



PIC QUESTION OF THE WEEK: 10/19/09

Q: What are the treatment options for hereditary angioedema?

A: Angioedema (formerly known as angioneurotic edema) is defined as a well-demarcated localized edema affecting the deeper layers of skin as well as subcutaneous tissue. Urticaria is a similar process; however, it involves only superficial layers of skin. Swelling may occur in many sites including the abdominal organs, tongue, face, eyes, larynx, etc. There are a number of etiologies of angioedema including reactions to allergens such as insect stings, some foods, and drugs. ACE inhibitors can induce angioedema in approximately 0.1-1% of patients. In this case, the reaction is not immunologically mediated. Occasionally, the exact cause cannot be determined resulting in a diagnosis of *idiopathic* angioedema. *Hereditary* angioedema (HAE) is a rare disorder that can affect all age groups. It is associated with deficiency of a protein known as C₁ esterase inhibitor (C₁ INH), a critical factor in regulation of the complement system. Absence of C₁ INH results in accumulation of C₁ and activation of other important proteins (e.g. C₂ – C₅) incorporated in the classic *complement* pathway. The complement system is extremely complex and comprised of approximately twenty serum proteins and various regulatory enzymes. It plays a key role in not only lysis of antibody-coated cells, but also in phagocytosis and reactions such as anaphylaxis and hemolysis. HAE is characterized by swelling of the skin, abdominal pain, and potentially life-threatening upper airway obstruction. Swelling is caused by excessive accumulation of bradykinin. This reduces vascular integrity and permits transfer of fluid to the extravascular space. Danazol, a synthetic steroid derived from ethinyl testosterone, is the only oral compound labeled for the chronic management of HAE. Although the exact mechanism is unknown, danazol increases circulating levels of C₁ INH and reduces the frequency and severity of attacks of angioedema. Cinryze® (human C₁ INH) was approved in 2008 and is labeled as an intravenous injection for the *prophylaxis* of episodes of HAE. It is only available through specialty pharmacies. The drug has been effective in reducing the number, severity, and duration of attacks of HAE. The FDA has recently approved another human C₁ INH (Berinert®) for the *treatment* of acute abdominal attacks and facial swelling associated with HAE. Distribution details for this product are not yet available. Although rare, HAE has a significantly negative impact on the patient's quality of life. Hopefully, these newer agents will prove beneficial in the management of this unusual disorder.

References:

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