Postmortem diagnosis of Factor V Leiden from paraffin wax embedded tissue

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Abstract

Activated protein C resistance resulting from Factor V Leiden is an important inherited thrombophilia disorder which is found in 3.5% of people in the UK. The genetic defect can be detected using the PCR and the diagnosis can be made post-mortem from paraffin wax embedded tissue. The presence of Factor V Leiden should be sought in all cases of unexplained sudden death resulting from venous thromboembolism.

Keywords: Factor V Leiden, thromboembolism, thrombophilia disorder.

Activated protein C resistance has been recognised recently as an important risk factor predisposing to venous thromboembolism. The disorder results from a specific missense mutation (G1691A) in exon 10 of the coagulation factor V gene, which is located in the sequence encoding the activated protein C cleavage site. Recent studies have shown that the mutant factor Va (Factor V Leiden) is 10 times less susceptible to deactivation by this natural anticoagulant. Factor V Leiden can be detected by means of the PCR as the nucleotide has been obtained matched those dextrase site for the restriction enzyme, MnlI. 2 Recently, we have demonstrated the importance of diagnosing this disorder retrospectively from postmortem paraffin wax embedded tissue.

Case report

A 24 year old man sustained a soft tissue laceration to the right leg following a road traffic accident. The wound was debrided and sutured and the patient was prescribed diclofenac sodium (Voltarol) as analgesia. One week later, he presented with lower abdominal pain and appendicitis was diagnosed provision-
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Figure 1 Detection of Factor V Leiden by PCR: amplified 147 bp fragment digested with MnlI for a normal subject (N), patient P who is heterozygous for the mutation and a homozygous control (C). M = molecular size marker (pBR322 digested with HaeIII).

Discussion

Heterozygous Factor V Leiden is found in 3.5% of the population of the UK. It can be identified in about 20% of subjects with de novo venous thrombosis and accounts for about 40% of familial thrombophilia. The genetic defect is an important cofactor for thromboembolism associated with use of oral contraceptives and pregnancy. Homozygous subjects and those patients who co-inherit a second thrombophilia disorder are probably at significantly higher risk.

Postmortem detection of Factor V Leiden from fresh or paraffin wax embedded tissue should be considered in all cases of unexplained sudden death where venous thromboembolism is suspected. Any tissue containing nucleated cells can be used as a source of DNA—e.g., for example, liver or lung tissue obtained by a “true-cut” biopsy. Retrospective diagnosis enables family studies and genetic counselling to be performed. The technique may also allow important studies to be undertaken on archival material—for example, to determine the significance of Factor V Leiden as a risk factor for maternal death resulting from thromboembolism in pregnancy.