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Editorial

Herpes simplex virus type-specific serology tests

Herpes Simplex Virus type 1 (HSV-1) and 2 (HSV-2) infections occur worldwide and the disease ranges from subclinical infection, to mucocutaneous vesicular lesions, to severe illnesses such as neonatal herpes and herpes encephalitis. These manifestations may be associated with primary infection or reactivation of latent virus. Laboratory confirmation of the diagnosis could yield prognostic information and guide specific antiviral therapy. Commonly used laboratory investigations include direct detection of viral components such as polymerase chain reaction (PCR) for HSV in the cerebrospinal fluid in cases of encephalitis, and viral culture of vesicular fluids in mucocutaneous disease such as genital herpes. These tests are sensitive, specific and yield reliable information on the HSV type. The PCR test provides results in one day, while viral culture for HSV could give a positive result in as early as two days.

Apart from the above tests for the virus or its components, another testing strategy is the detection of antibodies to the HSV types using type-specific serology tests. These tests are mainly performed in reference laboratories for epidemiological studies. Their applicability in the diagnostic laboratory is still limited, for a number of reasons. In most cases, the antibody of interest is that against HSV-2, since this is the major cause of genital herpes, sexual transmission, and neonatal infection. Nevertheless, HSV-1 is also known to result in the same spectrum of infections, so that a negative result for HSV-2 antibody could not rule out the development of genital and neonatal diseases.

Furthermore, HSV-1 and HSV-2 are antigenically closely related, and conventional antibody tests using crude viral lysates as antigens could not reliably differentiate antibodies of the two types. Type-specific HSV serology tests mainly employ two formats: Western blot to detect antibodies against proteins separated by electrophoresis, and enzyme immunoassays using the type-specific protein, glycoprotein G (gG), as antigens. These tests are not widely available and are expensive. More importantly, strict quality control of the reagents is essential to ensure the antibody test is type-specific.

With the currently available HSV type-specific tests, an important issue for consideration is the interpretation of the result for management purpose. In a primary infection, a person has not had any prior HSV infection, and antibodies to one type of HSV would become detectable by up to six weeks' time, while no antibody to the other HSV type would be present. In a non-primary first episode infection, a person had past infection with one HSV type and is currently infected with the other HSV type, such that antibodies against the previously acquired HSV type will be present in the acute serum, while the convalescent serum will contain antibodies to both HSV types. Finally, in a recurrent infection, no seroconversion to either HSV types could be detected. Apart from laboratory confirmation of a clinical illness, type-specific

HSV antibody testing could serve as a screening test for past infection, and thus latency, with an HSV type.

A number of scenarios have been proposed for utilisation of the test. Firstly, in the diagnosis of acute genital herpes simplex infection, when the patient presented late after crusting of the lesions, it has been proposed for using serology testing to document infection by seroconversion. Nevertheless, since over 60% of all HSV infections are asymptomatic, it is likely that the patient would be HSV-2 antibody positive for both acute and convalescent specimens. In such cases, only previous infection could be documented and the nature of the current infection could not be ascertained. Secondly, HSV-2 antibody "screening" tests are occasionally requested for the asymptomatic partner of a patient with documented HSV-2 infection. Since HSV infections are often asymptomatic, the partner may well have already been infected. Before the test is requested, it is recommended to formulate the counselling strategy in case the partner tested negative for HSV-2 antibody. Thirdly, an often debated problem is the offering of HSV-2 antibody screening routinely to pregnant women. Arguments for screening are mainly focused on identifying women serologically at risk for acquiring genital herpes, and providing counselling on strategies to prevent primary or non-primary first episode infections near term. In addition, women who tested positive for HSV-2 antibodies early in pregnancy would not require routine Caesarean section even when genital herpes is clinically diagnosed during parturition, since a recurrent infection is associated with minimal risk of neonatal herpes. On the other hand, the opposition considers that even with screening, there is no reliable means for prevention of acquisition of HSV near term and of transmission to the neonate. Current strategies rely on behavioural counselling on protected sex. There is at present no standard recommendation on the use of prophylactic acyclovir. Another important consideration is the limited availability of reliable tests for type-specific HSV antibody determination on a screening basis. The psychological and sociological impact of even one potentially incorrect result must be critically addressed.

In Hong Kong, HSV type-specific serology tests are not generally available. These tests are expensive and could be technically complex, such as the Western blot. Commercial test kits claiming to yield type-specific results should be regarded with caution, since cross-reaction between HSV-1 and HSV-2 is frequent. Even with the availability of a type-specific test, the options for management are ill-defined, mostly based on counselling and behavioural modification. Until the advent of an inexpensive and reliable test, and better-defined preventive and management strategies, the cost-effectiveness of HSV type-specific serology tests would be limited.

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