Intestinal thromboangiitis obliterans in a woman: A case report and discussion of chronic ischemic changes

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Although traditionally regarded as a disease of distal extremities, mesenteric vasculature can also manifest thromboangiitis obliterans (TAO). There are 31 cases of intestinal TAO in the English literature and the majority of subjects are male. However, cases of women with TAO are becoming more common, coinciding with an increased incidence of smoking in this sex. We describe the sixth case of a female patient with classic extremity manifestations paralleled by paroxysms of abdominal angina. Intestinal TAO can mimic extremity disease of smoldering chronic ischemia punctuated by unpredictable acute episodes of gangrene. In the present case, chronic ischemia manifested as partial bowel obstruction due to stricture deformity of the ileum and profound adipocyte atrophy of mesentery.

Key Words: *Buerger's disease; Female; Intestine; Lipid atrophy*

CASE PRESENTATION

The patient was an otherwise healthy 43-year-old woman with a 30-pack-year history of smoking and Raynaud's disease. Of note, she had no heart disease, hypertension, thrombophilia, repetitive pregnancy loss, connective tissue disorder or malignancy. She was prescribed a vasodilator (nifedipine 30 mg daily) for Raynaud's disease.

She complained of postprandial stomach cramps for four years, that intensified over the last 12 months, prompting multiple emergency room visits. The pain was vague and not associated with changes in bowel habit or stool appearance; she had lost 14 kg over the last year. Endoscopy examination was unremarkable. She was diagnosed with intestinal angina but continued to smoke against medical advice.

Three months before her most recent admission, she developed acute intractable pain of her left hand third digit. Angiograms of the aorta and extremities identified segmental occlusions of the splenic artery, midarm brachial arteries, radial artery of the right wrist, numerous digital arteries and tibial arteries. Larger vessels reconstituted distal to the occlusions via tortuous collaterals. Her left hand third digit began to ulcerate and an amputation was performed. Histological examination was negative for vasculitis.

Une thromboangéite oblitérante intestinale chez une femme : Rapport de cas et discussion des modifications ischémiques

Bien qu'elle soit généralement considérée comme une maladie des extrémités distales, la thromboangéite oblitérante (TAO) peut également se manifester dans le système vasculaire mésentérique. On répertorie 31 cas de TAO intestinale dans la documentation scientifique anglophone, et la majorité des sujets sont des hommes. Cependant, les cas de femmes atteintes de TAO deviennent plus courants, ce qui coïncide avec une augmentation de l'incidence de tabagisme au sein de cette population. Nous décrivons le sixième cas d'une patiente présentant des manifestations classiques des extrémités, accompagnées de paroxysmes d'angine abdominale. La TAO intestinale peut imiter une maladie des extrémités causée par une ischémie chronique latente ponctuée par des épisodes aigus de gangrène. Dans le cas présent, l'ischémie chronique a pris la forme d'une occlusion intestinale partielle causée par une difformité du resserrement iléal et d'une atrophie adipocytaire profonde du mésentère.

Two months before her most recent admission, she developed escalating right leg claudication. Serology showed a negative or normal antinuclear antibody, antineutrophil cytoplasmic antibodies (myeloperoxidase and proteinase-3), anticardiolipin, anti-DNA antibody, rheumatoid factor, homocysteine, hepatitis B and hepatitis C status. {Please confirm} A diagnosis of Buerger's disease was not established definitively due to splenic artery occlusion. Her painful and progressively ischemic right leg was recalcitrant to a course of cyclophosphamide and steroids.

Intractable right leg pain and abdominal angina prompted her most recent hospital admission. The initial abdominal radiographs revealed a marked distension of the stomach and loops of bowel, consistent with small bowel obstruction. Leg claudication was accompanied by absent popliteal and pedal pulses via Doppler ultrasound. An above-knee amputation was performed. Once again, histological examination of the limb was negative for vasculitis (Figure 1).

Two weeks later, she developed an acute abdomen with free air under the diaphragm identified radiographically. Exploration at laparotomy confirmed a stricture of the distal ileum, compatible with chronic ischemia. The distal jejunum was gangrenous. Two segmental resections of bowel with pri-

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Figure 1) Serial sections of the right popliteal artery delineate concentric segmental occlusion due to an acute thrombus (inset, hematoxylin and eosin, original magnification $\times 100$)

mary anastomoses were performed. She developed multisystem organ failure and died 35 days after admission.

Histomorphology of the extremity and the viscera vasculature was identical. No atherosclerosis, leukocytoclasia or fibrinoid necrosis was seen. The disease was almost exclusively confined to small and medium-sized arteries. On examination, the predominant vessel alteration was noted to be segmental thrombi of varying ages. Recent thrombi were associated with a mild lymphocytic and neutrophil transmural infiltrate but no giant cells, fibrous scarring or interruption of elastic lamina. Prominence of endothelial cells was obvious. Subacute thrombi had intraluminal pigment-laden macrophages and fibrin with an enmeshing of fibroblasts. These vessels had the most florid lamellar hypertrophy of internal elastic lamina. Small endothelialized channels recanalized chronic thrombi. The media of such vessels were intact.

Adipose tissue of the subcutis, mesentery and subserosa had localized lipoatrophy. Atrophy of adipocytes was mild in the finger and leg but profound in the mesenteric tissue (Figure 2). Presumably, both chronic ischemia and anorexia contributed to this atrophy.

DISCUSSION

Thromboangiitis obliterans (TAO) is an obliterative inflammatory disease of small arteries and veins. Young adult males who smoke heavily are at risk. However, women with TAO are becoming more common, coinciding with an increased incidence of smoking in this sex (1). As such, the disease may be a toxic angiitis or delayed hypersensitivity to vessel wall collagens I and III (2). A genetic predisposition is suggested (human leukocyte antigen-A9 or B5) and concurrent hyperhomocysteinemia may predict a poor prognosis (3,4).

The diagnosis of TAO necessitates the exclusion of vasculitides, atherosclerosis, thrombophilias, dysrhythmias and drug (ergot) ingestion. Specific diagnostic criteria, proven by long-term follow up, are all of a smoking history, disease onset before the age of 50 years, infrapopliteal arterial occlusions, either upper limb involvement or phlebitis migrans and absence of

Figure 2) Localized lipoatrophy of small bowel mesentery; typical lobular distribution of adipocytes about vessels is maintained (hematoxylin and eosin, original magnification $\times 400$). A subacute thrombus and elastic lamina lamellar hypertrophy is noted in an adjacent mesenteric artery (inset, elastic van Gieson, original magnification $\times 250$)

other atherosclerosis risk factors (5). Our patient satisfies these criteria. Her serology and angiograms were also indicative of TAO. Splenic artery occlusion was initially difficult to reconcile with our diagnosis; however, rare case reports verify splenic artery involvement in TAO (6,7). Thus, when histological examination proved negative for vasculitis, the diagnosis of Buerger's disease was confirmed.

Although traditionally regarded as a disease of distal extremities, Buerger indicated that mesenteric vasculature could manifest TAO (8). Intestinal TAO is an established entity with 31 cases described in the English literature. Approximately 50% of published cases indicate that Buerger's disease was verified by angiogram (9). Remaining subjects required a histological assessment of their necrotic bowel resections, as was the case presently. Intestinal TAO is a segmental process that preferentially afflicts the small bowel (70%) (7). Acute gangrenous episodes are ominous, with a 30% mortality rate (10). However, chronic ischemia may be managed successfully via bypass surgery (7,11,12).

Chronic ischemia of intestinal TAO appears to manifest as partial bowel obstruction (13). Symptomatology is usually nonspecific cramps or abdominal angina that contributes to significant weight loss (7,14). More specifically, postprandial cramping and pain, as noted in our patient, has been identified in four other cases (7,11,12,15). The morphology of segmental bowel disease includes occasional stricture formation, with or without confounding acute necrosis (14-17).

Anorexia, but also chronic arterial obstruction, classically causes localized lipoatrophy of the subcutis and omentum (18). In a series of 29 limbs amputated for end-stage TAO, 11 (38%) demonstrated membranocystic changes (19). Mild lipoatrophy was evident in the subcutis of our patient's extremities. In contrast, bowel subserosa and mesentery had profound atrophy. Variable arterial obstruction and degree of chronic ischemia probably contributed to such a heterogeneous pattern of atrophy (as presumably, confounding anorexia may facilitate a consistent distribution). More studies are warranted to verify our finding and characterize visceral lipoatrophy in Buerger's disease.

CONCLUSIONS

Cases of women with TAO are becoming more prevalent, including subjects with intestinal involvement. Our case demonstrates the chronic ischemic and acute gangrenous elements of intestinal TAO. Chronic ischemia manifested as partial bowel obstruction due to stricture deformity of the ileum. Postprandial cramping was experienced years before the acute gangrenous event. A novel finding presently is profound mesenteric lipoatrophy. Atrophy of visceral adipose tissue should be expected, as it is a well-documented feature of extremity TAO.

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