Inflammatory abdominal aortic aneurysms: A case-control study

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Purpose: **This study was designed to identify significant differences in the clinical and radiologic characteristics and outcome between patients with inflammatory and noninflammatory abdominal aortic aneurysms (AAAs).**

Methods: **We reviewed 29 consecutive patients who underwent repair of an inflammatory AAA between 1985 and 1994. This group was matched in a case-control fashion by date of surgery and by the performing surgeon to a group of 58 patients who underwent repair of noninflammatory AAAs.**

Results: **The two groups had comparable characteristics of age, gender, and cardiovascular risk factors. Patients with inflammatory AAAs were significantly more symptomatic than those with noninflammatory AAAs (93% vs 9%, $p < 0.001$), were more likely to have a family history of aneurysms (17% vs 1.5%, $p = 0.007$), and tended to be current smokers (45% vs 24%, $p = 0.049$). The most significant laboratory difference was an elevated sedimentation rate in patients with inflammatory AAAs (mean, 53 mm/hr vs 12 mm/hr, $p < 0.00001$). Inflammatory AAAs also were significantly larger than noninflammatory AAAs at presentation (6.8 cm vs 5.9 cm, $p < 0.05$). Although operative mortality was low in both groups, patients with an inflammatory AAA tended to have higher morbidity, including sepsis ($p < 0.01$) and renal failure ($p = 0.04$). Five-year survival rates, however, were similar for the two groups (79% for inflammatory and 83% for noninflammatory AAAs). On follow-up computed tomographic scans, the retroperitoneal inflammatory process resolved completely in 53% of the patients, but 47% of patients had persistent inflammation that involved the ureters in 32% and resulted in long-term solitary or bilateral renal atrophy in 47%.**

Conclusions: **This case-control study provides preliminary evidence that inflammatory AAAs may have a relatively strong familial connection and that current smoking may play an important role in the inflammatory response. The study also documents that persistent retroperitoneal inflammation may be more prevalent than has been previously reported, and stresses the need for an improved understanding of the pathogenesis and long-term management of inflammatory AAAs. (J Vasc Surg 1996;23:860-9.)**

In 1972, Walker and colleagues[1] used the term "inflammatory aneurysms of the abdominal aorta" to describe a distinct clinical syndrome. They emphasized the dense, white inflammatory wall and adhesion of some aneurysms to the adjacent duodenum and ureters. Subsequent reports characterized the typical clinical presentation of abdominal or back pain, malaise, weight loss, and an elevated sedimentation rate.[2-13] One multicenter study estimated that such an inflammatory process is associated with 2% to 14% of all abdominal aortic aneurysms (AAAs).[11] The precise cause of the inflammatory process, however, still remains unsolved.[10,14-22] Debate also continues over whether the process resolves after graft placement.[5,15] Some authors contend that graft repair results in dissipation of the inflammation,[5] whereas others report persistent inflammation in some patients.[23] Another important question is whether patients with inflammatory AAAs have a long-term survival rate different from patients with noninflammatory AAAs.[4]

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Supported by a Mayo Foundation Research Grant.

Presented at the Nineteenth Annual Meeting of the Midwestern Vascular Surgical Society, Chicago, Ill., Sept. 22-23, 1995.

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0741-5214/96/$5.00 + 0 **24/6/71743**

To address these controversies, we performed a case-control analysis of the clinical characteristics and surgical outcomes for 29 patients with documented inflammatory AAAs and 58 control patients with noninflammatory AAAs. Because the late outcome of the retroperitoneal inflammation has received minimal documentation in the literature,[23] we also ascertained the course of the inflammatory process by comparing preoperative imaging studies with postoperative computed tomographic (CT) scans at various times of follow-up.

METHODS

We reviewed the medical records of 29 consecutive patients who underwent surgery for an inflammatory AAA between 1985 and 1994 at the Mayo Clinic. We included only cases in which an inflammatory AAA was diagnosed unequivocally by CT, ultrasound, intraoperative, and pathologic findings.[1,3,4,7,10] We excluded all questionable cases of inflammatory AAA. In addition, 58 records of patients with nonruptured, noninflammatory (atherosclerotic) AAAs were identified in a case-control fashion for multiple variables comparison. Cases were matched by date of surgery and the performing surgeon.

We ascertained clinical characteristics and risk factors that may have predisposed patients to the inflammatory process or increased surgical risk and decreased the survival rate. These factors included gender, age, smoking history, hyperlipidemia, diabetes mellitus, family history of aneurysm (parent or sibling), clinically evident coronary heart disease, history of myocardial infarction or stroke, chronic obstructive pulmonary disease, clinically evident peripheral arterial occlusive disease, and chronic renal insufficiency (creatinine level >1.5 mg/dl).

In addition, we tabulated the typical clinical symptoms and signs of an inflammatory AAA: fever, abdominal or back pain, weight loss, tender AAA, elevated erythrocyte sedimentation rate (ESR), and abnormal serum creatinine level. Ultrasound and CT reports were reviewed to determine whether they had revealed the diagnosis of inflammatory AAA before operation. The mean diameter for both inflammatory and noninflammatory AAAs was compared. The anatomic extent of the inflammatory process was determined by preoperative ultrasound scans, CT scans, and operative descriptions. Whether the aneurysm ruptured or not was also ascertained.

Operative reports were reviewed to identify technical differences between the management of inflammatory and noninflammatory AAAs: ligation and division of left renal vein, tube rather than bifurcated aortic grafts, renal artery revascularization, renal stenting, and ureterolysis. Aneurysmal cultures were reviewed. When available, pathologic specimens were examined for inflammatory wall thickness and histologic signs of inflammation. Operative mortality and morbidity rates and late survival and complications were delineated.

In all 19 cases in which preoperative and late postoperative imaging were retrievable, we looked specifically for signs of persistence or resolution of the inflammatory process. These studies then were reviewed independently by a vascular radiologist (A.W.S.), who was unaware of the clinical symptom outcome.

In the statistical analysis, we used either a χ^2 test or Fisher's exact test to test for an association between the discrete factors of inflammatory or noninflammatory AAAs. We used the Wilcoxon rank-sum test to analyze the association for continuous variables. A Kaplan-Meier survival test was used to determine a possible difference in the patient survival rate between the two groups, with the p value based on the log-rank test.

RESULTS

Clinical characteristics. The two groups had comparable characteristics of age, gender, and medical risk factors. The mean patient age was 71.7 years for inflammatory AAAs and 71.3 years for noninflammatory AAAs. The gender mix was also comparable, with a male predominance of 3.4 to 1 in both groups. The inflammatory AAA group included 24 men and 5 women. When stratified according to their preoperative cardiovascular risk factors (Table I), only two variables achieved statistical significance. The most interesting was the strong familial tendency for inflammatory AAAs compared with noninflammatory AAAs (17% compared with 1.5%, $p = 0.01$). Although a history of cigarette smoking was comparable in the two groups (83% and 79%), more patients with inflammatory AAAs tended to be current smokers (45% compared with 24%, $p < 0.05$).

Clinical presentation. The vast majority of patients with inflammatory AAAs (93%) were symptomatic, compared with only 9% of patients with noninflammatory AAAs ($p < 0.001$). The leading symptom of an inflammatory AAA was abdominal pain (83%), followed by back pain (55%) and a weight loss of at least 10 pounds (mean, 25 pounds) in 41% of patients with inflammatory AAAs. On physical examination, more patients with an inflammatory AAA had a tender abdomen ($p < 0.001$). Fever (>37.5° C) was encoun-

Table I. Preoperative risk factors

	Inflammatory AAA (n = 29)	*Noninflammatory AAA (n = 58)*	*p*
Coronary artery disease	16 (55.2%)	32 (55.2%)	1.00
Past myocardial infarction	9 (31%)	19 (32.8%)	0.43
Hypertension	20 (69%)	38 (65.5%)	0.87
Past stroke	4 (13.8%)	9 (15.5%)	0.89
Chronic obstructive pulmonary disease	14 (48.3%)	17 (29.3%)	0.08*
Peripheral arterial occlusive disease	7 (24.1%)	14 (24.1%)	1.00
Hyperlipidemia	8 (27.6%)	13 (22.4%)	0.59
Diabetes	4 (13.8%)	12 (20.7%)	0.55
Chronic renal failure	6 (20.7%)	10 (17.2%)	0.83
Family history of AAA	5 (17.2%)	1 (1.7%)	0.01†
Cigarette smoker			
ever smoked	24 (82.8%)	46 (79.3%)	0.70
current smoker	13 (44.8%)	14 (24.1%)	0.04†

*Borderline significant; †statistically significant.

Table II. Clinical outcome of inflammatory AAA syndrome (n = 29)

	n	*(%)*
Preoperative clinical features		
Fever (≥37.5° C)	13	(45%)
Pain	25	(86%)
Abdomen	24	(83%)
Back	16	(55%)
Weight loss (≥10 lb)	12	(41%)
Elevated ESR	26	(89%)
Serum creatinine (≥1.2 mg/dl)	16	(55%)
Postoperative outcome		
Death	2	(6.8%)
Resolution of pain	25	(93%)
Resolution of fever	24	(89%)
Serum creatinine level (>1.2 mg/dl)	18	(67%)
Chronic renal failure/dialysis or ureteral stent	3	(11%)

tered more frequently in patients with an inflammatory AAA (45% compared with 9%; $p < 0.05$).

The most significant abnormality in results of laboratory tests was an elevated ESR in 89% of patients with an inflammatory AAA and in only 11% of patients with a noninflammatory AAA ($p < 0.001$). Mean ESR levels were 53 ± 3 mm/hr compared with 12 ± 2 mm/hr in patients with noninflammatory AAAs ($p < 0.0001$). Similarly, white blood count was elevated in approximately 40% of patients with an inflammatory AAA compared with 10% of patients with a noninflammatory AAA ($p < 0.05$), reaching means of 11,200 and 8600, respectively. Serum creatinine levels were similar in the two groups at 1.4 ± 0.2 mg/dl and 1.2 ± 0.1 mg/dl for inflammatory and noninflammatory AAAs, respectively.

The sensitivity of a preoperative imaging study for the correct diagnosis of an inflammatory AAA was 90% for CT scans of the abdomen compared with 60% for abdominal aortic ultrasound scans (Fig. 1). Angiography was of no benefit for the diagnosis of an inflammatory AAA. The mean preoperative diameter was greater for the inflammatory AAAs than for the noninflammatory AAAs (6.8 ± 0.2 cm compared with 5.9 ± 0.2 cm; $p < 0.05$). None of the inflammatory AAAs had signs of rupture before surgery. Ureteral involvement was noted in 32% of patients with inflammatory AAAs. Half of these patients had bilateral ureteral involvement. For comparison, we included only nonruptured, noninflammatory AAAs, although six (10.3%) of the originally matched noninflammatory AAAs were ruptured and were eventually excluded. None of the noninflammatory AAAs had ureteral involvement.

Operative pathologic findings. All 29 patients with an inflammatory AAA had adjacent organ adhesion to the aneurysm (Fig. 2). The inflammatory aneurysm surface was distinctively white and glistening compared with the yellowish appearance of noninflammatory AAAs. The most common organs involved in the inflammatory process were the duodenum (100%), left renal vein (48%), and the ureters

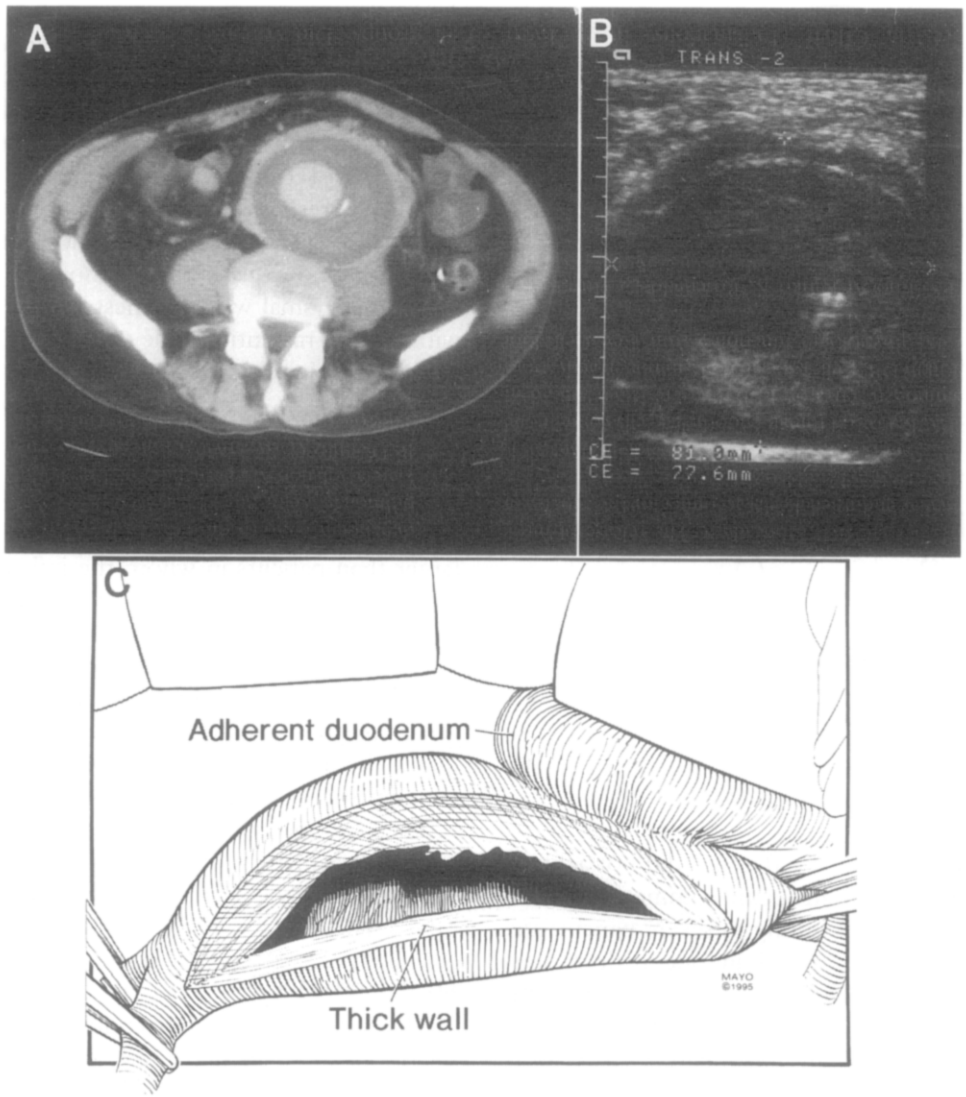

Fig. 1. A, CT scan of typical thick wall of inflammatory AAA. **B,** Ultrasound scan shows thick wall ("halo") of same inflammatory AAA. **C,** Intraoperative findings reveal thick, white, glistening aneurysm wall that is usually densely adherent to duodenum.

(45%). Other less common adhesions encountered were the small intestine (14%), colon and inferior vena cava (10% each), pancreas (7%), and common bile duct (3%).

Surgical management. All aneurysms were approached through a transperitoneal incision; none were exposed by a retroperitoneal incision. The extent of the AAA was similar in both groups, that is, infrarenal and iliac involvement. The use of straight and bifurcated grafts was also similar with approximately equal use of both types of graft. In the inflammatory aneurysm group, the left renal vein was ligated for better exposure in only two patients. Five patients with inflammatory AAAs (17%) had either preoperative or intraoperative placement of ureteral stents. Only one patient underwent ureterolysis. In the available pathologic specimens, the inflammatory aneurysm wall was markedly thickened (mean, 13 ± 2 mm) compared with noninflammatory AAAs (4 ± 1 mm; $p < 0.001$). The presence of germinal centers, lymphocytic inflammatory infiltrates, giant cells, fibrosis of nerves, and perivascular inflammation were also significantly more common in inflammatory aneurysms than in noninflammatory aneurysms ($p < 0.0001$).

Postoperative outcome (Table 2). Although the in-hospital mortality rate for inflammatory AAAs was higher than that for noninflammatory AAAs (6.8%

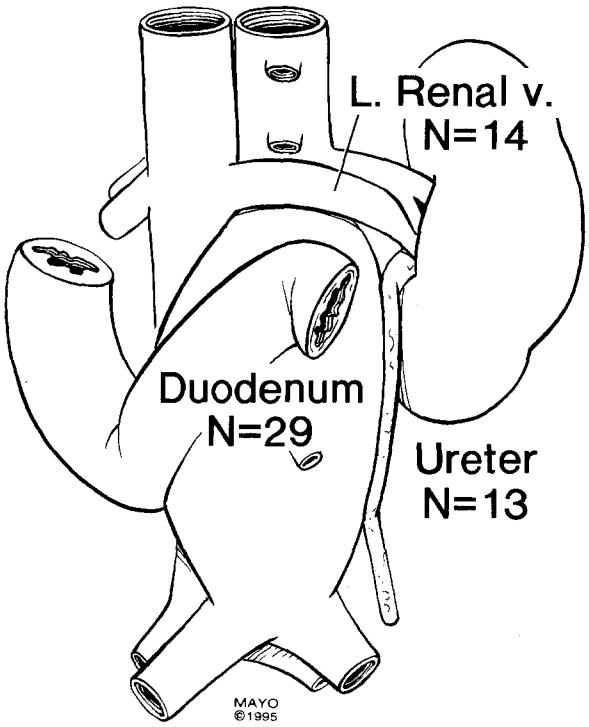

Fig. 2. Most common anatomic structures attached to the inflammatory aneurysm wall (n = 29).

and 0%, respectively), the difference did not achieve statistical significance. Iatrogenic common bile duct and pancreatic injury resulting in severe pancreatitis and bile peritonitis occurred in one patient, and septicemia led to the death of a second patient. The rate of other postoperative morbidity tended to be higher in patients with an inflammatory AAA compared with those who had a noninflammatory AAA (45% compared with 26%, $p = 0.07$). Patients with inflammatory AAAs tended to have higher rates of septicemia ($p < 0.01$) and renal failure ($p = 0.04$) than did patients with noninflammatory AAAs. Other early postoperative complications, which included myocardial infarction, stroke, respiratory failure, bleeding, thromboembolism, prolonged ileus, and wound infection, were divided equally between the two groups. The overall early reoperation rate was 7% and was similar between the two groups.

Twenty-five of 27 survivors (93%) had resolution of their preoperative clinical symptoms. Long-term survival rates were similar for the two groups, with 5-year rates of 79% and 83% for patients with inflammatory and noninflammatory AAAs (Fig. 3). The only late graft infection occurred in the inflammatory AAA group.

Late resolution of inflammatory process (Table II). Postoperative CT or ultrasound imaging was available in 19 of 29 patients with an inflammatory AAA. The mean follow-up was 12.9 ± 1.7 months (range, 3 to 51 months). The preoperative scans demonstrated that most of the periaortic inflammatory process occurs on the anterior surface of the aneurysm (Fig. 4), with a mean thickness of 7.6 ± 0.8 mm (range, 3 to 15 mm). This inflammatory process had completely resolved at late follow-up in only 53% of patients. None of these patients, however, had complete resolution earlier than 4 months. Their initial mean aneurysmal wall thickness was 5.4 ± 0.5 mm, with a mean resolution time of 1 year. The mean regression rate in this group was 1.5 ± 0.3 mm/month. In contrast, 47% of patients showed a persistent but slowly resolving inflammatory process on scans obtained at a mean follow-up of 17.7 ± 4.9 months (range, 3 to 48 months). Before surgery, the mean size of the inflammatory process in these patients was larger than patients in whom the inflammation had completely resolved (10.4 ± 1.0 mm compared with 5.4 ± 0.5 mm; $p < 0.01$). Their regression rate was relatively slow (0.7 ± 0.2 mm/month). Ureteral entrapment persisted in 32% of patients, with signs of renal atrophy in 47% of patients (Fig. 5). Chronic dialysis became necessary in 3.4% of patients with inflammatory AAAs. At last follow-up, the patients with residual retroperitoneal inflammation had a mean residual inflammatory thickness of 6.8 ± 0.5 mm, which was significantly less than the preoperative finding of 10.4 ± 1.0 mm ($p < 0.05$).

DISCUSSION

This case-control study confirms several past observations about inflammatory AAAs and reveals a few new preliminary but provocative findings. The triad of abdominal or back pain, a pulsatile (and sometimes tender) abdominal mass, and an elevated sedimentation rate is now the well-recognized clinical syndrome associated with an inflammatory aneurysm.[2,4] Although frequently missed in the past, the diagnosis currently can be made before surgery by the thick periaortic inflammatory rind that was seen in 90% of our patients on CT scan.[24-26] Our surgical experience also corroborates the technical challenge and dangers associated with the dense adhesions of bowel and veins to the inflamed aneurysm wall. These observations are not new, but the case-control method and our long-term imaging studies uncovered other unexpected findings of clinical relevance.

The most unexpected observation was the strong family tendency (17%) of inflammatory AAAs compared with noninflammatory AAAs (1.5%). Familial predilection has been recognized in several general atherosclerotic AAA series, but these reports have not addressed specifically the inflammatory versus nonin-

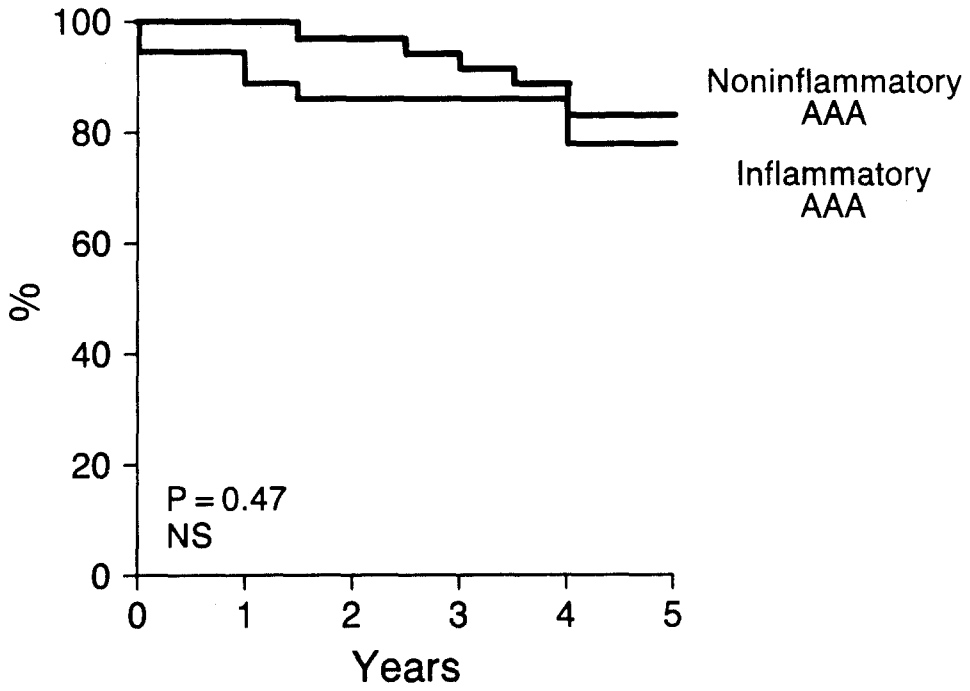

Fig. 3. Kaplan-Meier survival curves for inflammatory (n = 29; n = 8 at 5 years follow-up) and noninflammatory abdominal aortic aneurysms (n = 58; n = 19 at 5 years follow-up).

Table III. Late imaging findings (n = 19)

	n	*(%)*
CT scan	13	(68%)
Ultrasonography	6	(32%)
Residual inflammation	9	(47%)
Ureteral involvement	6	(32%)
Renal atrophy	9	(47%)
Unilateral	6	(32%)
Bilateral	3	(16%)

Follow-up: mean, 12.9 ± 1.7 months (range, 3 to 51 months)

flammatory nature of the aneurysms.[27-31] Because our previous review of inflammatory AAAs in 1985 had revealed a family history in 7.6% of patients, we prospectively ascertained family history (sibling or parent) in all subsequent cases both of inflammatory and noninflammatory AAAs. Although the numbers of patients we used for analysis were relatively small, the level of significance was strong ($p = 0.01$) and should be considered an important preliminary finding.

Such a familial tendency for inflammatory AAAs, however, may imply an abnormality in the cellular or humoral responses of the immune system. This provocative finding will obviously need corroboration by other similar case-control studies; but if it is confirmed, the explanation may lie in an altered cell-mediated immune response similar to the recent findings for giant cell arteritis by Weyand et al.[32-35] In our pathologic comparisons, inflammatory AAAs and giant cell arteritis share some common pathologic features.[36,37]

The second significant observation of this study concerns smoking. Several studies of inflammatory AAAs already have emphasized the extraordinarily high prevalence of cigarette abuse.[4,5] They have not, however, examined whether the patient had simply been a past smoker or was a current smoker. Although the percentage of patients who had ever smoked was similar for inflammatory and noninflammatory AAAs (83% and 80%, respectively), the patients with inflammatory AAAs were more likely to be current smokers (45% compared with 24%, $p = 0.04$). The precise mechanism by which cigarette smoking may alter the inflammatory response is not known, but Murphy et al.[38] have presented data suggesting that nicotine

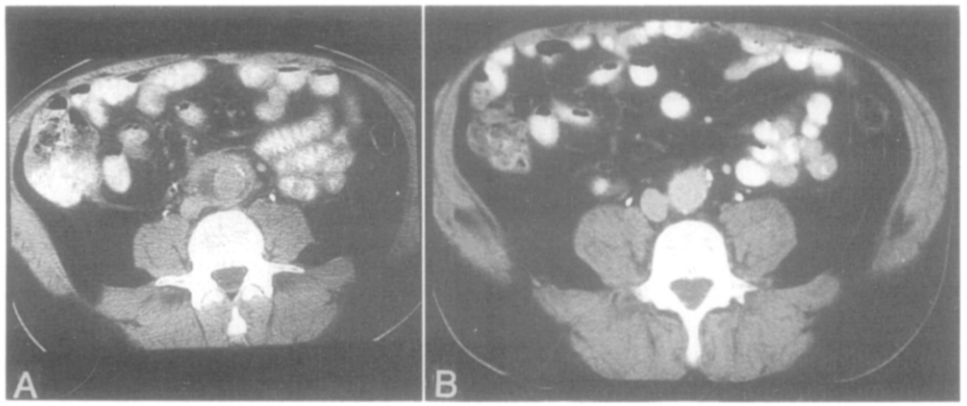

Fig. 4. Serial postoperative CT scans of inflammatory AAA in 64-year-old man. **A,** Six-week postoperative scan shows residual inflammatory rind around Dacron aortic graft. **B,** Nine-month postoperative scan shows resolution of inflammatory rind.

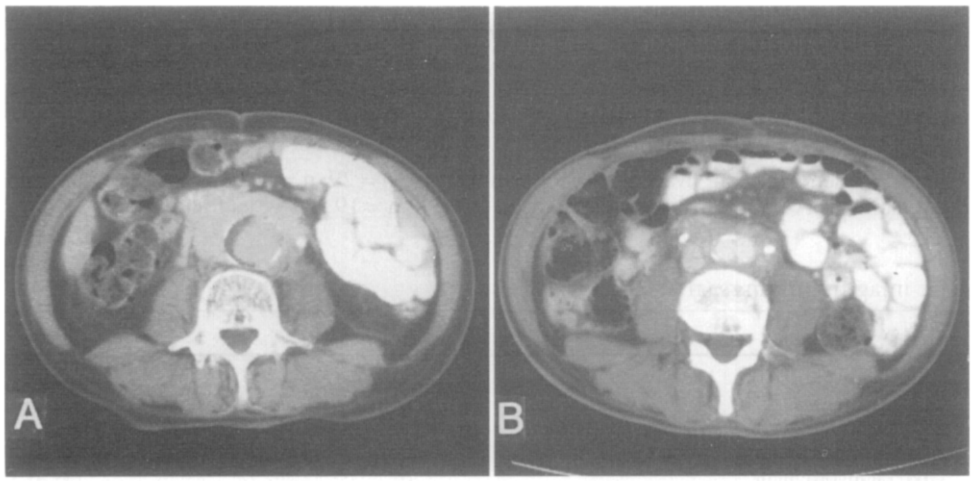

Fig. 5. This 65-year-old man had a 6.8-cm inflammatory AAA, occlusive uropathy, and a serum creatinine level of 4.7 mg/dl. **A,** Preoperative CT scan. **B,** Postoperative scan at 5 months with residual inflammation but entrapped ureters that required stenting.

induces elastase release by neutrophils. Other effects of nicotine or tobacco components on cell proliferation and fibrosis may also play a role in the development and persistence of an inflammatory retroperitoneal process. The clinical implication is that smoking cessation may be essential in resolving the inflammatory process surrounding the AAA. Because our follow-up records did not contain specific information on continued smoking in every patient, we can only speculate that continued smoking may be a driving factor in persistent inflammation.

Paramount to the final outcome of an inflammatory AAA is whether surgical repair by interposition grafting will result in resolution of the inflammatory process. The time-honored adage has been that grafting will lead to complete resolution of symptoms and inflammation.[5] Our findings challenge this adage. In follow-up ranging to 4 years, we documented complete resolution in slightly more than half of our patients, whereas the remainder had slow or no change. Despite improved symptoms, the inflammatory process persisted. In fact, it was associated with ureteral entrapment in one third of patients, with signs of silent unilateral or bilateral renal atrophy in half of this subgroup. A recent report from Stella et al.[23] in Italy agrees with our observations. They found that resolution occurred when the cellular density of the inflammatory rind was high, that is, when the cell/fibrosis ratio was greater than 1. We observed that resolution correlated with the initial thickness of the wall and was more likely when the initial wall thickness was less than 10 mm.

Whether the persistent inflammatory response can be modified pharmacologically remains debatable.

For years, the debate has centered around the use of steroids,[39] but could other mediators of the immune system help with healing? The answer is not known, but the question emphasizes the need for a clearer delineation of the pathogenesis of inflammatory AAAs.

One of the encouraging findings of this case-control study was the similar late survival for the two groups. Although inflammatory AAAs have a slightly higher perioperative mortality rate, the late outcome is not impaired in comparison with noninflammatory AAAs. This observation confirms the findings of our previous Mayo Clinic series of inflammatory AAAs that used historical controls to construct survival comparisons.[4] This past comparison was random and limited by selection bias. Consequently, we are more confident in the findings of this case-control study.

CONCLUSION

This study raises new questions about the familial tendency of inflammatory AAAs and stresses the potential importance of continued smoking in preventing the resolution of the retroperitoneal inflammation. In addition, we have documented the persistence of the inflammatory response in nearly 50% of patients after surgical grafting. The future challenge is to delineate the molecular and cellular pathogenesis of inflammatory AAAs so that better pharmacologic therapies can be developed for patients with the most exuberant inflammatory processes. For the moment, the best management of an inflammatory AAA remains repair by inclusion grafting because it alleviates the clinical syndrome in the majority of patients.

REFERENCES

1. Walker DI, Bloor K, Williams G, Gillie I. Inflammatory aneurysms of the abdominal aorta. Br J Surg 1972;59:609-14.
2. Goldstone J, Malone JM, Moore WS. Inflammatory aneurysms of the abdominal aorta. Surgery 1978;83:425-30.
3. Baskerville PA, Blankeney CG, Young AE, Browse NL. The diagnosis and treatment of periaortic fibrosis (inflammatory aneurysm). Br J Surg 1983;70:381-5.
4. Pennell RC, Hollier LH, Lie JT, et al. Inflammatory abdominal aortic aneurysms: a thirty-year review. J Vasc Surg 1985; 2:859-69.
5. Crawford JI, Stowe CL, Safi HJ, et al. Inflammatory aneurysms of the aorta. J Vasc Surg 1985;2:113-23.
6. Fiorani P, Bondanni S, Faraglia V, et al. Clinical and therapeutic evaluations of inflammatory aneurysms of the abdominal aorta. Int Angiol 1986;5:49-53.
7. Sterpetti AV, Hunter WJ, Feldhaus RJ, et al. Inflammatory aneurysms of the abdominal aorta: incidence, pathologic, and etiologic considerations. J Vasc Surg 1989;9:643-50.
8. Hill J, Charlesworth D. Inflammatory abdominal aortic aneurysms: A report of thirty-seven cases. Ann Vasc Surg 1988;2:352-7.
9. Boontje AH, van den Dungen J, Blanksma C. Inflammatory abdominal aortic aneurysms. J Cardiovasc Surg (Torino) 1990;31:611-6.
10. Leu HJ. Inflammatory abdominal aortic aneurysms: a disease entity? Histological analysis of 60 cases of inflammatory aortic aneurysms of unknown etiology. Virchows Arch A Pathol Anat Histopathol 1990;417:427-33.
11. Lindblad B, Almgren B, Bergqvist D, et al. Abdominal aortic aneurysm with perianeurysmal fibrosis: experience from 11 Swedish vascular centers. J Vasc Surg 1991;13:231-9.
12. Leseche G, Schaetz A, Arrive L, Nussaume O, Andreassian B. Diagnosis and management of 17 consecutive patients with inflammatory abdominal aneurysm. Am J Surg 1992;164:39-44.
13. Gans RO, Hoorntje SJ, Rauwerda JA, Luth WJ, van Hattum LA, Donker AJ. The inflammatory abdominal aortic aneurysm: prevalence, clinical features and diagnostic evaluation. Neth J Med 1993;43:105-15.
14. Stella A, Gargiulo M, Pasquinelli G, Preda P, Faggioli GI, Cenacchi G, D'Addato M. The cellular component in the parietal infiltrate of inflammatory abdominal aortic aneurysms. Eur J Vasc Surg 1993;5:65-70.
15. Koch AE, Kunkel SL, Pearce WH, et al. Enhanced production of the chemotactic cytokines interleukin-8 and monocyte chemoattractant protein-1 in human abdominal aortic aneurysms. Am J Pathol 1993;142:1423-31.
16. Keen RR, Nolan KD, Cipollone M, et al. Interleukin-1β induces differential gene expression in aortic smooth muscle cells. J Vasc Surg 1994;20:774-86.
17. Koch AE, Haines K, Rizzo RJ, et al. Human abdominal aortic aneurysms: immunophenotypic analysis suggesting an immune-mediated response. Am J Pathol 1990;137:1199-213.
18. Pasquinelli G, Preda P, Gargiulo M, et al. An immunohistochemical study of inflammatory abdominal aortic aneurysms. J Submicrosc Cytol Pathol 1993;25:103-12.
19. Cenacchi G, Guiducci G, Pasquinelli G, et al. The morphology of elastin in nonspecific and inflammatory abdominal aortic aneurysms: a comparative transmission, scanning and immunoelectronmicroscopy study. J Submicrosc Cytol Pathol 1995; 27:75-81.
20. Newman KM, Jean-Claude J, Li H, Ramey WG, Tilson MD. Cytokines that activate proteolysis are increased in abdominal aortic aneurysms. Circulation 1994;90(5 part 2):II224-7.
21. Newman KM, Malon AM, Shin RD, Scholes JV, Ramey WG, Tilson MD. Matrix metalloproteinases in abdominal aortic aneurysm: characterization, purification and their possible sources. Connect Tissue Res 1994;30:265-76.
22. Szekanecz Z, Shah MR, Pearce WH, Koch AE. Human atherosclerotic abdominal aortic aneurysms produce (IL)-6 and interferon-gamma but not IL-2 and IL-4: the possible role for IL-6 and interferon gamma in vascular inflammation. Agents Actions 1994;42:159-62.
23. Stella A, Gargiulo M, Faggioli GL, et al. Postoperative course of inflammatory abdominal aortic aneurysms. Ann Vasc Surg 1993;7:229-38.
24. Fitzgerald EJ, Blackett RL. "Inflammatory" abdominal aortic aneurysms. Clin Radiol 1988;39:247-51.
25. Tennant WG, Hartnell GG, Baird RN, Horrocks M. Radiologic investigation of abdominal aortic aneurysm disease: comparison of three modalities in staging and the detection of inflammatory change. J Vasc Surg 1993;17:703-9.
26. Ramirez AA, Riles TS, Imparato AM, Megibow AJ. CAT scans of inflammatory aneurysms: a new technique for preoperative diagnosis. Surgery 1982;91:390-3.

27. Tilson MD, Seashore MR. Fifty families with abdominal aortic aneurysms in two or more first-order relatives. Am J Surg 1984;147:551-3.
28. Darling RC III, Brewster DC, Darling RC, et al. Are familial abdominal aortic aneurysms different? J Vasc Surg 1989;10: 39-43.
29. Johansen K, Koepsell T. Familial tendency for abdominal aortic aneurysms. JAMA 1986;256:1934-6.
30. Webster MW, St Jean PL, Steed DL, Ferrell RE, Majumder PP. Abdominal aortic aneurysm: results of a family study. J Vasc Surg 1991;13:366-72.
31. Adams DCR, Tulloh BR, Galloway SW, Shaw E, Tulloh AJ, Poskitt KR. Familial abdominal aortic aneurysm: prevalence and implications for screening. Eur J Vasc Surg 1993;7:709-12.
32. Weyand CM, Hicok KC, Hunder GG, Goronzy JJ. The HLA-DRB1 locus as a genetic component of giant cell arteritis. J Clin Invest 1992;90:2355-61.
33. Weyand CM, Hunder NN, Hicok KC, Hunder GG, Goronzy JJ. The HLA-DRB1 alleles in polymyalgia rheumatica, giant cell arteritis, and rheumatoid arthritis. Arthritis Rheum 1994; 37:514-20.
34. Weyand CM, Hicok KC, Hunder GG, Goronzy JJ. Tissue cytokine patterns in patients with polymyalgia rheumatica and giant cell arteritis. Ann Intern Med 1994;121:484-91.
35. Wagner AD, Goronzy JJ, Weyand CM. Functional profile of tissue-infiltrating and circulating CD68+ cells in giant cell arteritis: evidence for two components of the disease. J Clin Invest 1994;94:1134-40.
36. Huston KA, Hunder GG, Lie JT, Kennedy RH, Elveback LR. Temporal arteritis: a 25-year epidemiologic, clinical, and pathologic study. Ann Intern Med 1979;88:162-7.
37. Banks PM, Cohen MD, Ginsburg WW, Hunder GG. Immunohistologic and cytochemical studies of temporal arteritis. Arthritis Rheum 1983;26:1201-7.
38. Murphy EA, Sarfati I, Lopes DA, Cohen JR. Nicotine stimulated elastase release from human neutrophils in abdominal aortic aneurysm patients [abstract]. Presented at the Forty-ninth Annual Meeting of the Society for Vascular Surgery, June 11, 1995.
39. Clyne CAC, Abercrombie GF. Perianeurysmal retroperitoneal fibrosis: two cases responding to steroids. Br J Urol 1977;49: 463-7.

Submitted October 11, 1995; accepted January 4, 1996.

DISCUSSION

Dr. Bruce L. Gewertz (Chicago, Ill.). I enjoyed this excellent presentation and landmark paper. A number of things about inflammatory aneurysms are really fascinating. It has been suggested that inflammatory aneurysms hold a key to our understanding of aneurysms in general. They are obviously a small subset of aneurysms but have many interesting features that the Mayo Clinic group has beautifully outlined. Let me ask you a few unanswerable questions, with my apologies.

You did exclude a number of cases in which inflammatory components were present that did not meet all the criteria that you rigorously set up. I think that was the right thing to do to gain insight into the questions you were asking, but many of us believe that there may be a spectrum of inflammatory aneurysms, from the small degree of inflammation in the typical aneurysm to these very pronounced inflammatory components. I wonder whether you think there is a spectrum, or do you think there is sort of an abrupt shift from a noninflammatory to an inflammatory aneurysm? Obviously, it begs the question of what comes first? Does the aneurysm come first or does the inflammation engender some local process that results in a weakening of the arterial wall and aneurysmal formation? This also raises the issue of whether inflammatory aneurysms rupture at the same rate as noninflammatory aneurysms. One could guess that the thicker the wall the less likely it would be to rupture.

Finally, the inflammation is almost always less on the posterior end. This fact led Bob Rutherford and many of us to use a retroperitoneal approach. Do you think that the localized nature of the reaction gives some clue as to the genesis of the inflammatory component?

I will finish with a couple of practical questions that may help us in our management. On the basis of your experience and longitudinal study and the fact that persistent renal problems may exist, do you stent or not stent the ureters at the initial operation? How long do you wait to decide that the inflammation is not resolving and you have to intervene in some way with a nephrostomy or a ureteral stent? Secondly, because you only lysed, as I recall, one patient's ureter during the course of the procedures, should we take a more aggressive tack, as is done overseas, to lyse the ureters and take the risk of inadvertent ureteral injury and devascularization of the ureter? Finally, I am interested in your thoughts on a problem that I have faced. What do you do when the component of inflammation is very significant in and around the iliac vessels and you have to go to the femoral vessels for whatever reason? Do you have any tricks in terms of tunneling to the groins?

Dr. John W. Hallett, Jr. Studying the pathogenesis of inflammatory aneurysms will lead to better understanding of all aneurysm pathogenesis. We agree that there is a spectrum of inflammatory aneurysms. In this study, we specifically selected the advanced end of this spectrum. When we did our case-control match, we hoped to discover greater differences between noninflammatory and inflammatory AAAs.

Which comes first, the aneurysm or the inflammation? We have seen patients who have had an inflammatory response around a relatively normal-sized aorta. Over time

these particular patients have shown aneurysmal degeneration of that particular aorta. So in some cases, the inflammation does precede the aneurysm.

The question about rupture is an interesting one. None of our 29 patients with inflammatory AAAs had a rupture. When we first did the case-control match, however, six of the 58 control aneurysms had shown signs of rupture. We excluded those ruptures and went to 58 nonruptured aneurysms for the study. In a previous study by Pennell et al. from the Mayo Clinic, rupture risk for the inflammatory aneurysms was one out of about 100. So the rupture risk is lower than noninflammatory AAAs.

The anterior location of the inflammation is also interesting. We have seen it on the posterior aspect too, but not in every case. I cannot explain why one would not see some inflammation on the posterior aspect except that not much tissue usually is present between the posterior aortic wall and the anterior spinal ligament.

Should we stent the ureters or not? Perhaps we should think more strongly about stenting. If ureters remain entrapped after AAA repair, a urologist should be consulted. The stenting should probably be done until one sees dissipation of the inflammation, which can take months or even a few years to occur. Obviously, one may not want to stent for a long period of time. If there is a lot of inflammation, you have to address the question of using steroids. In the future, I hope other antiinflammatory agents will exist that might be used.

Should we lyse the ureters? We do not believe strongly at all about lysing the ureters. In fact, performing ureterolysis can be a very risky thing to do. Thus we would not recommend routine lysis.

In terms of tunneling the graft limbs, most of these aneurysms have dissipation of the inflammation at the iliac artery level. If the inflammation extends into the pelvis, however, one alternative is to bring one graft limb down one side of the abdomen (e.g., the left side) to the external iliac artery and then do a femorofemoral crossover graft. This kind of approach may avoid the area where the ureter is densely bound into the aneurysm or where the bowel is bound up against the aneurysm. If you try to tunnel through severe inflammation, you can injure the ureter.

Dr. John W. Smith (Omaha, Neb.). We work in a hospital where Dr. Mardis, who first described stents, is the senior urologist, so when I had a patient like this that would not drain one kidney, I said, "Fix him up, put a stent in." He said, "Well, I will do it, but it will not work. Stents only work when the ureter has peristalsis." He put it in and, lo and behold, it did not work. So the question in my mind is that maybe we should be lysing these ureters, because the alternative is a nephrostomy. Then you have a hole in the body next to your graft that is potentially infected, and we do not want to be in that position either.

Dr. Hallett. In some ways, the ureteral entrapment may be an insoluble problem. If one looks at the risk of lysing of the ureters in some of these inflammatory areas, I am concerned that we may have more trouble with lysis than simple stenting. We are not, however, totally preserving the renal function by what we currently do in some patients. If we could identify more precisely the pathogenesis of inflammatory AAAs, other antiinflammatory agents might help. Inflammatory aneurysms have many histochemical features similar to giant cell arteritis.[32-35] A defect in the human lymphocytes may play into the abnormal inflammatory aneurysm reaction. If we could identify the antigen(s) in inflammatory AAAs and why the immune system produces such exuberant inflammation, we could progress in our total management of these difficult AAAs.