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Catastrophic antiphospholipid syndrome presenting with sudden renal failure: The lesson lies in vascular lesions

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Catastrophic antiphospholipid syndrome (CAPS), is a rare and potentially fatal form of the antiphospholipid syndrome (APS), characterized by an acute onset of multiple small vessel thrombosis in different organs that can lead to multi-organ failure. Its early diagnosis and energetic treatment are essential to prevent the usually high mortality (around 50%) associated with the disorder. It is necessary to increase the awareness of the lesion among the pathologists and the nephrologists from the developing countries for its early and accurate diagnosis and appropriate management.

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Catastrophic antiphospholipid syndrome (CAPS), is a rare and potentially fatal form of the antiphospholipid syndrome (APS), characterized by an acute onset of multiple small vessel thrombosis in different organs that can lead to multi-organ failure (1, 2). The resulting clinical manifestations are quite heterogeneous and protean reflecting the site and extent of small vessel obstruction (3-6). None of the various clinical or laboratory features is specific or pathognomonic of the condition. Many of the signs and symptoms resulting from small vessel occlusions are

also shared by related disorders of the thrombotic thrombocytopenic purpura (TTP) and hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, sometimes clumped together under the rubric, microangiopathic APS (1, 7). Thus, a need for the development of the diagnostic criteria for its early diagnosis was strongly felt soon after the recognition of the disorder in 1992 (1, 3). The preliminary international consensus criteria for the diagnosis of the condition were promulgated in late 2002 and published in 2003 (8). These criteria have been validated in a subsequent

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study of international cohort of 220 patients (9). It is evident from these criteria that the diagnosis of the condition is a clinicopathological one, requiring a high index of suspicion and prompt and appropriate laboratory investigation. The later requirement is even more important in cases of *de novo* form of CAPS. In the case of CAPS developing on the background of APS, the diagnosis is relatively easy. This progression is unpredictable in most instances.

The case presented in this issue of *Journal of Nephropathology* by Mardani et al represents a *de novo* CAPS, at least on the face of it (10). However, a deeper digging into the past history, reveals history of two abortions after six months of pregnancy. It may be that the patient was suffering from unrecognized APS, which is also reflected in the morphology of the kidney biopsy. There are foci of focal cortical atrophy (FCA), as shown in Figures 1A and B (11). Thus, the current complication of CAPS seems most probably to be superimposed on the background of hitherto undiagnosed APS. In my view, the case also represents a probable rather than a definite CAPS. The only organ whose involvement on clinical, laboratory and histopathological grounds seems definite is the kidney. The mental confusion which led to admission could very well be due to the thrombotic occlusion of cerebral small vasculature or a metabolic complication of uremia. Alternatively, it could also be a manifestation of cerebral edema resulting from the action of numerous cytokines involved in the pathogenesis of systemic inflammatory response syndrome (SIRS) (1). An imaging study of the brain might have been helpful in resolving this etiologic conundrum. A past history of psychosis is noteworthy as several cases have been recorded in the literature in which the thrombotic manifestations of APS have been preceded by symptoms of psychosis for several

years. Similar considerations also apply to gastrointestinal symptoms of nausea and vomiting. The fulfillment of second criteria for the diagnosis of CAPS is also not well documented. Although, the histopathological evidence of small vessel occlusion in the kidney is incontrovertible, a closer look at Fig. 2A discloses fibrinoid necrosis of the vessel wall, rather than the thrombotic occlusion. At least, the morphological evidence is less robust than “significant evidence of thrombosis as required by the preliminary criteria for the diagnosis of CAPS (1). Some sort of fibrin stain (eg. MSB) might have been very useful in confirming or refuting the thrombotic nature of the occlusion. Similarly, the fibrous intimal proliferations of the interlobular arteries and arterioles shown in figure 2B-C only remotely resemble those classically described and vividly depicted in a landmark paper on APS-nephropathy (APSN) (11). The disorder also represents primary rather than secondary disease, as the main autoimmune serology is reported negative.

It is also evident that a high index of suspicion was not exercised in this case, most probably due to an apparently *de novo* onset of the disorder. The diagnosis was only made on renal biopsy, which was actually undertaken for a suspicion of acute tubular necrosis (ATN) or tubulo-interstitial nephritis (ITN) 18 days after admission. The serology was also undertaken after the biopsy results. The anticoagulation and steroids were started late in this patient. However, the patient was lucky enough to survive the complication, which is fatal in around 50% of cases. The damage to the kidney is irreversible though. This most probably reflects acute on chronic insult to the kidney rather than resulting from the acute thrombotic complication *per se* (12-16).

One important consideration in this disorder relates to the identification of triggering factors

that are identifiable in roughly half of the reported cases (1). Identification of this is important for the proper management of the condition. For example, an identification of infection, which is the most common reported triggering factor, and its prompt treatment, can be life saving in majority of the cases. In the case under consideration, although antibiotics were used, there is no documentation of the source or type of infection, except for the history of fever.

Finally, an accurate documentation and reporting of such rare cases are necessary for determining the complete spectrum of the condition and a better understanding of the pathophysiology. Mardani et al. deserves compliments on bringing forth an important disease for discussion in the photo-nephropathology section of this journal. This will help increase awareness of the disorder among the nephrologists and pathologists, especially in developing countries. A word of caution is in order, however, when reporting such rarities. A very careful and diligent attention to all aspects of the condition is essential if such cases are to be included in the authentic international registries of these diseases.

Conflict of interest

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