Molecular genetic analysis of patients with rare bleeding disorders in South Iran

Looking Back — Looking Forward

In Iran, a country where the high rate of consanguinity makes RICDs 3 to 5 times more frequent than in Western countries (Peyvandi F, Mannucci PM et.al. Haemophilia, 2002), a registry of bleeding disorders has been kept since the early 1970s. Starting in 1996, we established a collaboration based upon visits, workshops, and exchange of technology and samples with Professor Mannucci and Professor Peyvandi. Working together has been developed in collaboration with the haemophilia treatment centers of the 2 main Iranian cities (Teheran in the North and Shiraz in the South) under World federation of Haemophilia (WFH) as a twinning program in the last few years.

Twinning has improved diagnosis and clinical care through coaching, training, and transfer of expertise, ultimately leading to improved quality of life for patients. Examples of our activities included consultation on the management of specific cases, clinical and laboratory training, donation of equipment and publication of research projects, working together on special projects such as creating a computerized rare bleeder patient registry in Milan, molecular diagnosis of inherited platelet disorder and hemophilia, organizing training workshops and conferences in Shiraz Medical University as host of other universities in Iran.

It should be mentioned that the twinning program can benefit centers in developed countries by giving them the opportunity to gain exposure to clinical problems no longer encountered in their own countries, as well as the experience of a different culture. Twinning can help to boost the profile of a treatment facility in an emerging country. Being twinned with a treatment centre can lend prestige and importance, as well as international recognition to an institution. This can be valuable in raising awareness of the center among Government officials and the media. All of the above has happened in our center and now our laboratory is a referral coagulation laboratory in the south of the Country with more than 600 patients registered. Urban patients and those living in rural areas are periodically summoned for clinical and laboratory evaluation. Training courses for staff and technicians from other universities are in progress. A program for genotyping is underway in Milan and in the near future in our center, with the goal to offer prenatal diagnosis to families that had already witnessed the birth of severely affected children.

RICDs and congenital platelet defects tend to be much less clinically severe than hemophilia, which can make it difficult for physicians and patients to recognize symptoms and diagnose the condition. Therefore, they have often been misdiagnosed and neglected. BSS patients have been diagnosed as Idiopathic thrombocytopenic purpura (ITP), and splenectomy has been wrongly performed without a sustained clinical benefit.

Advances through our experiments are being made in the study of the better known inherited platelet disorders such as GT and BSS, and our knowledge of them should accelerate as national centers become interested in such rare diseases, and as national networks are established.

Since the most common bleeding disorder is VWD, and since the majority of women with VWD experience menorrhagia from the onset of symptoms until diagnosis, a great amount of time can pass and more than half of the women had to be tested many times before obtaining a diagnosis. A large proportion of them underwent surgical procedures, including hysterectomy, to alleviate the discomfort and effects of menorrhagia. With appropriate diagnosis and patient management, many unnecessary and potentially harmful surgeries could have been avoided. Furthermore, unanticipated and excessive bleeding during childbirth and at surgery can be avoided with prophylactic treatment. A protocol needs to be established in order to address the problems associated with the diagnosis, treatment and health management of women with bleeding disorders.

Collaborative research projects with the goals of improving standardization of diagnostic techniques, including multimer analysis and molecular diagnosis, are in progress.

With the implementation in our center in the near future of the automated calibrated thrombin generation assay developed in the laboratory of Hemker and Béguin in Maastricht, [11-13] we will be able to diagnose and estimate bleeding risk more precisely, monitor treatment of bleeding disorders, and study thrombotic events.

Still for the undiagnosed patients asking whether these services provide information that is useful for disease avoidance, the prudent answer is: "Not now.... ask me again in the future".