CASE REPORT

Moderately increased albuminuria unmasked hypertension

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SUMMARY

The normal rate of albumin excretion is less than 30 mg/day (20 µg/min); persistent albumin excretion between 30 and 300 mg/day (20–200 µg/min) is called moderately increased albuminuria (formerly called microalbuminuria). In addition to being associated with diabetic nephropathy, moderately increased albuminuria has also been associated with cardiovascular disease in patients with as well as without diabetes. We present a case report of a man with moderately increased albuminuria who developed hypertension only detected by an ambulatory blood pressure monitoring procedure.

BACKGROUND

Persistent and progressive microalbuminuria could mask hypertension, which will only be revealed after performing an ambulatory blood pressure monitoring (ABPM). Because of the association between hypertension and microalbuminuria, patients could be considered at high cardiovascular risk and antihypertensive therapy should be started promptly.

CASE PRESENTATION

A 76-year-old man presented with borderline hypertension measured by blood pressure (BP) self-measurement at home over the past 10 months. He was not taking antihypertensive medication. He had a history of mitral valve prosthesis and bacterial endocarditis 5 years ago, and benign prostatic hypertrophy and hyperlipidaemia. He was on acenocumarol, tamsulosin 0.4 mg plus dutasteride 0.5 mg daily and fluvastatin 80 mg daily. Because of his history, two routine measurements of microalbuminuria were performed in the last year with result of 98 and 116 mg/L (normal range 0–20 mg/L). The physical examination was normal as was the result of the blood test.

INVESTIGATIONS

With the suspicion of masked hypertension, we performed an ABPM the result of which is shown in [figure 1](#): mean BP 24 h 139/67 mm Hg; activity 141/68 mm Hg and at rest 130/64 mm Hg with a non-dipper pattern.

Three months after the initial diagnosis, a new blood test showed normal biochemistry, including kidney function, liver function, lipid levels, glucose level and ions. Microalbuminuria in urine was 8 mg/L (0–20) and microalbuminuria/creatinine ratio was 13.3 mg/g (normal 0–20). A new ABPM of control ([figure 2](#)) showed: mean BP

116/63 mm Hg; activity 115/62 mm Hg and at rest 124/67 mm Hg with a riser pattern.

A third ABPM performed 9 months later ([figure 3](#)) showed: mean BP 109/54 mm Hg; activity 109/55 mm Hg and at rest 107/50 mm Hg with a dipper pattern.

DIFFERENTIAL DIAGNOSIS

Other causes of microalbuminuria as well as diabetes mellitus were ruled out.

TREATMENT

We advised the patient a change in lifestyle and started medical therapy with enalapril 20 mg/day, which was switched to valsartan 160 mg/day because of the presence of cough as an adverse effect. After a few weeks on therapy a new change to olmesartan 40 mg/day plus amlodipine 10 mg/day, in combination, was needed because his systolic BP remained high (160/81, 161/88 and 168/82 mm Hg).

Three months later, on therapy with amlodipine 10 mg plus olmesartan 40 mg taken in the morning, the patient's daytime BP was perfectly under control, he had no adverse effects, and showed good tolerance and compliance with medication.

Because of the riser pattern detected in his second ABPM, we advised him to take the antihypertensive drug at night, before going to bed, instead of in the morning.

The patient noted one episode of symptomatic hypotension during the heat of the past summer, so we decreased the dose of olmesartan to 20 mg/day leaving the dose of amlodipine taken at night unchanged, with improvement of symptoms and good control of his BP.

OUTCOME AND FOLLOW-UP

Our final diagnosis was masked isolated systolic hypertension and microalbuminuria as the target organ damage.

Our patient showed persistent and progressive microalbuminuria as part of masked isolated systolic hypertension, which was only revealed after performing an ABPM. Because of the association between hypertension and microalbuminuria, this patient was considered at high cardiovascular risk and antihypertensive therapy was started promptly with very good control.

Currently, the patient remains perfectly controlled and happy.

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Figure 1 First ambulatory blood pressure monitoring (October 2012).

DISCUSSION

Establishing the diagnosis of moderately increased albuminuria requires demonstration of a persistent elevation in albumin excretion. Transient elevations in the excretion of albumin can be seen in the following settings¹:

- ▶ Fever
- ▶ Infection
- ▶ Exercise
- ▶ Heart failure
- ▶ Non-specific joint inflammation
- ▶ Poor glycaemic control (glycated haemoglobin greater than 8%)
- ▶ Elevation in BP (greater than 160/100 mm Hg)
- ▶ Hyperlipidaemia (low-density lipoprotein (LDL) cholesterol greater than 120 mg/dL)

Although 24 h urine collection is the gold standard for the detection of moderately increased albuminuria, it has been suggested that screening can be more simply achieved by timed urine collection or an early morning specimen to minimise changes in urine volume that occur during the day.¹ The confounding effect of variations in urine volume on the urine albumin concentration can be avoided by calculation of the urine albumin-to-creatinine ratio in an untimed urine specimen. Currently, measurement of the urine albumin-to-creatinine ratio in an untimed urinary sample is the preferred screening strategy for moderately increased albuminuria.¹

Post hoc analyses in different patient populations have suggested that, in addition to its relation to renal disease, moderate increases in albuminuria over time are an important risk factor for cardiovascular disease and early cardiovascular mortality in patients with and without diabetes and/or hypertension.^{2–10}

How moderately increased albuminuria is associated with cardiovascular disease is not well understood. Moderately increased albuminuria in patients without diabetes appears to be a signal from the kidney that the vasculature, particularly the endothelium, is not functioning normally. The apparent association

between moderately increased albuminuria and cardiovascular disease is in part related to an adverse risk factor profile in patients with and without diabetes.^{7 11 12}

The association between moderately increased albuminuria and cardiovascular disease also extends to the development of moderately increased albuminuria and/or progression to severely increased albuminuria among patients at high cardiovascular risk.

Some guidelines recommend screening for moderately increased albuminuria among patients without diabetes at increased risk for chronic kidney disease and cardiovascular disease, such as those with hypertension and metabolic syndrome.¹³

As described above,⁴ there is evidence of an increase in mortality risk with moderately increased albuminuria that is independent of diabetes and hypertension. Nevertheless, some authors do not recommend screening for moderately increased albuminuria in the general population of patients without diabetes without any such risk factors, as the value of screening in these patients is unclear; the ability of any therapies to provide benefit in this setting is unknown, and it is not cost effective.¹⁴

There is increasing evidence that even stage 3 chronic kidney disease (serum creatinine ≥ 1.5 mg/dL (133 μ mol/L) or estimated glomerular filtration rate ≤ 60 mL/min) is associated with an increased risk of cardiovascular disease. As a result, chronic kidney disease is considered by many to be a coronary equivalent that should be managed according to secondary prevention goals.

Several studies have examined the effects of antihypertensive therapy on moderately increased albuminuria and clinical cardiovascular outcomes.^{15 16} Our patient was started on enalapril 20 mg/day, which was switched to valsartan 160 mg/day because of the presence of cough as an adverse effect. After a few weeks on therapy, a new change to olmesartan 40 mg/day plus amlodipine 10 mg/day, in combination, was needed because his systolic BP remained high. After reading his second ABPM we applied chronotherapy,^{17–20} switching the medication time of

Figure 2 Second ambulatory blood pressure monitoring (January 2013).

Figure 3 Third ambulatory blood pressure monitoring (October 2013).

administration from morning to night, before going to bed. Although intriguing, further study is required to determine whether therapy specifically aimed at decreasing albuminuria in patients without diabetes will improve cardiovascular outcomes.

In the absence of clear data, the current recommendations for patients without diabetes who are noted to have moderately increased albuminuria are as follows:

- ▶ Testing for moderately increased albuminuria should be repeated at least twice to make certain that it is a persistent abnormality.
- ▶ Among patients with persistent moderately increased albuminuria who are hypertensive, an ACE inhibitor or angiotensin II receptor blocker could be used because of the greater ability of these drugs to reduce albuminuria compared with other antihypertensive drugs.
- ▶ The BP goal is <140/<90 mm Hg in the absence of proteinuric renal disease or atherosclerotic cardiovascular disease.
- ▶ Aspirin therapy as well as consideration of a statin are recommended in patients who also have other risk factors for cardiovascular disease. The LDL cholesterol concentration goal is less than 100 mg/dL (2.6 mmol/L).
- ▶ Albumin excretion should be monitored at regular intervals.

Learning points

- ▶ Moderately increased albuminuria has also been associated with cardiovascular disease in patients with as well as without diabetes.
- ▶ The usual approach in patients without diabetes who are noted to have moderately increased albuminuria is:
 - Testing for moderately increased albuminuria should be repeated at least twice to make certain that it is a persistent abnormality.
 - Among patients with persistent moderately increased albuminuria who are hypertensive, an ACE inhibitor or angiotensin II receptor blocker could be used because of the greater ability of these drugs to reduce albuminuria compared with other antihypertensive drugs.
 - Albumin excretion should be monitored at regular intervals.
- ▶ As target organ damage, microalbuminuria could be an indicator of masked hypertension. Ambulatory blood pressure monitoring could be useful and necessary to reveal it.

Competing interests None.

Patient consent Obtained.

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