Patent Foramen Ovale: When the Innocent Bystander Becomes a Medical Threat

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The flap of the oval fossa has a central role in the fetus, since it is responsible for the diversion of oxygenated umbilical venous blood from the right to the left atrium and from there through the aorta to the rapidly developing brain. After birth, a concomitant increase in the left and decrease in the right atrial pressures bring the two parts of the flap together, disabling further passage of blood. In most people, the two layers of the flap fuse completely, so that even unusual hemodynamic circumstances do not enable the reopening of the passage and right-to-left shunting.

Even in people who may have a minimal patency, so-called probe patency (occurring in as many as one-quarter of the adult population according to autopsy series), there is no clinical risk of any sort. However, there is a much smaller and not well-defined subgroup of people with a potentially larger inter-atrial communication, who are at risk of adverse clinical events should the hemodynamic circumstances lead to reopening of the communication. Many of them can be recognized by a floppy inter-atrial septal aneurysm comprising the septum primum part of the flap.

Several diseases and pathologic conditions have been attributed to the patent foramen ovale in patients with a proven potential for at least transient significant right-to-left shunting: cryptogenic stroke or visceral/limb ischemia from paradoxical embolism, migraine with aura, decompression sickness of the divers, platypnea ortho-deoxya syndrome, and other rare causes of cyanosis, e.g., post-pneumonectomy. Except for migraine, these conditions are rare [1].

The discrepancy between the relatively high prevalence of a patent foramen ovale in the population and the rarity of the associated clinical conditions has evoked many a scholarly debate as to whether this association is well established. The embolic events are extremely difficult to document because the passage of thrombus occurs very quickly, and only as a rare coincidence may this moment be captured by echocardiography. (Occasionally in patients with a disseminated malignancy, the thrombus may be sizable and gets caught in the foramen ovale for a prolonged period.) In most cases, the diagnosis is made by exclusion of other causes of stroke or embolism.

Clinically important cyanosis with significant arterial oxygen desaturation due to right-to-left shunt through a patent foramen ovale is rare, but when it occurs, it is relatively easily demonstrated by the injection of echo contrast (bubbles). It may be the result of chronic disease that causes a constant elevation of right atrial pressure, e.g., pulmonary hypertension or congenital heart disease with right ventricular diastolic dysfunction, or a result of a transient increase in right atrial pressure as in acute pulmonary embolism or myocardial infarction with right ventricular involvement [2-4]. It is enough for the right atrial pressure to be slightly higher than left atrial pressure to cause significant right-to-left shunt. In the catheterization laboratory we have seen marked arterial desaturation despite a small mean inter-atrial pressure difference of 2 mmHg. In such cases, it is enough to mildly increase left heart filling pressure by increasing the peripheral vascular tone with neosynephrine to eliminate the shunt.

For permanent elimination of the shunt, device closure of the foramen ovale is required, but such a procedure requires careful judgment, because in cases with very high right atrial pressure the right-to-left shunting decompresses the right atrium, and closing it leads to further increase of right atrial pressure and worsening right heart failure.

In extreme cases of right atrial hypertension, as in end-stage primary pulmonary hypertension, it is even recommended that an inter-atrial communication be created by atrial septostomy in order to reduce right heart filling pressure and increase left ventricular preload, at the cost of controlled clinical cyanosis [5]. It is well known to people who perform this procedure that resting oxygen saturation should not be reduced by more than 10% from baseline. If too large a communication is created, the deep cyanosis that ensues is often fatal.

In their case report in this issue of IMAJ, Buber et al. [6] describe a patient with acute myocardial infarction involving mainly the right ventricle, who had a very significant and sudden decrease of arterial saturation due to right-to-left shunting through a patent foramen.
ovale, which proved to be the cause of medically uncontrollable deterioration and death. In such cases, pharmacologic treatment, particularly systemic vasconstrictors, should be tried first, but if not helpful, prompt catheterization and device closure of the patent foramen ovale may be the only life-saving solution [7,8].

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References

The AIM2 inflammasome is essential for host defense against cytosolic bacteria and DNA viruses

Inflammasomes regulate the activity of caspase-1 and the maturation of interleukin 1β (IL-1β) and IL-18. AIM2 has been shown to bind DNA and engage the caspase-1-activating adaptor protein ASC to form a caspase-1-activating inflammasome. Using Aim2-deficient mice, Rathinam et al. identified a central role for AIM2 in regulating caspase-1-dependent maturation of IL-1β and IL-18, as well as pyroptosis, in response to synthetic double-stranded DNA. AIM2 was essential for inflammasome activation in response to Francisella tularensis, vaccinia virus and mouse cytomegalovirus, and had a partial role in the sensing of Listeria monocytogenes. Moreover, production of IL-18 and natural killer cell-dependent production of interferon-gamma, events critical in the early control of virus replication, were dependent on AIM2 during mouse cytomegalovirus infection in vivo. Collectively, these observations demonstrate the importance of AIM2 in the sensing of both bacterial and viral pathogens and in triggering innate immunity. Nature Immunol 2010; 11: 395

Eitan Israeli

Natural killer T cells and infection with Borrelia burgdorferi

Natural killer T cells (NKTs) express a limited T cell receptor repertoire and recognize lipid (rather than protein) antigens presented by the non-classical major histocompatibility complex CD1d. Although NKTs have been implicated in antimicrobial, inflammatory and autoimmune responses, their dynamics during an immune response and the antigen-presenting cell (APC) populations that mediate their activation are not well defined. Lee et al. (Nat Immunol 2010; 295; 303) have visualized the response of NKTs in the liver to infection with Borrelia burgdorferi (the causal agent of Lyme’s disease), whereas Barral et al. followed NKTs in lymph nodes in response to particulate lipid antigens. In mice infected with Borrelia, they proliferated rapidly and produced cytokines; in response to antigen, NKTs slowed down and formed long-lasting contacts with their relevant APCs, which in both cases were macrophages. In the liver, sinusoid-localized Kupffer cells activated NKTs, whereas lymph node NKTs were activated by a subset of macrophages located in the subcapsular sinus.

Eitan Israeli

“An age is called Dark not because the light fails to shine, but because people refuse to see it”

James Michener (1907-1997), American author of more than 40 novels, mostly sweeping sagas covering the lives of many generations in a particular geographic locale and incorporating historical facts into the story. Michener was known for the meticulous research behind his work. His major books include Tales of the South Pacific (for which he won the Pulitzer Prize for Fiction in 1948), Hawaii, The Drifters, Centennial, The Source, The Fires of Spring, Chesapeake, Caribbean, Caravans, Alaska, Texas, and Poland