



Takayasu's Disease with Predominant Pulmonary Arterial Involvement

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Pradeep Vaideeswar

73.1 Clinical History

A 20-year-old male had been symptomatic for the past 2 years with grade 1 dyspnea. He had been diagnosed as a case of rheumatic heart disease (RHD) and had had been on regular penicillin prophylaxis. During the past 10 days, the dyspnea had progressed to grade 4 and was accompanied by right-sided chest pain, generalized anasarca, and ascites. On examination, the pulse rate was 96 per minute, irregular with raised jugular venous pressure. There was a diffuse, hyperdynamic apical impulse with systolic/diastolic thrill and pan-systolic/early diastolic murmur at pulmonary area. Right bundle branch block with right ventricular strain, and aneurysmal right atrium, right ventricular hypertrophy, severe tricuspid regurgitation with small left ventricle were noted on ECG and echocardiography, respectively. Computed tomographic angiography revealed thrombotic occlusion of distal right pulmonary artery. The patient was transferred to intensive care unit for continuous hemodynamic monitoring and was treated with inotropics, anti-failure drugs, and anticoagulants. The patient's relatives had refused consent for thrombolytic therapy. Due to unstable hemodynamics, surgical

pulmonary thrombectomy could not be considered as a viable option. The condition did not improve and was complicated by development of basal consolidation with expiry on 5th day of admission.

73.2 Autopsy Findings

At autopsy, there was moderate cardiomegaly (weight 400 g) with ballooned right atrium and marked enlargement of right ventricle (Fig. 73.1a). Both chambers had marked pearly white endocardial thickening (Fig. 73.1a) with moderate myocardial hypertrophy. The pulmonary trunk (Fig. 73.1b) and its branches were markedly dilated with extremely thick, rugose, wrinkled, grey-white intima and thick, leathery walls. The extrapulmonary branches were devoid of thrombi, but right pulmonary artery and inferior division of left pulmonary artery at their respective hila were occluded by fresh and organizing thrombi. There were no features of chronic rheumatic heart disease. Fresh thrombi were also present within some intrapulmonary branches. Dilatation of the airways, firmness at the bronchovascular bundles, and bronchopneumonia were also noted.

The pulmonary trunk and both branches showed thickening of their walls due to moderate to marked fibro-cellular intimal thickening and adventitial fibrosis (Fig. 73.1c, d). The media was attenuated with paucity/fragmentation of elastic

P. Vaideeswar (✉)
Department of Pathology (Cardiovascular and Thoracic Division), Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai, India

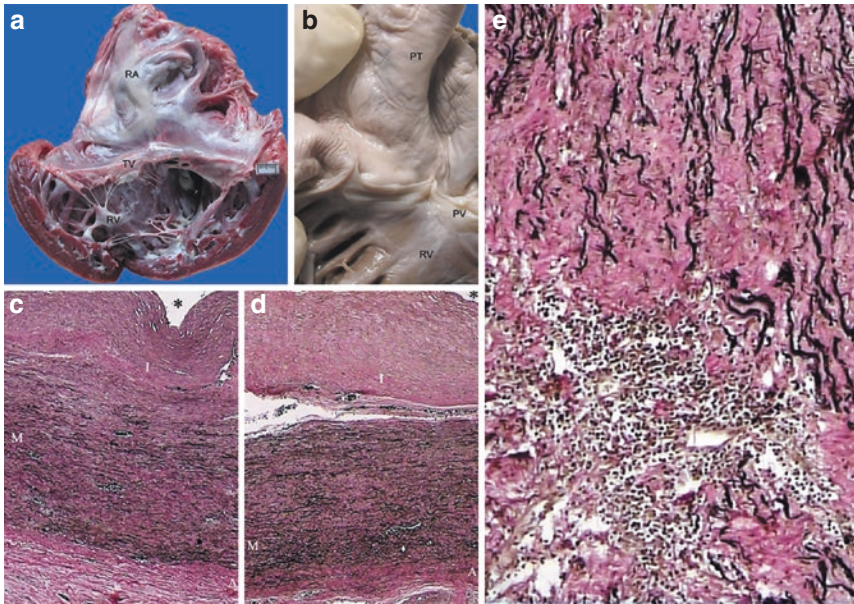


Fig. 73.1 (a) Opened out right ventricular RV inflow tract in the fresh state showing marked dilatation of right atrium RA and RV with dilated tricuspid annulus. Note marked patchy endocardial thickening; (b) Thick, wrinkled whitish intima of the pulmonary trunk PT imparting a vague tree-bark appearance (PV pulmonary valve, TV

valve); (c) and (d) The wall of the main pulmonary artery showed thickened intima I with adventitial A fibrosis. The media M also shows fibrosis with paucity of elastic fibers (Elastic van Gieson $\times 250$); (e) Scarred media with foci of lymphocytes (Elastic van Gieson $\times 400$)

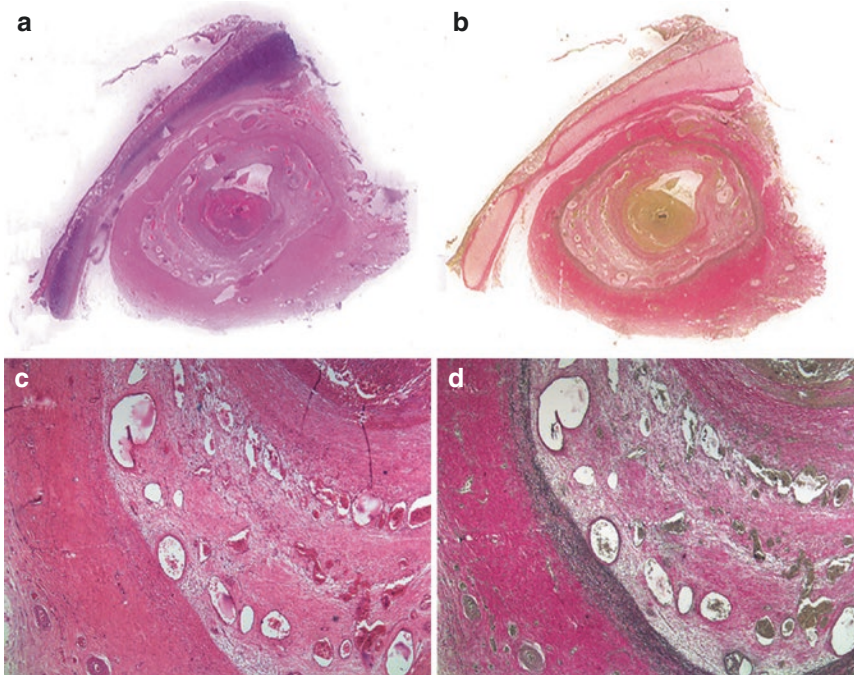


Fig. 73.2 Scanned image of the inferior division of the left pulmonary artery showing luminal occlusion by fresh and organizing thrombus, (a) H&E and (b) Elastic van Gieson; The organization shows intense collagenization

towards the luminal aspect, imparting a ‘vessel-in-vessel’ appearance, (c) H&E $\times 100$ and (d) Elastic van Gieson $\times 100$

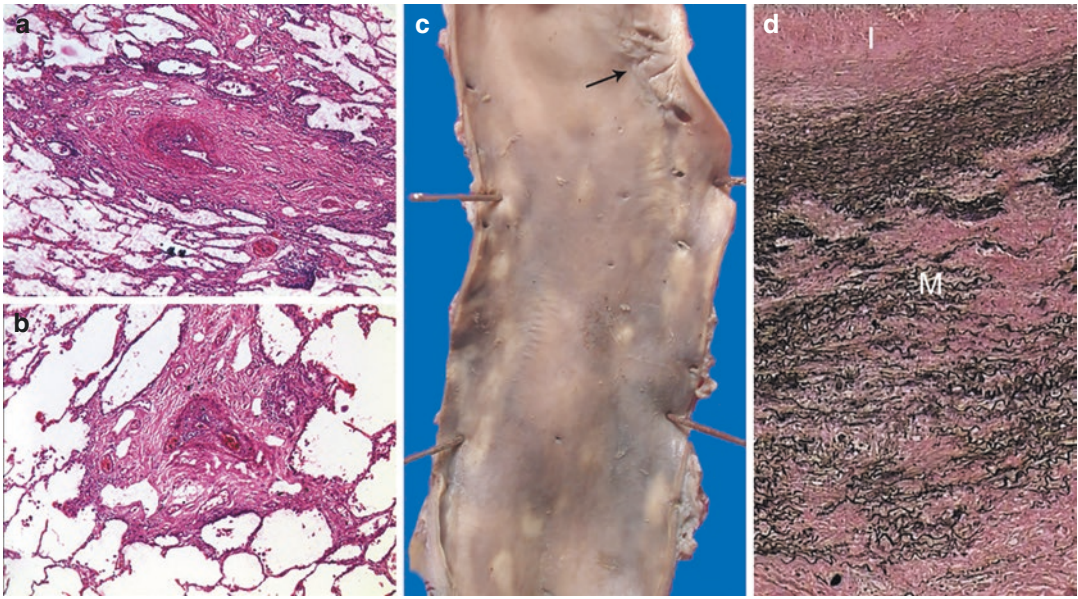


Fig. 73.3 (a) and (b) Thickening of the walls of the small muscular arteries with extensive peri-arterial fibrosis with vascularization; (c) Small area over the greater curvature of the proximal thoracic aorta showing intimal plaque and

rugosity (arrow); (d) Extensive scarring of the media M with intimal fibrosis was seen in the region of the aortic pathology (Elastic van Gieson $\times 100$)

fibers and fairly extensive collagenization (Fig. 73.1c, d). Small clusters of lymphohistiocytes were also present (Fig. 73.1e). The branch lumina had occlusive fresh thrombi superimposed over organizing thrombus, giving it a classic ‘vessel-in-vessel’ pattern (Fig. 73.2a–d). Similar lesions were also present in the intrapulmonary branches. A striking feature was the presence of prominent peri-arterial fibrosis (Fig. 73.3a, b), leading to ectatic bronchi/bronchioles, acute inflammation, bronchopneumonia, and simple aspergilloma. Interestingly, a small segment of cobble-stoned intima with wall thickening was present in proximal thoracic aorta (Fig. 73.3c), revealing histology of a healed aortitis (Fig. 73.3d).

Cause of Death: Right heart failure due to predominant pulmonary arterial Takayasu’s arteritis (TA) with chronic thrombosis.

73.3 Discussion

A vasculitic process involving the pulmonary trunk and its extra- and intrapulmonary branches had produced the clinical features of pulmonary

thromboembolism (PTE) in a young adult male. The histopathology revealed destruction of the wall with fibrosis and minimal inflammation, which was suggestive of a healed phase of Takayasu arteritis (TA). TA (See Chaps. 63–65) is an example of a large-vessel vasculitis of an unknown etiology, which targets the aorta and its major branches (including the coronary arteries) and commonly occurs in young women of usually Asian descent. The various stages (viz. active, chronic, and healed) of granulomatous or non-granulomatous pan-arteritis lead to triphasic clinical phases (i.e., pre-pulseless, vasculitic, and burnt-out). The ongoing and dissipating inflammation produces arterial stenosis, occlusion, and/or aneurysms with end-organ ischemia. The clinical presentations depend on the location and extent of the stenotic aorto-arteriopathy and hence the clinical criteria for diagnosis of TA and the angiographic classification for distribution of lesions are based primarily on the aorto-arterial disease. In this instance, the clinical scenario was entirely orchestrated by a dominant pulmonary arterial involvement.

The pulmonary artery (PA) is the second large artery to be involved by TA and there is an extremely wide range of incidence (8–80%) depending on the ethnicity of the population studied and the diagnostic modalities. It must be realized that PA involvement is often clinically overlooked since it is usually coexists with the more morbid aorto-arterial disease, particularly in Type II TA (ascending aorta, arch and its branches, and descending thoracic aorta, See Chap. 63), which warrants careful analysis of the pulmonary vasculature by noninvasive techniques like echocardiography. However, exclusive or predominant PA inflammation (which is not classified as an independent type) is rarely reported and is said to affect about one-third of the patients with TA with increased frequency in males and without racial or geographic predilection. Again, the incidence may be an overestimate as many of these patients do not have adequate follow-up to document a possibly subsequent aortic involvement. In our case, the dominant pulmonary arterial disease showed only subtle aortic involvement, which may not have been picked up by the routinely used imaging techniques.

In the reported case, there was involvement of the PA, its left and right branches, and many of the intrapulmonary arteries in both the lungs. Literature reveals a varied distribution, most often affecting the right PA along with segmental and subsegmental branches of the upper lobes. In the present case, the trunk and the proximal portions of the branches were dilated with intimal thickening and had features of healed arteritis. However, the distal portions and their intrapulmonary branches revealed stenotic and occlusive lesions with the characteristic vessel-in-vessel appearance, which was well seen. Dilatations or plexiform lesions were not seen within the lungs. Patients with predominant pulmonary vascular disease present a challenge to clinical diagnosis. Owing to the absence of the aortic disease, the insidious pulmonary arterial inflammation does not present any symptoms. The patients develop symptoms like progressive dyspnea, chest pain, or hemoptysis in the late stages of disease when there is stenosis or occlusion, which are indistinguishable from chronic thromboembolic phenomenon (See Chap. 68)

with pulmonary hypertension (PH). TA-related PH is included in the subset WHO Category 4. Our patient was symptomatic for the past 2 years, but had been misdiagnosed as a case of RHD (See Chap. 5) and had a diagnosis of thromboembolism in the current admission. Some cases can also develop pulmonary infarctions or pulmonary hemorrhage, which develops due to systemic-pulmonary shunts. The shunts are better demonstrated by angiography and not well-appreciated on gross or histopathological examination. Infarction or hemorrhage was not seen at autopsy. We also noted that the peri-arterial fibrosis had also lead to ectasia of the airways and there were foci of bronchopneumonia and even fungal colonization. These superadded infections (including tuberculosis) can occur in the patients with TA of PA and the diseased parenchyma may have to be resected in some cases. Steroids are the first line of therapy in all cases of TA, which was delayed in our case leading to severe dyspnea due to PH and right heart failure. The delay in diagnosis can range from 3 to 72 months. The stenosing lesions may also require interventional or surgical pulmonary revascularization. In conclusion, pulmonary vasculitis should be borne in mind whenever young patients present with features suggestive of pulmonary arterial thrombosis or PH.

Further Reading

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