An overview in acquired hemophilia A

Impact Paragraph

Acquired hemophilia is a rare autoimmune disease whose incidence is inexorably destined to increase over the years.

The average age of the population has grown from around 50 years in the 1950s to 74 years today and is still growing. This leads to an increase of an elderly population often affected by numerous comorbidities, including those form the cardiovascular tract, such as atrial fibrillation and heart failure, pulmonary system, such as chronic bronchitis and asthma, autoimmune disorders such as rheumatoid arthritis, or oncological diseases, all requiring pharmacological care and treatments. Underlying diseases and drugs account for 50% of non-idiopathic AHA cases, while age over 65 years appears to be another risk factor for developing this bleeding disorder.

These patients who present to the hospital with extensive hematomas and anemia are subjects without a family or personal bleeding history, therefore the diagnosis of AHA becomes difficult and may be delayed for many days, causing a similar delay in starting the necessary treatments. Other reasons for such delay are comorbidities and/or the use of antithrombotic medication. Unlike what happens in the case of congenital hemorrhagic diseases, where well-identified patients are immediately referred to specific treatment centers for acute and prophylactic therapies, in case of acquired hemophilia, patients after a first visit to an emergency room, are hospitalized in general internal medicine departments where clinicians are not always able to recognize this autoimmune hemorrhagic disorder

in time. Given the potentially life-threatening consequences of delayed diagnosis and treatment, the impact of timely management has substantial impact. The guidelines therefore recommend prompt intervention to stop bleeding and eradicate inhibitor.

It is therefore necessary to train these specialists who can be the first to meet subjects affected by AHA to immediately understand the signs and symptoms of the disease and to immediately request those laboratory tests that can help to correctly frame the patient.

In the case of AHA, the severity of the bleeding does not always correlate with the level of FVIII present in the circulation and with the inhibitor titer, so it is necessary to subject the patient to periodic checks over a long period of time.

Patients with AHA should be monitored after discharge to prevent relapse, but these follow-ups should preferably be performed at hemophilia centers where the laboratory is able to evaluate both plasma coagulation FVIII and inhibitor titers, while doctors are able to promptly intervene in case of need.

Today there are several first-line drugs for the treatment of AHA such as rFVIIa, aPCC and rpFVIII, but often these are only available in large hospitals where there is a congenital hemophilia treatment center, while in smaller peripheral hospitals these expensive products are not always available, or if they are, it occurs with a certain delay, after a specific purchase request.

Given these difficulties and given the costs associated with treatment, clinicians must nevertheless be informed

that the use of plasma-derived concentrates can also be effective in stopping acute. They must know which are the most suitable drugs for this type of therapy and the method of administration. The cost of treatment with different anti-hemostatic drugs to solve the acute AHA bleeding in Italy is reported in table 1. The example is based on a man/woman, weight 70 kg, needing a treatment for seven days. Mean IU or mg were derived from published studies and registries.

	Cost (€)/IU (or mg)	IU (or mg)/Kg/week	Treatment Cost (€)
rpFVIII (Obizur®)	3.882	56,000	217,392
rFVIIa (NovoSeven®)	971.2	353	342,833
aPCC (Feiba®)	1.224	73,500	89,964
*pdFVIII or pdFVIII/vWF	0.771	60,000	46,260

* Continuous infusion

In the future, especially for the prophylactic treatment necessary to prevent dangerous relapses, estimated at around 20% of cases after the first acute episode, there may be more often a place for emicizumab, which is a bispecific monoclonal antibody that has been quite

successfully applied in congenital hemophilia. However, it is not an easy-to-manage drug; its interference with some laboratory tests, the need for a loading dose to achieve full efficacy, the associated thromboembolic risk, especially when plasma FVIII levels tend to rise, suggest the use of this drug should be confined to experts in the treatment of congenital hemophilia, who can best oversee the advantages and disadvantages of emicizumab.

Information and training are therefore the basis of the treatment of acquired hemophilia, necessary so that this disease is increasingly easily recognized and correctly managed, which may reduce related mortality to zero.