Hyperlipidaemia in hyperuricaemia and gout

The finding of hyperlipidaemia in patients with hyperuricaemia and gout is common. The usual abnormality is hypertriglyceridaemia (type IV hyperlipoproteinaemia), being reported in between 25% and 60% of patients with gout. This finding has been related to reports of an increased frequency of coronary artery disease in some patients with gout and has contributed to the suggestion that the urate concentration might be an indicator of coronary risk. Now that gouty arthritis itself is so treatable, an associated disorder that might reduce the life span becomes even more important in the management of a patient with gout.

However, our understanding of the mechanism of any association between hypertriglyceridaemia and hyperuricaemia is far from complete and this becomes increasingly important when determining the factors that contribute to the development of hyperuricaemia and gout in a particular person. No longer can it be assumed that there is a common aetiology for the hyperuricaemia in patients who present with an acute urate crystal arthropathy and refer to it as “primary gout”. Similarly, it is no longer expected that each patient with gout would have inherited a “gouty diathesis”, unless you regard this concept as meaning a relatively poor renal clearance of urate in the presence of otherwise normal renal function.

Hyperuricaemia in most patients is found to have multiple causes, some genetic and others environmental, with many of the latter being able to be modified, potentially correcting the contribution of that cause to the hyperuricaemia. In such an assessment, the contribution of each factor to the hypertriglyceridaemia may also need to be considered and a series of inherited and environmental factors have been sought. Of the genetic causes, an uncommon allelic variant of the apoprotein CIII gene (the S2 allele) was found to be more common among a group of hypertriglyceridaemic patients with gout and, more recently, a higher frequency of an apo e4 allele has been found in such patients. That such a search revealed relatively so little frequency of an apo e4 allele has been found in such others environmental, with many of the latter being able to be modified, potentially correcting the contribution of that cause to the hyperuricaemia.  

In this syndrome, clustering of the various adverse cardiovascular risk factors is common, including an association with hypertension and the development of coronary artery disease. Endothelial dysfunction has also been described in insulin resistant subjects and this may be the mechanism for the associated increase in the risk of atherosclerosis. The insulin resistance syndrome may present clinically in many different ways, particularly as impaired glucose tolerance with moderate increase in the fasting blood sugar. It may also present as hypertension or as hyperlipidaemia with myocardial ischaemia.

Now that hyperuricaemia has come to be recognised as an intrinsic part of the syndrome, it is being realised that one of the clinical presentations may be as gouty arthritis. Indeed, the degree of hyperuricaemia has been proposed as a simple marker of the degree of insulin resistance. The renal clearance of urate has also been shown to have an inverse relation with both the degree of insulin resistance as well as with visceral fat area as measured by abdominal computed tomography. Thus, as we look more closely at some of
our patients presenting with gout, we are increasingly recognising the presence of other features of this syndrome. The perception of this insulin resistance syndrome really depends upon the perspective from which its presentation is viewed. When the presentation is as gout, you usually find evidence of the associated hypertriglyceridaemia or impaired glucose tolerance or hypertension only if you seek it specifically. Also, a clinical presentation as acute gout may well occur earlier than one resulting from complications from other components of the syndrome, which may be asymptomatic for years.

Many studies have examined different aspects of the relation between the manifestations of the insulin resistance syndrome, studying different types of subjects and using different study techniques.27-29 A consensus is emerging that hypertriglyceridaemia is an intrinsic component of the syndrome and that this hypertriglyceridaemia is caused by a reduction in the renal clearance of urate leading to under-excretion of urate. There has been no clear evidence that the syndrome incorporates a component of over-production of urate. The recent demonstration that exogenous insulin can reduce the renal excretion of both urate and sodium in both healthy and hypertensive subjects28-30 provides a ready mechanism to explain the association of hyperinsulinaemia with hyperuricaemia and hypertension, especially if the kidney retains its sensitivity to the effects of insulin at a time when other organs are insulin resistant. Dietary reduction of the triglyceride concentration with a low calorie diet increases renal excretion of urate in hypertriglyceridaemic hypertriglyceridaemic subjects, but the effect is reversed when the triglycerides are again increased.31

Several studies have examined the link between the hyperuricaemia and gout. Abdominal obesity, suggested by visceral fat accumulation and increased fasting urine uric acid excretion in hyperuricaemic-hypertriglyceridemic persons. Ann Intern Med 1974;80:143-9.


