Takayasu’s aorto-arteritis
A report of 11 cases at King Edward VIII Hospital, Durban

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Summary
Eleven cases of histologically confirmed Takayasu’s aorto-arteritis seen at King Edward VIII Hospital, Durban, are presented. The morphological features of the various histological stages are highlighted. The anatomical distribution of lesions is also discussed.

Takayasu’s aorto-arteritis was first reported in South Africa by Isaacson et al. in 1959. In 1961 Isaacson and Shnier reported a further 6 cases of this condition and called it an ‘idiopathic aortitis in young Africans’. Subsequently Isaacson has concluded that clinically and pathologically idiopathic aortitis is indistinguishable from Takayasu’s aorto-arteritis. A further 11 cases are presented.

Patients and methods
Eleven cases of Takayasu’s aorto-arteritis were seen at King Edward VIII Hospital, Durban, over a 6-year period. All the patients required corrective surgery. Specimens were submitted for histological examination. The material received was formalin-fixed, embedded in paraffin, and stained with haematoxylin-eosin and Verhoeff-Van Gieson. Stains for spirochaetes and acid-fast bacilli were negative. The clinical notes and relevant angiograms were studied.

Results
The ages of the patients ranged from 11 to 49 years (mean 27.8 years, median 26 years). There were 8 females and 3 males. Nine were black and 2 were Asian.

Distribution of lesions
The lesions were classified according to the categories proposed by Ueno et al. in 1967, together with angiography studies (Table I). Of the 7 patients with type I disease, 4 had lesions involving the common carotid arteries; of these 3 were aneurysms and 1 was an occlusive lesion. Two patients had occlusive lesions of the axillary artery, and the remaining patient had an occlusive lesion of the brachiocephalic artery.

The 4 patients in the type II category included 3 with thoraco-abdominal aneurysms and 1 with occlusive aorto-iliac disease. Furthermore, 2 patients in this group had renal artery involvement with resultant established hypertension.

Laboratory data
All serological tests for syphilis in the 8 patients available for testing were negative. Three patients had a strongly positive Mantoux skin test, in 2 this test was negative, and 1 had a strong family history of tuberculosis. The erythrocyte sedimentation rate (6 patients) ranged from 12 to 130 mm/1st h (Westergren). Autopsy performed in 1 case showed tuberculosis involving carinal and pancreatic lymph nodes. This patient had type I disease (Table I).

Histological analysis
In accordance with Pokrovsky et al. the histological features of the 11 cases were categorised into three stages of the disease.

Acute stage (4 cases)
The inflammatory process involved all layers of the vessel wall (Fig. 1), the most characteristic feature being inflammatory destruction of the outer half of the media (Fig. 2). This contrasts with giant-cell arteritis, in which there is inner medial and outer intimal involvement.

Medial changes. A consistent finding in all 4 cases was outer-half disruption of the medial elastica with an inflammatory infiltrate.
comprising lymphocytes, histiocytes, occasional plasma cells and polymorphonuclear leucocytes. Occasional multinucleated giant cells of the foreign-body type were found, especially at the site of destruction of the elastica. Associated smooth-muscle disruption was also noted. One patient had focal areas of necrosis.

**Intimal changes.** The intima showed thickening with loose concentric proliferating connective tissue. Although the intima was largely devoid of inflammation, focal spillover into the intima was noted in 2 cases.

**Adventitial changes.** Typically thickening and fibrosis of this layer was seen. Inflammation was noted in 2 cases — perivascular mononuclear in one and granulomatous in the other. The remaining 2 patients were free of inflammation.

**Intermediate stage (4 cases)**

In this stage the acute inflammation had subsided and there was established destruction and fragmentation of the medial elastica with continued presence of inflammatory cells, mainly lymphocytes. A striking feature was intensified vascularisation of the media (neo-angiogenesis) (Fig. 3).

**Sclerosing stage (3 cases)**

This was characterised by transmural fibrosis and scarring with mild thickening of the vaso vasorum and scattered mononuclear cells (predominantly lymphocytes) in the adventitia. The media was reduced to a sea of collagen with scattered islands of residual elastic fibres. The intima was more dense and somewhat collagenous.

**Discussion**

This is a further report of Takayasu's aorto-arteritis in South Africa, following on previous documentation. Although most cases have been described in young females, Takayasu's aorto-arteritis may be found at any age and in either sex, as was noted in this series.

It should be noted that a fourth type of distribution has been described, encompassing types I, II and III together with pulmonary involvement. Cases of type IV disease have been reported by Rose et al.

In determining the distribution of lesions, comprehensive angioraphy (complete aortogram from origin to pelvic bifurcation including the major branches) is necessary whenever Takayasu's aorto-arteritis is suspected. In general, the findings on angioraphy correlate with clinical manifestations.

A good correlation is noted between the histological stage and the anatomical lesion. All our patients with acute-stage disease were found to have occlusive arterioopathy, leading to the classic 'pulseless disease'. Similarly, the sclerosing stage had given rise to saccular aneurysmal lesions. These findings support the concept that Takayasu's aorto-arteritis evolves from an acute phase through to a sclerosing stage. Furthermore, it is distinguishable from other forms of arteritis.

Necrosis, an unusual feature seen in 1 of our cases, has been reported previously by Nasu, and the well-known association of tuberculous lymphadenopathy and Takayasu's aorto-arteritis was seen in 1 of our cases.

Although Takayasu reported his first case over 75 years ago, the causation of the disease is still obscure. However, current trends support an auto-immune pathogenesis with the detection of an anti-aorto antibody in the serum of patients. This has been supported more recently with genetically related factors which support auto-immunity as a cause. Others have postulated that the immunological mechanism is delayed hypersensitivity to tubercul protein.

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**REFERENCES**

Rhinocerebral mucormycosis in diabetic keto-acidosis
A case report

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Summary
A case of diabetic keto-acidosis complicated by rhinocerebral mucormycosis is described. Early diagnosis, control of the diabetes, aggressive surgical debridement, and systemic antifungal therapy resulted in a successful outcome.

Fungi belonging to the taxonomic order Mucorales are widespread in nature and show minimal intrinsic pathogenicity in normal subjects. However, under certain clinical conditions, they can initiate aggressive and fulminant infections. Diabetic keto-acidosis predisposes to the life-threatening condition of rhinocerebral mucormycosis.

Case report
A 37-year-old black man was admitted to Baragwanath Hospital complaining of abdominal pain of recent onset, vomiting, polyuria and weight loss. There was no previous or family history of diabetes mellitus. Examination revealed an obese, dehydrated man who had a tachycardia and Kussmaul's respiration. No other abnormalities were noted. Urinalysis showed glycosuria and ketonuria. The diagnosis of diabetic keto-acidosis was confirmed by the finding of a plasma glucose value of 48.6 mmol/l, an arterial pH of 7.0 together with ketonaemia, and a serum urea level of 12.1 mmol/l.

Intensive therapy was instituted which included rehydration with normal saline, low-dose insulin regimen, potassium replacement, and bicarbonate administration. He responded within 12 hours and was given a diabetic diet and subcutaneous soluble insulin as per sliding scale. Ketonuria persisted although plasma glucose and arterial pH were stable. No evidence of infection was found. On day 8 he had a recurrence of keto-acidosis while on treatment, and again, no infection was found. He responded well to intensive treatment. On day 10, keto-acidosis recurred, only this time he complained of left-sided headache of sudden onset associated with epistaxis. He now appeared drowsy, pyrexial, and there was no previous or family history of diabetes mellitus. Examination revealed an obese, dehydrated man who had a tachycardia and Kussmaul's respiration. No other abnormalities were noted. Urinalysis showed glycosuria and ketonuria. The diagnosis of diabetic keto-acidosis was confirmed by the finding of a plasma glucose value of 48.6 mmol/l, an arterial pH of 7.0 together with ketonaemia, and a serum urea level of 12.1 mmol/l.

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Amphotericin B therapy was started. However, eye involvement proved progressive with blindness of the left eye developing secondary to central retinal artery occlusion. Evisceration of the orbit was performed on day 15.

Pathology
Tissue removed at the time of initial fronto-ethmoidectomy showed extensive necrosis of the respiratory mucosa and submucosa accompanied by a heavy mixed inflammatory-cell infiltrate comprising neutrophils, lymphocytes and histiocytes. Widespread intravascular infiltration by broad non-septate fungal hyphae consistent with mucormycosis was present, which in many vessels resulted in complete vascular occlusion (Fig. 1). Free-lying fungal hyphae were evident in the fibrous connective tissue stroma of the submucosa and also extended deep into the sinus wall between bone trabeculae.

Tissue removed at the time of exenteration of the left orbit appeared necrotic with striking infiltration of the left eye by similar phycomycectye hyphae. Involvement of the optic nerve, retina and scleral vessels was noted (Fig. 2). A biopsy of the cribriform plate, performed at the same time, also showed invasion by fungal hyphae.