Case Report

Rapidly Progressive Intracranial Vasculopathy in Graft Versus Host Disease

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After allogenic hematopoietic stem cell transplantation, cerebrovascular complications are uncommon, occurring in approximately 2%, and typically due to coagulopathy or infection. Graft versus host disease has been rarely reported to affect the central nervous system but these cases typically describe leukoencephalopathy, encephalitis, or perivascular infiltrates or vasculitis with subcortical ischemia or hemorrhage. We report a previously undescribed noninflammatory vasculopathy causing multifocal intracranial arterial occlusions and cerebral infarctions in a man following allogenic hematopoietic stem cell transplantation for chronic lymphocytic leukemia, which we propose to be a central nervous system manifestation of graft versus host disease.

Key Words: Cerebrovascular disease—Graft versus host disease—Vasculopathy—Vasculitis—Central nervous system—Stroke—Cerebral infarction—Chronic lymphocytic leukemia

Case Report

Eighteen months after receiving an allogenic hematopoietic stem cell transplantation (HSCT) for B-cell chronic lymphocytic leukemia complicated by cutaneous sclerodermoid graft versus host disease (GvHD), a 54-year-old man presented with an acute ischemic stroke. Over the next 2 months, he suffered recurrent, stereotyped transient ischemic attacks of left ataxic hemiparesis which failed multiple antiplatelet agents, then decreased in frequency with tacrolimus. Cerebral angiography revealed multifocal stenoses and dilatation of medium-sized intracranial arteries and occlusion of the right middle cerebral artery (MCA). He was treated with high-dose oral steroids and cyclophosphamide with improvement in his headaches and cutaneous GvHD, but continued to suffer cerebral infarcts and died 2 months later from bacterial meningitis. Neuropathology demonstrated the neutrophilic inflammation involving the adventitia of the MCAs, a finding consistent with the bacterial meningitis that was the ultimate cause of the patient's demise. The lumen of the MCAs was occluded by prominent intimal hyperplasia with collagen deposition and medial disruption consistent with a noninflammatory vasculopathy (Fig 1).

Discussion

Central nervous system complications of GvHD are rare and often limited to single center case series.[1] Most case reports have described an inflammatory vasculitis characterized by perivascular lymphomononuclear infiltrates.[2] The key finding present in this case is prominent intimal hyperplasia in the absence of classically described perivascular lymphomononuclear infiltrate. To our knowledge, this is the first pathologic case description of a rapidly progressive noninflammatory occlusive vasculopathy due to central nervous system GvHD.

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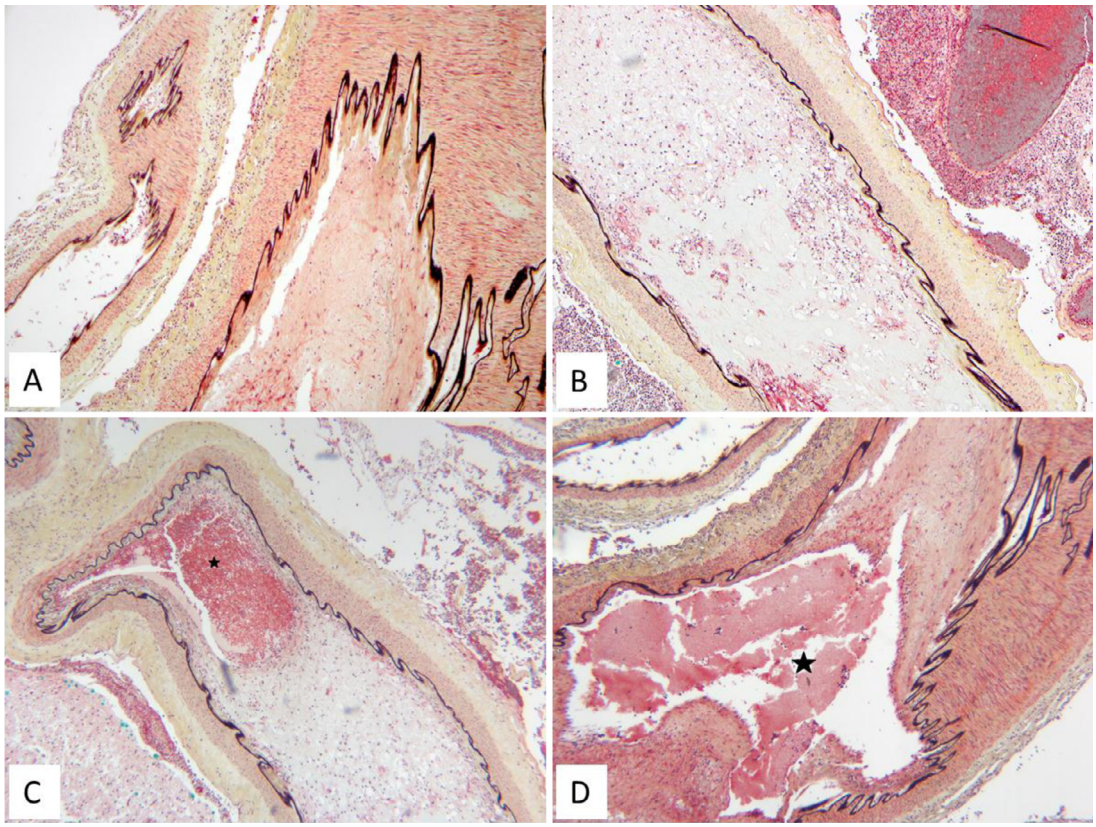

Figure 1. *Movat stain (10×) of representative sections of the MCA demonstrating neutrophilic inflammation involving the adventitia (A and B) without involvement of the media and intima; this finding is consistent with bacterial meningitis. The lumen of the vessel, denoted by the star, is occluded by extensive intimal hyperplasia, which is a separate pathophysiological process (C and D). Abbreviation: MCA, middle cerebral artery.*

Although this vasculopathy involved the native cerebral arteries, pathologically it is most similar to the allograft vasculopathy complicating solid organ transplants. The best described is cardiac allograft vasculopathy, which affects 75% of patients at 3 years, represents the leading cause of death in that time period, and is considered an accelerated form of coronary artery disease.[3] The temporary symptomatic improvement with tacrolimis but otherwise poor response to multiple antithrombotic and immunosuppressive therapies in our patient is similar to cardiac allograft vasculopathy, where treatment relies on prophylaxis with calcineurin inhibitors and, once established, can only be palliated with mechanical interventions (i.e., angioplasty and stenting).

Although still exceedingly rare, there is increasing evidence to suggest that the vascular endothelium can be a target of GvHD.[4]

A case series of 6 pediatric patients after BMT found vasculopathy in small muscular arteries in lung and gastrointestinal tract, described similar to our case as "*concentric intimal or medial hyperplasia with luminal narrowing*."[5]

Cerebrovascular complications from GvHD are rare and although vasculitis is often considered in the setting of rapidly progressive and multifocal cerebral arterial stenoses, this noninflammatory vasculopathy of cerebrovascular GvHD needs to be included in the differential diagnosis. Future cases of cerebrovascular GvHD should consider management strategies that are effective for cardiac allograft vasculopathy, such as maximizing calcineurin inhibitor therapy and palliative intracranial angioplasty or stenting.

References

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