Chapter 8

Ischemia in children

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Ischemia is a pathophysiological state of hypoperfusion with cellular, local and systemic consequences that can be severe and threatening to tissue and organ function and consequently to the life of the patient. Brief ischemia may result in reversible injury with preservation of cellular integrity, and may even be protective against the harmful effects of subsequent and more prolonged ischemia. If the underlying abnormality has been corrected and perfusion restored after prolonged ischemia, reperfusion injury may occur. Reperfusion injury is caused by an imbalance between increased production of reactive oxygen and nitrogen species and decreased availability of such free-radical scavengers as nitric oxide. This results in a cascade of effects characteristic of an acute inflammatory reaction and most profoundly affecting the endothelial cells lining microscopic blood vessels. The intensity of this inflammatory reaction may extend to involvement of remote tissues and organs, leading to multiple organ dysfunction with a high degree of morbidity and mortality. When uncorrected, prolonged ischemia leads to irreversible injury: necrosis or cell death.

The final common pathway of disorganized and contiguous cell death after prolonged ischemia is indistinguishable from that evoked by other nonphysiological disturbances such as metabolic poisoning, hypoxia, trauma, lytic viruses, hypothermia and complement attack. This stands in opposition to the highly organized and tightly regulated process of programmed cell death, or apoptosis. Interestingly, damage to the cell related to ischemia or ischemia-reperfusion injury may *induce* cell death from apoptosis. The imaging findings and related approaches to imaging management of ischemia and its consequences in the broader sense of unregulated cell death from nonphysiological disturbances will be the primary focus of this chapter.

Clinicians seldom consider consulting radiologists to diagnose and treat ischemia *per se*. The imaging findings related to ischemia are often subtle and nonspecific, related to hypoperfusion, visualized as absence of contrast where it might be expected, and to increased extravascular and extracellular edema, visualized as free fluid where it might not be expected. These findings are often interpreted in the more familiar context of organ-based pathologies such as stroke, necrotizing enterocolitis, coronary artery disease, avascular necrosis, frostbite, etc. In turn, radiologists should anticipate the prior probability of these subtle findings in the face of relevant history, and similarly should seek a relevant history in the face of these subtle findings!

Sickle cell disease: a prototype for pediatric ischemia

While there are many potential examples of medical conditions that predispose to ischemia, a few serve well to illustrate the principles. For example, the child with sickle cell anemia accompanied by factors that potentiate decreased end-organ oxygen tension (e.g., dehydration) may develop microvascular occlusions due to sickled erythrocytes that manifests most characteristically as recurrent painful vaso-occlusive crises which present variously as stroke, acute chest syndrome, splenic infarction, aseptic necrosis of bone, low-flow priapism, and leg ulcers. The sickle cell acts as a procoagulant with exposed phosphatidylserine, and as an irritant that provokes an inflammatory response and impairs perfusion. Secondary effects of sickling may relate to increased degradation of erythrocytes as well as local and distant effects of hypoxia, inflammatory mediators, and activated cells that result in reperfusion injury and organ dysfunction manifesting as stroke, pulmonary embolic disease, acute splenic sequestration crisis, renal failure, cholelithiasis and pain.

Because the combined effects of the decreased immunocompetence and local tissue ischemia or necrosis that commonly accompany sickle cell disease predispose both to localized infection and to overwhelming sepsis, abnormal imaging findings in children with sickle cell disease must be interpreted with a high degree of suspicion for both ischemic changes and infection (Figure 8.1). So-called "acute chest syndrome" is emblematic of this concept, as a new pulmonary infiltrate on the chest radiograph of a child with sickle cell disease, usually accompanied (or preceded) by pain in the chest or extremities, fever, respiratory distress and decreased oxygen saturation, may develop because of infection, infarction or both (Figure 8.2).

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