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Invited review

Chronic periaortitis – a new interpretation of Ormond's disease

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Chronic inflammation leading to fibrosis can affect the periaortic tissue throughout the entire course of the aorta in its ascending and descending thoracic, abdominal and iliac sections [17]. So far, the etiology of this chronic inflammation without any microbial cause is not known. The inflammatory process usually occurs in the abdominal aortic region, presenting as retroperitoneal fibrosis. In the retroperitoneum there are different predilection sites for fibrotic change. The most frequent type of retroperitoneal fibrosis was first described in 1905 by Albarran [2], and since 1948 has been commonly known as Ormond's disease [22]. The pathological process begins in the periaortic tissue and can impair the ureter causing deviation. Further sites of retroperitoneal fibrosis are the iliac [28] and the mesenteric regions [8, 9, 12, 16], and also the porta hepatis; in these sites it is designated iliac fibrosis, sclerosing mesenteritis and sclerosing cholangitis, respectively. The mediastinal fibrosis surrounds the thoracic aorta and can lead to vena cava obstruction, as has been known for over 100 years [21]. Idiopathic fibroses can also surround the arteries coming from the aorta, thyroid and even coronary arteries, as known in Riedel's thyroiditis and recently described in chronic coronary periarteritis [17, 26]. For all these fibrotic diseases with similar histopathological features and unknown etiology the name „systemic idiopathic fibrosis" has been proposed, indicating that the multifocal occurrence of the fibrosis is not rare [8, 13, 17, 21]. The frequency of multifocal fibrosis is 10% in 481 cases of Ormond's disease [13]. New results in etiological research in retroperitoneal fibrosis suggest the introduction of the new term "chronic periaortitis" [7, 20]. This term would also include inflammatory aneurysm of the aorta and perianeurysmatic fibrosis. The actual [10] etiological concept is based upon the observation that a chronic inflammation spreading from the atherosclerotically changed aortic wall leads to periaortic and periarterial fibrosis. The clinical signs and symptoms and the etiology of Ormond's disease are presented, this being the most frequent and best known form of chronic periaortitis.

Clinical features of retroperitoneal fibrosis

The important diagnostic methods are computer-assisted tomography, urography and surgical revision with biopsy. Histologically the disease is characterized by an inflammatory process with lymphoplasmocytic infiltration of the periaortic fat tissue [20]. Lipid deposition is found in the interstitium [9, 30], and intracellular accumulation occurs in foam cells [9] identified as macrophages [1]; in addition, giant cells are observed [9, 30]. With the development of the chronic inflammation the fibrotic involvement of the retroperitoneal fat tissue increases. The lymphatic system and blood vessels can also be involved in this fibrotic process, the final stage being an extensive fibrosis. The disease is usually diagnosed in this advanced stage be biopsy, and obvious clinical symptoms occur when organs are impaired in their function by fibrotic involvement or retraction. Minor chronic inflammatory infiltrations in the periaortic and mesenteric retroperitoneum [14] are frequent but still do not cause any symptoms in this early stage; such subclinical periaortitis [24] is diagnosed at autopsy. Advanced fibrotic stages are accompanied by two different forms of symptoms, i.e., local symptoms with atypical pains in the back, sides, and abdomes and systemic symptoms. An abdominal mass might be palpable. Severe local complications, such as deviation or obstruction of the ureters, call for surgical treatment [3, 5, 20, 29] to restore ureterial and renal function. Obstructions of the small bowel, colon, vena cava or main bile duct may also require surgical intervention. The systemic signs of the disease are malaise, weight loss and elevation of the sedimentation rate [13, 29], and severe wasting disease [8, 30], possibly, though rarely, with fatal consequences [4]. Successful medical treatment of these rare but severe cases with cyclophosphamide [8] and azathioprine [30] has been described. However, even when the disease has a severe course, there is often a spontaneous recovery, first in the general condition and then in body weight and sedimentation rate. Regression of the inflammatory fibrosis can be monitored by CT [5, 7, 16, 20]. Steroids inhibit the

Table 1. Chronic periaortitis/periarteritis. Possible localizations of fibrosis. Synonyms on the right

Retroperitoneal fibrosis	
Ormond's disease	
Sclerosing mesenteritis	Mesenteric fibrosis
	Mesenteric panniculitis
	Mesenteric lipodystrophy
	Retractile mesenteritis
	Mesenteric liposclerosis
Iliac fibrosis	
Inflammatory aneurysm of the aorta	Perianeurysmal fibrosis
Sclerosing cholangitis	
Mediastinal fibrosis	
Pleural fibrosis	
Pericardial fibrosis	
Riedel's thyroiditis	
Chronic coronary periarteritis	
Pseudotumor orbitae	
Peyronie's disease	Induratio penis plastica

periaortic process [3, 5, 9, 10, 13, 20, 21, 30] and are useful when no spontaneous recovery occurs, with or without surgery. With mild courses success is often evident even after as little as 24 h [17]. A spontaneous recovery can be observed after surgical biopsy alone [16], probably caused by endogenous corticosteroid release. After clinical recovery an asymptomatic and unimportant fibrosis persists [5, 16], which requires regular monitoring [3, 5].

The results of three studies involving long-term observation of different patient groups confirm this experience. All 11 patients enrolled in the first study are reported to be disease-free and alive after steroid treatment; the average follow-up period is 5 (range 0.5–20) years. In 5 cases ureterolysis was performed because of severe obstruction [3]. In a second study of 60 uremic patients the mean age was 56 years (12 years higher than in the first study mentioned). A two-year survival rate of 78% was reported [5]. In a third study, 25 patients between the ages of 34–74 years underwent ureterolysis and omentum plasty; the average follow-up time was 9 (range 2–22) years, and the survival rate was 92% with the deaths not being caused by fibrosis. Steroids were used in cases of inoperability or recurrence only [29]. Reliable data on the course and the prognosis of severe retroperitoneal fibrosis are difficult to obtain owing to the lack of published case material throughout the world. Severe local complications with secondary systemic illness (uremia, ileus) must be distinguished from the very rare primary systemic symptomatology; the extensive consuming inflammatory and fibrotic process with cachexia makes this possible. Mild courses are common with spontaneous or steroid-inducible remissions.

Etiology of retroperitoneal fibrosis

Different hypotheses have been put forward to explain the etiology of retroperitoneal fibrosis (reviewed in [17]), such as an autoimmune process [8, 17], lymph obstruction, traumatic aortic leakage, operations and malignant tumors or, quite often, side effects of medication, mostly of methysergide [27] and beta-blockers [25]. Retroperitoneal fibrosis can be induced experimentally by vitamin E deficiency (insufficient antioxidative protection [11]). It is mostly middle-aged and elderly men who are affected by the disease [3, 5, 9, 29] which is now diagnosed more frequently. The existence of a direct correlation between atherosclerotic plaques of the aorta and the retroperitoneal fibrosis seems more and more likely particularly in light of the publications of Mitchinson [1, 6, 19, 20, 24]. Periaortitis is found in the region of advanced atherosclerotic plaques [19] and can be detected by gallium scintigraphy [15]. Chronic inflammatory tumefaction and fibrous retraction lead to the clinical symptoms. The antigen that has been implicated in the atherosclerotic plaques, which causes an inflammatory autoimmune reaction, is ceroid, an insoluble polymer of oxidated lipoproteins, which is produced only in pathological conditions (chronic hypoxically or oxidatively damaged tissues, hyperlipidemia [6]).In atherosclerotic plaques ceroid is found mostly in macrophages (foam cells), but also occurs extracellularly [1]. Ceroid has also been demonstrated in tissue and lymph-node macrophages [20]. Antibodies of the IgG and IgM classes from plasma cells [23] may be identified by fluorescent microscopy at the same places as the antigen [24]. In plaque ruptures ceroid can penetrate through a thin media into the adventitia and thus into the periaortic tissue, and as an antigen can explain the spreading of the inflammation. A systemic circulation of antibodies to ceroid could be found and may well open new perspectives in a serologic diagnosis of periaortitis [19, 20]. The periaortic and periarterial autoimmune process may explain several diseases whose pathogenesis is unclear and not seen as directly connected (Table 1). It is still not known why a harmless minor inflammation can take a severe course or be severely exacerbated; the possibility of different responses of the immune system has been postulated [20].

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