AMPATHLAB UPDATE

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N-Terminal Procollagen-III Peptide (P3NP)

Biochemistry

Type III collagen is an important component of connective tissue. N-terminal procollagen-III peptide (P3NP) is a cleavage product of the precursor of Type III collagen and is formed in equimolar proportions to Type III collagen. Serum levels of P3NP can therefore be used as a measure of Type III collagen and reflects the rate of extracellular matrix synthesis or breakdown.

Clinical significance

P3NP is a direct biomarker for the diagnostic and prognostic assessment of hepatic fibrosis.

Active proliferation of connective tissue in the liver is reflected by raised serum P3NP levels, e.g. fibrosis, cirrhosis, chronic active hepatitis, acute hepatitis, alcoholic liver disease, primary biliary cirrhosis.

P3NP is the most widely validated direct biomarker to diagnose and monitor methotrexate-induced hepatic fibrosis. Methotrexate (MTX) is a recognised hepatotoxin that occupies a key place in the management of many autoimmune and inflammatory skin diseases. Long-term use in psoriasis is associated with a 22% increased risk of hepatic fibrosis. The prevalence of psoriasis is 1–3% in Western Caucasian populations and 0.65% in a black KwaZulu-Natal cohort.

P3NP in hepatic fibrosis

Although liver biopsy is the gold standard for assessing hepatic fibrosis, biochemical markers and radiological techniques are increasingly being favoured for their safety, accuracy and cost-efficiency.

Serum P3NP measurement shows superior performance for the detection and monitoring of hepatic fibrosis, particularly in MTX-induced hepatic fibrosis (sensitivity 77.3%, specificity 91.5%). Consistently normal P3NP levels correlate with a minimal risk for the development of substantial hepatic fibrosis, and serial measurements reduce the need for liver biopsy.

Standard liver function tests (LFTs) in isolation demonstrate a low diagnostic accuracy to detect hepatic fibrosis and would miss many cases (sensitivity 38%, specificity 83%). The Fibrotest patented panel (a2-macroglobulin, apolipoprotein A1, haptoglobin, gamma glutamyl transferase and total bilirubin) is well investigated and correlates best with liver biopsy staging. A 2011 systematic review demonstrated similar sensitivities between P3NP and the Fibrotest (P3NP sensitivity=77.3%, specificity=91.5%, Fibrotest sensitivity=83%, specificity=61%), with P3NP having the advantage of measurement of a single analyte only.

Guidelines for monitoring hepatic fibrosis in psoriasis patients

Pre-treatment and 2–3 monthly measurements are recommended.

Interpretation of results

Pre-treatment P3NP

i) > 1.00 U/mL (> 8 ug/L): do not commence MTX, obtain hepatology opinion, consider biopsy

Monitoring during MTX treatment

Consider hepatology opinion/ biopsy if P3NP is:

i) > 1.25 U/mL (> 10 ug/L) on one occasion
ii) > 1.00 U/mL (> 8 ug/L) on two consecutive occasions
iii) > 0.53 U/mL (> 4.2 ug/L) on three occasions in a 12-month period

Consider MTX withdrawal if P3NP is:

i) > 1.25 U/mL (> 10 ug/L) on three occasions in a 12-month period

Raised P3NP levels are also encountered in non-hepatic diseases, including pulmonary fibrosis, rheumatoid disorders, myocardial infarction, acromegaly and multiple trauma. P3NP may be raised as a result of active bone remodelling and is not reliable for monitoring hepatic fibrosis following orthopaedic surgery, skeletal fractures, erosive psoriatic arthritis or in growing children.

References available upon request.

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Please contact your local Ampath pathologist for more information.