SydPath
ST VINCENT'S PATHOLOGY

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INSULIN ANTIBODIES INFORMATION SHEET

INTRODUCTION

Antibodies directed against insulin may be found in a number of clinical circumstances: at the time of onset of type 1 diabetes mellitus, in the autoimmune insulin syndrome, and secondary to treatment with exogenous insulin. As with other auto-antibodies, insulin antibodies are not specific and may be found in patients with other autoimmune diseases which reduces their potential value as a diagnostic test.

INSULIN ANTIBODIES AS A MARKER FOR TYPE 1 DIABETES MELLITUS

Patients with new onset type 1 diabetes mellitus (DM) may have insulin antibodies detected in their blood stream along with islet cell antibodies and GAD antibodies. These immunoglobulins have also been measured in relatives of patients with type 1 DM patients with their presence indicating an increased risk of developing DM. Insulin antibodies are less sensitive than GAD antibodies for confirmation of type 1 DM and it has been recommended that all three antibodies be measured when performing research studies for prediction in relatives.

AUTOIMMUNE INSULIN SYNDROME

This syndrome classically presents with hypoglycaemia several hours after a meal. Auto-antibodies against endogenous insulin bind the hormone which is released later after the meal. The best described clinical situation is the use of methimazole in the treatment of Graves disease in Japanese women. Other sulphydryl-containing drugs such as carbimazole, penicillamine, thioprine, and glutathione have also been implicated, possibly by rendering insulin more antigenic by linkage to an insulin sulphydryl group. The syndrome has also been described after treatment with drugs without cysteine groups such as hydrallazine and procainamide. The pathological findings in the islet are of hyperplasia without evidence of inflammation indicating that the condition is distinct from type 1 DM. This condition is very rare in the Australian population.

ANTIBODIES TO EXOGENOUS INSULIN

The development of low levels of antibodies to exogenous insulin is an expected consequence of insulin treatment in diabetes mellitus. In some cases they may lead to higher post-prandial glucose levels and increased risk of delayed hypoglycaemia. Very rarely this condition may cause extreme insulin resistance leading to very high daily insulin requirements. Immune mediated lipodystrophy at the injection site may also occur. This incidence of this phenomenon has markedly decreased due to the use of human insulin of high purity. Treatment may include concentrated insulin, plasmapheresis or short-duration high-dose corticosteroids. The insulin analogue Lispro has been used in cases of insulin antibodies against exogenous human insulin (Lahtela, 1997).

ASSAY

The assay for insulin antibodies used at SydPath detects the binding of radio-labelled human insulin (^{125}I-insulin) to immunoglobulin in the patient's serum. In the assay a trace amount of labelled insulin is incubated with dilutions of serum followed by separation of immunoglobulin-bound and free insulin using polyethyleneglycol. The binding of insulin is a product of the avidity and concentration of the antibodies in the patient's serum. Non-specific binding is detected by additionally running the samples with a high concentration of added unlabelled human insulin which blocks only specific binding with the antiserum.

If no binding is detected the test is reported as negative. If a positive result is obtained, the result is reported as the highest dilution that still yields significant binding. Most positive samples only yield significant binding for the undiluted serum.

Note that insulin may interfere with the measurement of insulin antibodies, and that insulin antibodies may interfere with the accurate measurement of serum insulin.

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