Recent views on Buerger’s disease

GEORGE WILLIAMS

From the Department of Pathology, University of Manchester

SYNOPSIS Eighty-two biopsy specimens of vessels from 37 patients with clinical Buerger’s disease were examined histologically and classified. The aetiology of this vascular disorder is discussed and a basis suggested for its pathogenesis as primarily a thrombotic disorder complicated by vasculitis. Thus both acute and chronic lesions are acceptable as entities.

Thromboangiitis was established as a clinicopathological entity by Buerger in the early part of this century. Despite the extensive literature which has accumulated around this disease, its aetiology remains unknown, its pathogenesis controversial, and its clinical course unpredictable. In this paper, some aetiological factors long associated with Buerger’s disease are considered in the light of the more recent literature and its pathology is studied in 82 biopsy specimens from clinically affected patients.

CONTRIBUTORY AETIOLOGICAL FACTORS

Sex, age, race, tobacco, and infection have all received attention as contributory factors.

Thromboangiitis is predominantly a disease of males. Buerger (1924) recorded only two females in 500 cases and this bias has been maintained in every major series. A few cases have been recorded in women (Poteete and Lynch, 1956; Montorsi and Ghiringhelli, 1961). Gailis (1957) reckoned that of 4,467 cases collected from the literature, probably fewer than 10 could be regarded as genuine occurrences in women, an assessment reinforced by Kaiser, Musser, and Shumacker (1960). The age group mainly involved is between 25 and 50 years, although patients well outside this range have been recorded (Allen, Barker, and Hines, 1962).

Buerger’s view of the disorder as being largely restricted to the Jewish race reflected a strong racial bias in the population from which his own patients were drawn; this view is no longer tenable. Over the years a wider incidence has been recorded: McKusick and Harris (1961) and Inada, Hayashi, and Okatani (1964) have described the disease in Japan. In 120 cases Lynn and Burt (1949) recorded only five Jewish patients; Hershey, Pareira, and Ahlvin (1962) found none, and Szilagyi and Elliott (1964) only one in their respective series of seven and 22 cases. Studies of the disorder in an almost exclusively Jewish population in Israel (Goodman, Elian, Mozes, and Deutsch, 1965) showed an 80% incidence in Ashkenazim as opposed to Sephardic stock.

The harmful effects of cigarette smoking on the course of the disease, emphasized by Silbert (1935, 1945, and 1948), have been substantiated by more recent studies (McKusick and Harris, 1961; Hershey et al, 1962). Goodman et al, however, found that the consumption of tobacco of patients with arteriosclerosis and of those classified as having Buerger’s disease did not differ significantly and that cessation of smoking was beneficial only if maintained for at least 12 months. The collective evidence shows that chronic vascular insufficiency is aggravated by tobacco consumption, an effect to which patients in the Buerger category seem particularly susceptible.

The striking inflammatory component of the active phase of the disease has prompted several workers to seek an infective cause. In this context the most significant association has been between Buerger’s disease and fungal infection as indicated by Thompson (1941) and Naide (1941), and later by Boyd, Ratcliffe, Jepson, and James (1949) and Boyd (1950). The latter emphasized that the patchy, superficial phlebitis which may precede involvement of larger vessels was commonly associated with dermophytosis of the interdigital folds. The role of fungi is difficult to assess; in the present study a minority of patients had fungal infections but their vascular lesions differed in no way from the larger non-infected group.

PATHOLOGICAL STUDY

In this study, a specimen was defined anatomically
in terms of its vessel of origin. Thus, in some instances, for example, from amputated limbs or as a result of repeated biopsies, several specimens were obtained from individual patients. A total of 82 specimens (Table I) – 10 from upper limbs, 72 from lower limbs – were examined from 37 patients (34 males, three females). Microscopically, four upper limb specimens were normal, the remaining six were abnormal. Of the lower limb specimens, four were normal and 68 abnormal. The lesions were classified as acute, subacute, or chronic in terms of the tissue changes. Arteries and veins were commonly both involved though not necessarily at the same stage of the process. Different stages were occasionally seen in one group of vessels or in different vessel groups from individual patients. In this series, 66% of all specimens showed chronic lesions, 15% acute or subacute, the remaining 19% showing either bland thrombosis in normal vessels, atheroma (one case), or simply normal vessels.

Macroscopically longstanding lesions showed arteries, veins, and sometimes nerve trunks bound together as fibrous cords. Multiple transverse sections showed obliteration of the vascular lumina by dense grey tissue with variable canalization. Acute and subacute lesions appeared as friable brown-red thrombus occupying short lengths of the vessels, either as isolated occlusions or as terminations of more chronic obliterated segments.

Microscopically, the acute stage showed luminal obstruction by thrombus containing dense aggregates of polymorph leucocytes. The vessel walls showed infiltration with polymorph leucocytes, an intact, elastic lamina, and no significant muscle damage. In the subacute stage, mononuclear as well as polymorphonuclear leucocytes contributed to the cell infiltrates, and foamy giant cells were present within the lumen, usually at the cell-fibrin interface (Fig. 1). Chronic lesions evinced a wide spectrum of fibrous occlusions with variable chronic inflammatory infiltrates, lymphoid aggregates, and perivascular fibrosis (Figs. 2, 3, 4, and 5); arterial muscle coats were penetrated by extensions of the vasa vasorum linking up with the luminal canalizing vessels. Superficial thrombophlebitis (Fig. 6) was seen in three cases. The acute phases may occur in terminal portions of occluded vessels or occasionally in isolated segments, sometimes in superficial veins, a point which Buerger emphasized. The acute lesion in both arteries and veins consists of a thrombus associated with an intense inflammatory reaction involving the vessel coats and frequently adjacent vascular channels and nerves. In the material under study I have not seen vasculitis in the absence of thrombosis, though the reverse may occur, for example, at the extremity of a recent occlusion.

**DISCUSSION**

Acute and subacute lesions are relatively rare and their significance has been questioned. Gery, Fontaine, and Branzeu (1939) found none in arterectomy specimens and amputated limbs from 14 patients. However, Schatz, Fine, and Eyler (1966) described inflammatory vessel changes in nine of the 12 cases they studied pathologically, and McKusick, Harris, Ottesen, and Goodman (1962) described micro-abscess formation as a feature of the acute lesions affecting many vessels in four of their patients. The intense inflammatory reaction in the acute lesions and their subacute counterparts is not a feature of ordinary thrombi; their appearances suggest an inflammatory response to constituents of the thrombus, at first limited to the vascular lumen, then later spreading to involve the vessel coats and adjacent structures.

Emphasis on the distinctive nature of the active lesions does not detract from the concept of Buerger’s disease as primarily a thrombotic disorder. Indeed, there is considerable evidence in support of such a view. De Takats (1943) and Hagedorn and Barker (1948) found increased tolerance of heparin in patients with Buerger’s disease and arteriosclerotics as compared with controls. Eisen, Tyson, Michael, and Baumann (1951) showed that platelet adhesiveness was markedly increased during active
Recent views on Buerger's disease

FIG. 1. Subacute lesion showing polymorph and mononuclear leucocytes, fibrin, and giant cells in vessel lumen. × 120.

FIG. 2. Popliteal artery showing recurrence of subacute lesion (fibrin and giant cells) within a recanalized old thrombus. × 50.

FIG. 3. Posterior tibial artery showing recanalized thrombus, lymphocyte infiltration, and penetrating mural capillaries. × 40.
FIG. 4. Popliteal vein showing recanalized thrombus containing lymphoid aggregates. $\times 35$.

FIG. 5. Lymphocytic aggregates surround collateral adventitial vessels. $\times 100$.

FIG. 6. Thrombophlebitis in a superficial vein. $\times 120$. 
phases of thromboangiitis, and remained higher than that of control patients during quiescent periods of the disease. By studying a range of coagulation factors Craven and Cotton (1967) showed that in contrast to atherosclerotic and control groups, patients with Buerger’s disease have raised plasma levels of heparin-precipitable fibrinogen, indicating a hypercoagulable state.

The chronic lesions of Buerger’s disease comprise organized recanalized thrombi within muscular walls frequently distorted by fibrosis and ingrowths of adventitial vessels. As such they represent the end products of vascular injury or occlusion. The degree of perivascular fibrosis and of lymphoid infiltration of the luminal tissue varies throughout the obliterated vessel segments. These features are consistent with a disease process in which focal or segmental vasculitis, combined with thrombosis and possible end-arteritic changes, effect a variable pattern of vascular obliteration quite distinct from that of atherosclerosis.

In recent times it has been argued that Buerger’s syndrome is not a distinct entity. Fisher (1957) studied its cerebrovascular manifestations in five cases and concluded that they resulted from ‘stagnation thrombosis’ complicating proximal occlusions of the carotid or midcerebral arteries. By applying this hypothesis to lesions of the major limb vessels he viewed the latter as secondary to obstruction of the proximal arterial trunks by atherosclerosis. Gore and Burrows (1958) drew similar conclusions from their review of necropsy and amputation specimens. Ming, Wessler, Gurewich, and Freiman (1959) examined pathological specimens from 26 patients and concluded that the lesions of Buerger’s disease could be explained in terms of multiple embolization, thrombosis, and athrotem. Later studies by the same group of workers (Wessler, Ming, Gurewich, and Freiman, 1960; Wessler, 1961) reinforced their conclusions. However, others, including Horwitz (1961), Barker (1962), Ishikawa, Kawase, and Mishina (1962) and particularly McKusick and his colleagues (1961, 1962a and b), have rejected this concept. The latter group, after extensive studies in Japan and the Orient, failed to demonstrate embolization, athrotem, or thrombosis as the basis of Buerger’s disease which they viewed as a distinct clinicopathological entity. Clinical and angiographic differences between Buerger’s disease and atherosclerosis have also been indicated. McPherson, Juergens, and Gifford (1963) found that survival times for patients with Buerger’s disease were comparable to those of the normal population, indicating a self-limiting disorder, whereas atherosclerosis, on account of its progressive nature, killed at least 30% of patients within 10 years of diagnosis. Angiographically, in Buerger’s disease, the main arterial trunks proximal to occluded segments have a smooth lining (Steiner, 1956) with regular, tapered outlines (Hershey et al., 1962) in contrast to the irregular lining and serpiginous outlines of atherosclerotic vessels.

This dichotomy of views regarding the nature of Buerger’s disease may be partly reconciled by accepting it as an episodic thrombotic disorder which produces, possibly on an allergic basis, focal or segmental vasculitis in response to the thrombus or its breakdown products. Thus the acute lesion would be acceptable as an entity. The variable patterns of luminal obliteration, chronic inflammatory infiltration, and vascular distortion which characterize the chronic lesions could logically represent the long-term residue left by repeated acute episodes, thrombosis, and end-arteritic change.

I am indebted to Dr J. Davson for reading the manuscript and to Mr N. Mowat and Mr J. T. Stopford for the photomicrographs.

REFERENCES


