OP17. PATHOLOGIC FEATURES OF TAKAYASU'S ARTERITIS (NON SPECIFIC AORTOARTERITIS)

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Takayasu’s arteritis or Non-specific aortoarteritis (NSAA) is an uncommon form of large vessel vasculitis and has been known by various names.

The morbid anatomical features of NSAA described here are based on the autopsy findings of 80 cases seen in a 30-year period. These autopsies were carried out at Seth GS Medical College & KEM hospital, Mumbai. With an active autopsy service, the incidence of NSAA is about 0.15%. 46.25% of these cases were in the pediatric age group.

In the aorta, the disease had 2 patterns of involvement: (a) Segmental lesions either single or multiple, with skip areas in between. (b) Diffuse extensive disease. Marked periadventitial and adventitial fibrous thickening with adhesions to neighboring structures with enlarged lymph nodes is often noted around the involved segments. The aorta is stiff and rigid, sometimes with dilated segments and aneurysms.

Localized stenotic lesions are fairly common (37.5%), seen particularly in children and is noted in the descending thoracic (DTA) and abdominal aorta. In our material the DTA is the segment maximally affected. The lesion starts at the level of L subclavian or just beyond it to involve variable lengths of DTA. Abdominal aorta (renal artery segment) disease is more common in adults. This is often associated with renal artery stenosis. In diffuse disease the thoracic abdominal aorta is affected, sparing the ascending aorta. In autopsy material, isolated arch vessel disease is rare. When arch vessel is diseased, it involves mainly the L Subclavian and there is always associated aortic arch disease.

Arch vessel disease is in the form of complete block or ostial narrowing with occlusive luminal thrombi. Coronary ostial stenosis is not uncommon.

The intimal surface of the aorta is covered with gelatinous or whitish plaques or is diffusely thickened. Mural thrombi are sometimes present in the constricted segment.

Histopathological features: Inflammation may be in the active or more commonly in the chronic healed phase. In the active phase, diffuse or granulomatous inflammation is seen consisting of Langhans giant cells, foreign body giant cells, mixed inflammatory cells and sometimes-fibroinoid necrosis. Inflammatory reaction is maximal at the junction of the media and adventitia and is marked around vasavasorum though there is no vasculitis. Adventitia shows increase in ground substance with acid mucopolysaccharides. Media shows neovascularization and inflammatory cells. Intima is thickened with increase in ground substance. There is no intimitis. In chronic phase there is sparse inflammation around vasavasorum, adventitial thickening, fibrosis, scarring in the media, disruption of elastic fibres and hyaline intimal thickening. Pulmonary artery and coronary artery involvement is infrequent.

The commonest associated pathology noted at autopsy is tuberculous lymphadenitis (55%). Matted enlarged Para aortic and mediastinal lymph nodes are particularly present around the involved segments of aorta.

It is not easy to reconstruct the natural course of the disease. Symptoms are related to well establish lesions in the aorta or its branches. The inflammatory process may be self limiting in most cases. Regression of lesions has been documented in a few case reports. Prognosis is influenced by clinical course, age of onset and complications like hypertension, rapid development of congestive cardiac failure, and left ventricular failure.

As of today, there is no specific disease activity marker and treatment should be aimed at preventing vital organ ischemia and cardiac failure.

OP18. FACTORS INVOLVED IN THE PERSISTENCE OF INFLAMMATORY LESIONS IN GIANT CELL ARTERITIS (GCA)

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Patients with GCA usually experience a dramatic relief of their cranial, polymyalgic and systemic symptoms with corticosteroid treatment. However, recurrences are frequent during steroid tapering and corticosteroid requirements are highly variable among individuals: while some patients easily enter sustained remission, others require remarkable cumulated corticosteroid doses with their ensuing adverse effects.

We and others have empirically observed that the intensity of the acute phase response is associated with different disease outcomes. Patients with a weak acute phase response have higher risk of developing disease-related ischemic events. These patients have weaker expression of pro-inflammatory cytokines in their lesions, lower concentrations of pro-inflammatory cytokines in their sera, weaker angiogenic response in their lesions and lower expression of endothelial cell adhesion molecules.

In contrast, patients that develop a perpetuating disease with sustained inflammatory activity have higher risk of ischemic complications, perhaps facilitated by the scarring process itself, whereas other patients would develop a perpetuating disease with sustained inflammatory cascades with vascular regeneration and remodelling, leading to a more refractory and relapsing outcome.

Pro-inflammatory cytokines IL-1β, TNFα and IL-6 may have an important role in contributing to these different outcomes. Their tissue expression correlates with the intensity of the acute phase reaction. In addition, TNFα and, IL-1β, mRNA concentrations in lesions correlate with subsequent corticosteroid requirements. Based on their known biologic functions, pro-inflammatory cytokines may have important roles in perpetuating the inflammatory process by amplifying inflammatory cascades such as endothelial adhesion molecule expression, chemokine and cytokine production and by triggering the acute phase response leading to the general feeling of sickness in patients with GCA. Alternatively, these cytokines may be the downstream products of more relevant factors or may be co-ordinately regulated with other molecules with a more direct impact on the course of GCA.

Comparison of gene expression in vascular inflammatory lesions between easy responders and refractory patients may help to identify additional factors involved in persistence of inflammation in GCA. Using this approach we have identified CCL-2 (MCP-1) a powerful chemotactic factor for monocytes and Th1 lymphocytes, as a significant molecule associated with disease refractoriness.

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control mAb or 99mTc-labelled leukocytes. We have since shown focal and intense than those obtained with an isotype matched iron oxide nanoparticles.

Using anti-E-selectin conjugated ultrasmall superparamagnetic iron oxide nanoparticles.

Monoclonal antibody 1.2B6 is a mouse antibody generated in our laboratory, which primarily reacts with E-selectin but also reacts with P-selectin at about four-fold lower affinity. Using this mAb, antibodies are taken with E-selectin into the cell, allowing E-selectin is internalised, and agents conjugated to anti-E-selectin accumulating of targeting agent and increased imaging signal. Furthermore, following expression, molecular imaging of endothelial activation, since it is readily accessible to targeting agents.

E-selectin represents a potentially useful target for the molecular imaging of endothelial activation in vivo in patients with RA [1–3] and inflamed bowel in Crohn’s Disease [4]. More recently we have investigated the possibility of imaging E-selectin by magnetic resonance using anti-E-selectin conjugated ultrasmall superparamagnetic iron oxide nanoparticles.

In contrast to the temporal arteries pathologies do not ultrasound image is identical to that of the temporal arteries. The lumen; 4, consideration of wall swelling, stenosis, and occlusion of normal temporal arteries; 2, high-end ultrasound equipment without temporal arteritis to be sure about the appearance of most of the other arteries is now widely used in diagnosis of GCA.

Duplex ultrasound of the temporal arteries but also for months or years. In such risk over the longer term, though a causal link has yet to be proven in humans. Products of the inflammatory response have effects on the vascular endothelium that might attenuate its normal atheroprotective functions, and could provide a mechanistic link between inflammation and cardiovascular disease. Whether interventions to modify the inflammatory response would be efficacious in reducing cardiovascular events in acute or chronic settings is yet uncertain.

Despite the important role that endothelial activation plays during inflammatory responses, molecular changes in endothelium are relatively inaccessible to clinical investigation. E-selectin (CD62E, ELAM-1) is an adhesion molecule expressed on the luminal surface of vascular endothelial cells in inflammation. It serves the function of initiating interactions between the endothelial cell and circulating leucocytes, preceding leucocyte diapedesis into inflamed tissue. E-selectin is not constitutively expressed by endothelial cells but is induced in response to cytokines during many inflammatory conditions, including sepsis, inflammatory bowel disease, atherosclerosis, and rheumatoid arthritis. E-selectin represents a potentially useful target for the molecular imaging of endothelial activation, since it is readily accessible to targeting agents. Furthermore, following expression, E-selectin is internalised, and agents conjugated to anti-E-selectin antibodies are taken with E-selectin into the cell, allowing accumulation of targeting agent and increased imaging signal.

Monoclonal antibody 1.2B6 is a mouse antibody generated in our laboratory, which primarily reacts with E-selectin but also reacts with P-selectin at about four-fold lower affinity. Using this mAb, we have successfully imaged activated endothelium in vivo using radiospectroscopy. The technique was first evaluated in porcine models of phytohaemagglutinin-induced and MSU crystal-induced arthritis, in which we found that the images of synovitis obtained with 111In-labelled mAb 1.2B6 F(ab)₂ were significantly more focal and intense than those obtained with an isotope matched control mAb or 99mTc-labelled leukocytes. We have since shown that 111In-labelled mAb 1.2B6 F(ab)₂ could image inflamed joints in patients with RA [1–3] and inflamed bowel in Crohn’s Disease and Ulcerative Colitis [4].

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Results: The meta-analysis describes a sensitivity of 87% and a specificity of 96% for duplex ultrasound with regard to clinical diagnosis. Sensitivity is similar in our cohort, but specificity is >99%. Results are varying considerably between studies. Sensitivities with regard to histology vary between 40% and 100% for colour Doppler and between 91% and 100% for duplex ultrasound. Specificities vary between 68% and 100% for histology and between 78% and 100% for the clinical diagnosis. According to the meta-analysis a pre-test probability of 10% correlates with post-test probabilities of 71% and 2% for positive and negative ultrasound, respectively. A pre-test probability of 50% correlates with post-test probabilities of 96% and 12%, and a 90% pre-test probability correlates with post-test probabilities of 99% and 55%. Four aspects are essential to receive good results: 1, sonographer experienced for positive and negative ultrasound, respectively. A pre-test probability of 50% correlates with post-test probabilities of 96% and 12%, and a 90% pre-test probability correlates with post-test probabilities of 99% and 55%. Four aspects are essential to receive good results: 1, sonographer experienced