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Title Biology of haemostasis disorders: Lupus anticoagulant detection

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Aim

The National Salaried Workers' Health Insurance Fund (CNAMTS) asked HAS to assess the value of the different laboratory tests for haemostasis abnormalities with a view to updating the section in the Nomenclature of Procedures in Laboratory Medicine (NABM) containing the procedures in laboratory medicine for measuring abnormalities of haemostasis (subsection 5-02). One of those procedures is detection of the lupus anticoagulant.

Venous thromboembolism (VTE), the two main forms of which are deep-vein thrombosis (DVT) and pulmonary embolism (PE), is a complex disorder resulting from the interaction of numerous genetic and environmental risk factors which constitute an individual's predisposition to thrombotic events. In France, the annual incidence of VTE is said to be 120 per 100,000, that of PE between 60 and 111 per 100,000. VTE is responsible for a mortality rate of 7.2 per 100,000. In pregnant women, the prevalence of VTE is 1 case per 1000 to 2000 pregnancies. Numerous studies have shown that there is a connection between VTE and biological risk factors (BRF), including antiphospholipid syndrome (APLS) which is one of the acquired causes of thrombophilia and thus of VTE.

Conclusions and results

APLS is defined by the combination of:

- one clinical criterion: vascular thrombosis or obstetric disease;
- and one laboratory criterion showing the presence of heterogeneous antiphospholipid antibodies: anticardiolipin (aCL), anti-β2 glycoprotein 1 antibody (anti-β2GP 1) or lupus anticoagulant (LA).

According to the various documents analysed, lupus anticoagulant is detected in several phases: screening, demonstration of an inhibitory effect, and confirmation. It requires the performance of two coagulation tests (at the screening phase) based on different principles:

- the recommended tests are, firstly, dilute Russell's viper venom time (dRVVT) and, secondly, activated partial thromboplastin time (aPTT) using silica in the presence of low concentrations of phospholipids;
- the indications for the detection of lupus anticoagulant are generally vascular thrombosis (venous or arterial thromboembolic accident in elderly patients, provoked venous thromboembolic accident in a young patient, unprovoked venous thromboembolic accident or unexplained arterial thromboembolic accident in young patients under 50 years of age, thromboses at unusual sites, thrombosis in patients with an autoimmune disorder, first episode of unprovoked VTE occurring before age 60 years, VTE, whether or not provoked, in women of child-bearing age, any recurrence of proximal DVT and/or provoked or unprovoked PE, the first episode of which occurred before age 60 years, any recurrence of unprovoked distal DVT, episode of DVT or PE with no obvious cause, recurrence of DVT or PE, cerebral vascular accident or peripheral arterial thrombosis in the absence of any risk factors, recurring arterial thromboses despite preventive anticoagulant treatment, systemic lupus erythematosus) and/or obstetric disorders (multiple spontaneous abortions, late intrauterine death in patients with an autoimmune disease, early or severe preeclampsia or severe placental insufficiency, unexplained intrauterine death, severe unexplained intrauterine growth retardation in women with a history of VTE and in asymptomatic pregnant women with a family history of VTE or hereditary thrombophilia);

- it is recommended that a positive test should be repeated at least 12 weeks after the initial test to check whether lupus anticoagulant is still present;

- the result must always include a complete laboratory assessment of the APLS profile with a check for anticardiolipin and anti-β2 glycoprotein 1 antibodies (NABM code 1460);

- the reports on the results must be easy to interpret. It is important for these tests to be carried out at experienced laboratories and repeated in the same laboratory.

Recommendations

On the basis of the literature identified and analysed, detection of lupus anticoagulant is necessary as part of the diagnostic investigation of APLS which is a serious disease, and can be used to adjust patients' treatment. The lupus anticoagulant can be detected in three stages: screening, demonstration of an inhibitory effect (mixing stage) and confirmation (LA neutralisation stage). It requires the performance of two coagulation tests (at the screening phase) based on different principles: the dilute Russell's viper venom time and the activated partial thromboplastin time using silica. These tests must be supplemented by a check for anticardiolipin and anti-β2GP 1 antibodies.

Methods

This assessment is based on a critical analysis of the literature carried out by the Haute Autorité de Santé, and reviewed by experts in haemostasis. It takes into account the arguments of a group of experts assembled by CNAMTS on which CNAMTS based its request. The assessment of this procedure is based on a critical analysis of the literature consisting of six documents comprising four guidelines, one HAS technological assessment report of 2006 and a position paper, plus the review by three experts in haemostasis.

Written by

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