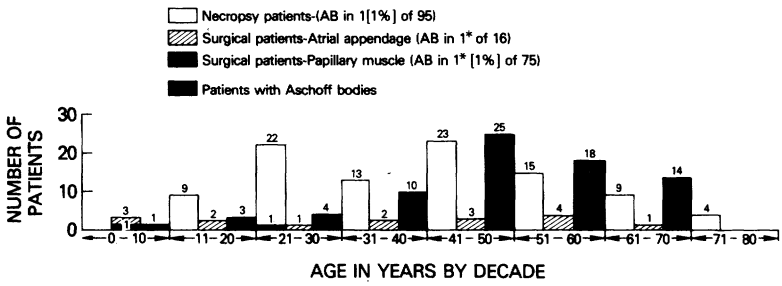


FIGURE 3. *Frequency by decade of Aschoff bodies (AB) in necropsy and surgical patients with mitral stenosis with or without dysfunction of other cardiac valves.*



*Same patient. AB in both atrial appendage and in papillary muscle.

FIGURE 4. *Frequency by decade of Aschoff bodies (AB) in necropsy and surgical patients with pure mitral regurgitation with or without dysfunction of other cardiac valves.*

meaningful (figs. 2 and 3). Thus, among our 206 necropsy patients with mitral stenosis, with or without other valve lesions, nine (4%) had Aschoff bodies, whereas among 390 surgical patients with mitral stenosis in whom left atrial appendage or papillary muscle or both were examined, 44 (11%) had Aschoff bodies ($P < 0.01$) (fig. 2). Because Aschoff bodies are observed infrequently in papillary muscle, the most meaningful comparison between the necropsy and surgical groups is made by comparing only the patients in whom left atrium was examined histologically. Thus, of the 206 necropsy patients with mitral stenosis, 9 (4%) had Aschoff bodies in the wall of left atrium, whereas of the 192 surgical patients with mitral stenosis, 40 (21%) had Aschoff bodies in the left atrium ($P < 0.01$) (fig. 2). The explanation for the difference in frequency (4% versus 21%) of Aschoff bodies in the necropsy and surgical group is uncertain. The average age of the necropsy and surgical patients, however, is different. The 206 necropsy patients with mitral stenosis, with or without other valve lesions, averaged 47 years of age (range 21–85), and the 192 surgical patients who underwent mitral commissurotomy for mitral stenosis aged 38 years of age (range 7–67) ($P < 0.01$) (fig. 3).

Aschoff bodies are significantly more frequent in patients with mitral stenosis than in patients with pure mitral regurgitation. Thus, of 95 necropsy patients examined who had pure mitral regurgitation, with or without dysfunction of one or more other cardiac valves, only one (1%) had Aschoff bodies (figs. 2 and 4), whereas of 206 necropsy patients with mitral stenosis, with or without dysfunction of one or more other cardiac valves, 9 (4%) had Aschoff bodies (fig. 2).

Among our 11 patients with Aschoff bodies at necropsy, nine had good historical evidence in the past of acute rheumatic fever. Although we are aware that historical evidence always represents "soft" data, the frequency of a positive history of acute rheumatic fever is strikingly different between patients with mitral valve disease compared to those with aortic valve disease. Among our 192 patients with clinically isolated aortic stenosis (table 2), only 12% had a history compatible with acute rheumatic fever. In contrast, of our 206 patients with mitral stenosis, with or without dysfunction of one or more other cardiac valves, 72% had a positive history of acute rheumatic fever. Thus, in general, *among patients with chronic valvular heart disease,* a positive history of acute rheumatic fever indicates a diffuse anatomic lesion of the mitral valve. The anatomic lesion, however, may or may not be of functional significance.

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