Review

Aortic involvement in rheumatic diseases

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ABSTRACT

Objective. *To review the prevalence, mechanisms, presentations and clinical significance of aortic involvement in rheumatic inflammatory diseases.*

Methods. The medical literature, available through a PUBMED search was reviewed and the relevant information was summarized. In addition, selected articles related to aortic involvement in rheumatic diseases were included in this review.

Results. *Rheumatic disorders may be categorized by their propensity to involve the aorta: conditions with a prevalence of 10% and more (Takayasu's arteritis, temporal arteritis, long-standing ankylosing spondylitis, Cogan's syndrome and relapsing polychondritis), disorders with uncommon but well documented aortic involvement and rheumatic conditions with rare case reports of such involvement. Clinical presentation of aortic disease is dependent on the part of aorta involved and may manifest by aortic pain and/or other symptoms caused by aortic dilatation, narrowing or aneurysm. The histopathology of inflammatory aortitis is characterized by lymphoplasmacytic infiltration with or without giant cells or granulomas. On the other hand, non-inflammatory aortic damage in rheumatic diseases may include Marfan-like cystic disintegration of the aortic media as well as accelerated atherosclerosis. Awareness of rheumatic conditions with a high potential for clinically significant aortic involvement may promote referral of such patients for aortic imaging and sometimes surgery before fatal complications intervene.*

Conclusions. *Early diagnosis of aortic involvement can be advanced by informed consideration of such a complication in a rheumatic patient.*

Introduction

Rheumatic conditions may involve the aorta and, though relatively rare, aortic disease may be fatal in patients with connective tissue disease or vasculitis. Though clinically significant aortic involvement is in general considered to be a feature of large vessel vasculitis such as temporal arteritis and Takayasu's disease, it has also been well-described in spondyloarthropathies and less so in rheumatoid arthritis (RA). There is substantial evidence, however, that aortic disease may be a manifestation of many other systemic rheumatic disorders. Occasionally, a rheumatologist may face patients who are first referred for consultation after surgery for aortic aneurysm, which turns out to be 'inflammatory' on histological evaluation.

The medical literature contains multiple case and case-series reports of aortic involvement in rheumatic diseases. Presently, there exists no comprehensive review of this subject in the rheumatologic literature. The aim of the present work is to organize this data, dispersed among journals of different medical and surgical specialties, and review the subject from a rheumatological perspective.

Awareness of the potential of aortic complications in rheumatic patients should, hopefully, lead to their early diagnosis and appropriate management.

Methods

A PUBMED search of articles published in 1960 - 2004 using the key word combinations: (Aorta or Aortitis) with (ANCA, or Arteritis, or Arthritis, or Behçet's disease, or Cogan's syndrome, or Dermatomyositis, or Systemic Lupus Erythematosus, or Relapsing Polychondritis, or Polyarteritis Nodosa, or Polymyositis, or Rheumatoid Arthritis, or Sarcoidosis, or Scleroderma, or Sjögren's syndrome, or Spondyloarthropathy, or Takayasu's disease, or Vasculitis, or Wegener's granulomato-

sis) was performed. Not all papers published and numerous case reports on the subject are exhaustively listed but those series felt to contribute new knowledge and understanding of the subject at the time of their publication were included in this review. In addition, selected articles and book chapters related to aortic involvement in rheumatic diseases were analyzed. The available information regarding aortic involvement in inflammatory rheumatic disorders was summarized. Hereditary disorders of connective tissue are not included in this review.

General principles of aortic involvement in rheumatic diseases: Clinical signs suggestive of aortic involvement

Aortic involvement in rheumatic disease presents a spectrum of manifestations (Table I). Stenosing lesions are the hallmark of Takayasu's disease, while dilatations or aneurysms of the aorta represent a more common pattern of damage in rheumatic disease and may occur in a variety of specific and non-specific forms of aortitis, leading to diverse clinical presentations, including aneurysm-related or ischemia-related symptoms, as well as general symptoms of inflammation, like fatigue or malaise (1). Both the thoracic and/or abdominal aorta may be involved. Aneurysms may leak, dissect, rupture or initiate thrombus formation and release thromboemboli. With involvement of the ascending aorta, aortic root dilatation may trigger aortic valve incompetence and heart failure, while angina pectoris or myocardial infarction may represent aortitis expanding to the ostia of coronary arteries.

While there is a paucity of symptoms pointing to early aortic disease, aortic pain may be an early sign and its timely recognition is of primary importance. Best known is the pain of acute thoracic aorta dissection. It is classically described as of abrupt onset, anterior chest or posterior suprascapular in location with downwards radiation, searing or tearing in character and pulsating, sometimes with an odd sensation in the legs. Partial aortic tears or evolving aortic dissection may well masquerade as angina pectoris, with only a high level of suspicion leading to timely diagnosis in these patients. In our experience, persistent descending aortitis may simulate inflammatory-type thoracic and lumbar spine pain, including restriction in anterior flexion of the torso. Aortic root dilatation, stretch and distension without tear also often cause chest pain, but less well-defined. The symptoms are sometimes low-grade, chronic or recurrent, with variable duration or frequency (2).

Correspondingly, a rheumatic disease patient with unexplained aortic regurgitation, arterial embolic events or pain, suspected to be of aortic origin, should be assessed for the presence of inflammatory aortic disease.

Awareness of those cohorts of rheumatic patients with a higher probability of developing aortic complications, a high index of suspicion in such groups, and, a low threshold for referral of candidate patients for aortic imaging would serve to aid early diagnosis of aortic disease.

Diagnostic imaging of the aorta

Choice of the optimal method of imaging should take into account the localization and pattern of suspected aortic involvement.

Enlargement of the thoracic aorta on chest radiographs has been found to predict higher mortality in patients with RA (3). The presence of a thoracic aortic aneurysm may be easily go undetected on chest X-ray, however, despite its usefulness as a screening tool in asymptomatic patients, and thus additional imaging needs to be ordered in a patient with suspected aortic involvement. Two-dimentional transthoracic or trans-esophageal echocardiography is a sensitive non-invasive tool for imaging of the aortic valve, aortic root and ascending aorta (4, 5). Of interest, patients with RA, spondyloarthropathies, and Behçet's disease may have a very high, up to 30%-50%, prevalence of subclinical aortic abnormalities when examined by echocardiography, but the practical significance of these findings is not clear (6-8). Abdominal ultrasound may be useful in evaluation and monitoring of abdominal aortic aneurysms.

Computed tomography (CT) and magnetic resonance imaging (MRI) have had a major impact on the workup and diagnosis of aortic disease since the 1980s. Both have proven to be very effective in evaluating mural aortic changes, aortic aneurysms, aortic dissection and differentiation of the aorta from adjacent tissue. Techniques, like helical CT, CT angiography, MR angiography provide a highly accurate overall picture of aortic pathology in any part of aorta but at higher expense. MRI has also proved valuable in evaluating the results of aortic repair (4, 9). Conventional thoracic aortography still has a role in preoperative evaluation and planning, while it gives less information on the anatomy of the aortic wall than MRI (9). Positron-emission tomography with 18-fluorodeoxyglucose (FDG PET) detects metabolic changes in the arterial wall and is comparable with MRI in the diagnosis of aortitis but may be more reliable in monitoring disease activity during im-

Table I. Clinical presentations of aortic disease in rheumatic patients.

Asymptomatic	
General syndrome:	- fever, malaise, weight loss, high sedimentation rate.
Pain (chest, back, abdominal):	- acute typical pain of aortic dissection; - vague or nonspecific recurrent pain;
Aortic valve incompetence:	- due to aortic root dilatation; - due to direct involvement of the aortic valve;
Ischemic symptoms:	- coronary ischemia; - abdominal ischemia; - limb claudication;
Embolic phenomena	

munosuppressive treatment and thus holds some promise for the future (10). Unfortunately, there are no studies that present percentages or figures as to the sensitivity, specificity or predictive value of the above mentioned modalities in inflammatory rheumatic disorders.

Pathogenesis and anatomical pathology

Much of aortic involvement in rheumatic diseases is due to aortic wall inflammation, i.e. aortitis. The pathology of aortitis is frequently non-specific, contributing little to differential diagnosis, and, at times, provoking confusion. A thickened aortic wall with an accompanying shiny, white periaortic inflammatory reaction is representative of the gross pathology of aortitis. The inflammatory adhesions, often quite prominent, may involve structures adjacent to the thoracic or abdominal aorta, with findings identical to those of retroperitoneal fibrosis reported (11-13). Microscopically, a thickened adventitia is frequently unseparable from the media and contains inflammatory cells - lymphocytes, plasma cells, histiocytes - in diffuse distribution or in follicle-like arrangement. Vasculitis of the vasa vasorum may be prominent. It has been suggested that inflamed vasa vasorum produce a variety of adhesion molecules and serve as port of entry for critical player-cells, like CD4^{+} cells in giant cell arteritis, into the aortic wall (14). Of note, granulomas as well as giant cells of all types may be present in the aortic wall of patients with a variety of rheumatic diseases, including Cogan's syndrome, sarcoidosis, RA, idiopathic inflammatory aneurysms, and probably others, not being specific for Takayasu's disease and giant cell (temporal) arteritis (11, 12, 15-17). The morphologic findings in Takayasu's arteritis include, in addition to that described above, the presence of a thickened, fibrotic intima and an aortic lumen with narrowings alternating with aneurysmal dilatations (18). This picture of multiple narrowings and coarctations of aorta has been proposed as specific to Takayasu arteritis (8). Aside from the presence of granulomas and giant cells, histopathology usually reveals lymphoplasmacytic infiltrate of adventitia and media, a non-specific finding present in a number of rheumatic disorders, such as relapsing polychondritis, systemic lupus erythematosus (SLE), ankylosing spondylitis, as well as in aortitis of infectious or toxic etiology (1, 19, 20).

Non-inflammatory aortic damage has been infrequently described in rheumatic diseases. Though in SLE 'true' lupus aortitis with deposition of IgG, C3 and fibrinogen, or numerous lymphoplasmacytic infiltrates in the wall of aorta has been described, a majority of reported patients with SLE and aortic aneurysm or dissection have had medial cystic degeneration of Marfan type on histopathological analysis (21-26). Long-term glucocorticosteroid treatment may be a contributing factor to connective tissue disintegration in the aortic media in patients with SLE and other rheumatic disorders (27). In addition, accelerated atherosclerosis recently demonstrated in SLE and RA patients, may be another important mechanism of aortic damage in patients with rheumatic inflammatory diseases (28-31).

Treatment

Treatment of aortic involvement in rheumatic disease typically involves aggressive drug therapy of the underlying disease with high dose steroids and additional immunosuppressive therapy, as needed. Follow-up is usually that of acute phase reactants with an aim to maintain these at the normal level, with periodic echocardiographic/CT/MR angiographic monitoring. Close cooperation of rheumatologists and vascular surgeons is mandatory for considerations of aortic bands in cases of stenosis, aneurysm resection and aortic grafts, as indicated. Detailed surgical consideration is beyond the scope of present work. Specifics of therapy will be addressed under discussion of each rheumatic disease entity with aortic involvement.

Takayasu's arteritis (TA)

TA is the prototypical disorder of aortic inflammation. TA has a female predominance, affecting mostly young adults. The disease usually presents between ages of 15 and 25 in Japan, but is diagnosed at a mean age of 41 years in Italy and Sweden (32). The aorta and its major branches are the main target of TA involvement. The classification of TA, as proposed in 1994, with division to five subgroups by segment of involved aorta, reflects the ability of the disease to affect any aortic segment (33). Of interest, ascending aorta involvement has been described as more typical for Japanese patients, while abdominal aortic involvement is more frequent in patients from India and Thailand. Clinical manifestations of TA are extremely variable and may include hypertension, signs of generalized inflammation and/or ischemic complications in the territory of occluded vessels, such as myocardial ischemia or limb claudication. It has been emphasized that the possibility of TA should be considered when symptoms and signs of any patient, especially a young women can not be explained clearly (34). Children with TA usually suffer a more aggressive course, with high prevalence of hypertension and heart failure (35). Angiography is presently the method of choice to confirm the diagnosis at an advanced stage of TA as well as to assess disease extent, while MRI can detect earlier alterations of the vessel wall (36). Typical findings include stenoses and, often, aneurysms with a variable distribution along the aorta. It has been stressed that whereas dilatations and aneurysms of the aorta may be found in other forms of aortitis of known and unknown origin as well as by TA, narrowings and coarctations of the aorta are a specific feature of TA (1). The recently reported high accuracy of FDG PET in detection of aortic inflammation, even in clinically silent areas, in patients with TA may significantly contribute to earlier diagnosis in patients suspected to have the disease and serve as an important tool in monitoring disease activity (37).

Giant cell (temporal) arteritis (GCA)

GCA, which usually affects individuals 50 years of age and older, may be associated with aortitis in at least 15% of

cases with aortic aneurysms, ruptures, dissections, aortic valve incompetence and aortic arch syndrome reported (38). Aneurysms of the ascending thoracic aorta were found 17-fold more often in patients with GCA than in a control group, with abdominal aortic aneurysms 2.5-fold more frequent (39). Aortitis and its complications represent an important cause of mortality in patients with GCA (40). Given its frequency and potential severity, aortic involvement in patients with GCA may warrant a standardized approach, aiming at early detection. One study of newly diagnosed patients with GCA investigated the value of routine helical computered tomography (hCT) of the aorta to look for evidence of aortitis. Thickening of the ascending thoracic aortic wall was detected in 5 out of 22 patients and thickening of abdominal aortic wall in 6 out of 22 patients, versus 0/22 in control group. Three of the GCA patients already had aneurysms of the thoracic aorta, versus 1/22 of controls (41). There was hCT evidence of resolution of aortic inflammation under glucocorticoid therapy (42). FDG PET scintigraphy was shown to have even greater potential in detection aortic inflammation in GCA patients, though the possibility of false-positive uptake by atherosclerotic plaques should always be taken into consideration in this elderly cohort of patients (10, 36). These data relate to the benefit of routine aortic imaging in all patients with GCA, and suggest the importance of monitoring this one additional endpoint in this condition.

Spondyloarthropathies
Ankylosing spondylitis was probably the first chronic rheumatic disease known to be associated with aortitis (43). Numerous case reports have confirmed the causality of this relationship since that time. The primary manifestation of aortic involvement in spondyloarthropathies is insufficiency of the aortic valve. Inflammation and dilatation of the aorta are the main causes of aortic incompetence in this context, but fibrotic changes of the valve have also been described (44). It is generally held that the prevalence of aortic insufficiency in ankylosing spondylitis goes up with disease duration, being rare in the first decade and rising to the level of 10% in patients with disease duration of more than 30 years (45). In contrast, hemodynamically significant aortic incompetence, or even aortic aneurysm, have been described as early events in patients with juvenile HLA B27-related arthritis and reactive arthritis (46, 47).

Rheumatoid arthritis (RA)
Paucity of recently reported cases of aortic involvement in patients with RA may indicate that, nowadays, the aorta is a rare target in this disease. In the largest series reported, 10 cases of aortitis were identified from among 188 consecutive cases of RA examined by autopsy from 1958 to 1985; seven patients had associated vasculitis involving small and medium sized arteries and all but one had nodular seropositive disease. Three of these 10 patients died as a direct result of aortitis and four others developed a fatal myocardial infarction secondary to vasculitis (17). Typically, the diagnosis of aortitis was not appreciated premortem and was only made at autopsy (17, 43). Asymptomatic aortic regurgitation is probably more frequent in RA than overt aortitis and may be detected by transesophageal echocardiography in up to 30% of patients (7). The clinical significance of this finding is not clear, however.

Systemic lupus erythematosus (SLE)
While cardiovascular manifestations frequently complicate SLE, aortic involvement has rarely been reported. Most SLE patients presenting with aortic aneurysm or dissection reported had in common young age of disease onset, long-term corticosteroid therapy and arterial hypertension (23-26). Of interest, medial degeneration of the Marfan type and not an inflammatory infiltrate of the aortic wall dominated the histopathological picture in these cases, raising suspicion as to the possible causative role of steroids as well as mechanical factors in damaging the aorta. The prognosis for dissecting aortic aneurysm in patients with SLE may be grim, with the additional difficulty involved in replacement of an affected segment of the aorta further weakened by chronic steroid therapy (24). In view of the predominant reported localization of aortic involvement in SLE in the ascending aorta, we speculate that periodic echocardiography may be a reliable method of monitoring SLE patients with risk factors for potentially fatal aortic involvement.

Behçet's disease (BD)
The frequency of aortic involvement in BD varies according to different studies. Reports from Turkey and Italy have shown that dilatation of the ascending aorta on transthoracic or transesophageal echocardiography is present in 1/3 to 1/2 of patients with BD (8, 48). On the other hand, CT screening for thoracic aneurysm was negative in all 53 BD patients in one study from Israel (49). Clinically significant aortic aneurysms are probably infrequent, being reported in 4 out of 450 BD patients seen over 10 year period in another study (50). Insufficiency of the aortic valve is another reported manifestation of BD, with acute aortic regurgitation necessitating surgery diagnosed in 6 patients in one study (51). Redundant motion of the elongated aortic cusp, with periaortic echo-free space and paravalvular leakage were suggested as echocardiographic signs differentiating BD from Takayasu's disease in a recent work (52).

The propensity of patients with BD to develop false aneurysms is well-known, especially at anastomoses and sites of trauma, leading to the recommendation to restricted use of angiography in favor of non-invasive imaging when possible (53). This peculiarity is also a consideration when surgical intervention for aortic aneurysm is indicated in BD, where both open and endovascular treatment have given satisfactory results (49, 54-56). Consequently, meticulous long-term follow-up is recommended to monitor for post-surgical pseudoaneurysms in patients with BD.

Relapsing polychondritis (RP)
The aorta, as a proteoglycan-rich tissue, can serve as a target in RP (57).

Aortic damage may result in aneurysm formation in any part of aorta in this disorder, but ascending aortic involvement is most frequent, in up to 10% of the patients (1, 58). In addition, aortic root dilatation, rather than direct involvement of the valve, may lead to aortic regurgitation, which may be hemodynamically significant and require aortic valve replacement. In a review of 20 patients with RP referred for surgery the mean interval between first disease manifestations and cardiac valve replacement was 6.5 years (59). During the initial four postoperative years, 24% of these required reoperation for valve leak or aortic aneurysm, with 53% dying of a cardiovascular cause. Due to the progressive course of aortitis in RP, which is at times refractory to intensive immunosuppressive therapy, periodic imaging evaluations of the aorta for therapy planning in selected patients has been suggested (60).

Cogan's syndrome (CS)

CS is a disease of young adults, with a mean age of 29 years at disease onset, defined by the presence of both ocular and inner ear inflammation (16). While different forms of eye involvement have been described in patients with CS, acute interstitial keratitis is the most typical one. Acute Meniere-like disease usually occurs within 1 to 6 months before or after the onset of eye symptoms (61). Aortitis with valvulitis and aortic insufficiency has been documented as occurring from 2 weeks to 12 years after the initial diagnosis of the syndrome and has an estimated prevalence of up to 10% (61, 62). Of practical relevance, the strong association of the aortitis with ostial coronary artery disease provides a rational for recommending cardiac catheterization to any patient with CS having evidence of aortic involvement (16). As acute aortitis may be life-threatening in CS, a low threshold for patient referral for imaging procedures is warranted (61). Successful surgical treatment of aortitis, related aortic regurgitation and coronary artery disease in patients with CS has been described (63, 64).

Sarcoidosis

While some do not consider sarcoidosis a rheumatic disease per se it frequently comes up in the differential diagnosis of inflammatory rheumatic conditions, with arthritis and multiorgan involvement. The occurrence of aortitis in sarcoidosis has been described infrequently with the similarity of the histopathologic picture to that of Takayasu's arteritis adding further to confusion (65, 66). Due to the relatively low prevalence of sarcoidosis, and even more so the rarity of clinically significant aortitis in these patients, no studies regarding aortic involvement in sarcoidosis have been done. Nevertheless, the possibility of aortitis should be considered in this setting when clinically appropriate.

Polyarteritis nodosa (PAN) and ANCA-related vasculitides

The rare reports of aortic involvement in systemic vasculitides serve to underscore the exceptionality of this phenomenon. In one patient with PAN necrotizing vasculitis of the vasa vasorum led to aortic dissection (67). Wegener's granulomatosis presenting with aortic dissection and periaortitis is another *rara avis* reported (68). A recent review summarized published case reports concerning aortic damage in ANCA-associated vasculitides (69). Finally, the association of a Takayasu's-like disease with positive pANCA has been described (70).

Juvenile idiopathic (rheumatoid) arthritis (JIA)

Solitary case reports of probable aortic involvement in pauci- and polyarticular JIA were identified. These cases along with a report of juvenile spondyloarthropathy with aortic regurgitation due to aortitis, attest to the rarity of aortic involvement in children with chronic arthritis (47, 71, 72).

Idiopathic aortitis and inflammatory aortic aneurysms (IAA)

'The surgeons just operated on that young woman, young man or middle-aged or older person and they were not particularly ill other than they had an aortic problem, and the pathologist found profound inflammatory changes and necrosis sometimes, giant cells may be there, maybe not, and you get the consult' (73).

There is no consensus about the nature of IAA in the medical literature. An opinion that IAA is an inflammatory variant of the well-known atherosclerotic aneurysm, on the one hand, and the conclusion that there are no morphological findings which would justify the separation of IAA from Takayasu's disease on the other hand, reflect this confusion (12, 74). The mean age of the patients with IAA is about 60 years old in the studies reported (11, 12, 75). These studies differ, however, in their finding on male versus female predominance, as well as the predominant location of aneurysms or/and dissection in the thoracic versus abdominal aorta.

The patients with IAA, representing about 4% of all patients with aortic aneurysms, may be symptomatic and often present with the triad of aortic pain, weight loss and elevated erythrocyte sedimentation rate (ESR) (75). Weight loss occurs in 20% to 40%, and an elevated ESR in 40% to 88% of patients with IAA (11). The importance of preoperative diagnosis of IAA has been emphasized. High resolution ultrasound, CT scan or MRI can detect aneurysmal wall thickening and perianeurysmal soft tissue changes suggestive of IAA (11). The postoperative management of patients with IAA is not standardized. In a survey from the Cleveland Clinic, recurrent aneurysms were not identified among 11 corticosteroid-treated patients, while in those not treated with steroids new aneurysms were identified in 6 out of 25 cases. The steroid regimen was not standardized, however, with varying doses/duration used. The experience, thus, was not considered clear cut enough to support the recommendation of steroid treatment for all patients with IAA. The authors recommended immunosupressive therapy only upon detection of signs of residual vasculitis beyond that identified in the resected surgical specimen (75).

Conclusions

Aortic disorders play an important role in morbidity and mortality of patients

with certain rheumatic diseases. Aortitis, or inflammation of the aortic wall, is a leading reported cause of aortic involvement in rheumatic patients, but its histo-morphologic picture is common in different entities and is rarely of help in the differential diagnosis of rheumatic disorders. By our analysis, we were able to categorize rheumatic disorders by their propensity to involve the aorta: conditions with a prevalence of 10% and more (chosen arbitrarily to represent relatively frequent involvement), those with uncommon but well reported aortic involvement and those conditions with rare case reports of such involvement (Table II). Clinical presentation of aortic involvement in rheumatic patients may vary and is not well distinguished in some patients (Table I).

Knowledge of both the manifestations of aortic involvement and rheumatic conditions with a high propensity for such involvement is critical for early referral of patients for appropriate aortic imaging and timely diagnosis. Echocardiography may be an effective means for evaluation and follow-up of rheumatic patients with a high risk for the disease of an ascending aorta. CT or MR imaging is usually required for imaging of the descendent thoracic and abdominal aorta when the clinical presentation suggests such involvement. FDG PET scintigraphy may be an increasingly useful tool in early diagnosis and monitoring a disease activity in rheumatic patients with aortic involvement.

Future studies are required to establish the cost-effectiveness of prophylactic routine aortic imaging in selected groups of rheumatic patients, especially in patients with giant cell arteritis.

Optimal management of rheumatic patients with diagnosed aortic involvement is another unresolved issue, with glucocorticosteroids, immunosuppressives, biological agents, endovascular or open surgery being the available options nowadays.

Acknowledgments

Table II. Rheumatic diseases with reported aortic involvement.

Rheumatic diseases with high (10% and more) prevalence of aortic involvement.	Rheumatic diseases with uncommon, but well reported, aortic involvement.	Rheumatic diseases with isolated case reports of aortic involvement
Takayasu's arteritis	Rheumatoid arthritis	Sarcoidosis
Giant cell (temporal) arteritis	Spodyloarthropathies	Wegener's granulomatosis
Long-standing ankylosing spondylitis	Behçet's disease	Polyarteritis nodosa
Cogan's syndrome	Systemic lupus erythematosus	Juvenile Idiopathic Arthritis
Relapsing polychondritis		ANCA-associated Aortitis

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