CASE REPORT

Sepsis-related hypertensive response: friend or foe?

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SUMMARY

In daily practice acute arterial hypertension may occur during acute sepsis. No management guidelines concerning this issue figured in the latest sepsis campaign guidelines. Arterial hypertension occurring during sepsis could be an overlooked condition despite its potential haemodynamic harmful consequences. In this paper, a clinical study of acute hypertensive response related to sepsis is detailed. It shows that arterial hypertension, renal salt wasting and glomerular hyperfiltration can occur simultaneously during sepsis. Mechanisms and management options of sepsis-related arterial hypertensive response are also discussed.

BACKGROUND

Circulatory failure during sepsis is a major problem in critical care setting and septic shock-related short-term mortality is near 50% even in recent reports.¹ Guidelines for management of circulatory failure during sepsis have been recently reactualised.² These guidelines pointed out the importance of raising arterial blood pressure to a predefined target level. Management of arterial hypertension when present was not mentioned because by definition acute sepsis is usually associated with hypotension. In addition, recent clinical investigations dealing with haemodynamic support during acute sepsis were focused on the optimal level of arterial blood pressure to be achieved when hypotension occurs.³ Again, arterial hypertension during sepsis was not mentioned. However, in daily practice the occurrence of acute arterial hypertension during the early stages of some sepsis-related conditions is a reality especially when the patients are not sedated. We found no available data concerning this issue despite its relative frequency in daily practice. This lack of interest is surprising because besides inducing end-organ failure acute arterial hypertension might also induce negative fluid balance⁴ and lower cardiac output, which would be harmful in the setting of acute sepsis where adequate blood volume and cardiac output are early goals in patients resuscitation.

CASE PRESENTATION

We had to manage a 30-year-old male patient admitted in our intensive care unit for acute pneumococcal meningitis. Our patient's medical history was marked by chronic alcoholism. The weight and height of the patient were 90 kg and 1.80 m, respectively. The patient presented with persistent arterial hypertension (190/110 mm Hg), tachycardia (pulse rate 140 bpm) associated with a fever of around 40°C and he was obnubilated. Neurological examination showed photophobia

and clinical signs of meningeal irritation. The Glasgow Coma Scale was 13/15.

Cardiovascular examination showed cold extremities and extensive skin livedo covering nearly 60% of the patient's body surface area. Urine output was high (5 mL/kg/h) despite clinical evidence of low cardiac output.

Pulmonary examination was normal and transcutaneous oxygen saturation was 97% and required no oxygen supplementation.

INVESTIGATIONS

Cerebrospinal fluid (CSF) analysis and culture showed 550 altered neutrophils/mm³ associated with high protein levels (2 g/L) and numerous *Streptococcus pneumoniae* colonies. The CSF glucose level was undetectable.

Brain contrast-enhanced CT showed no brain oedema or hydrocephalus. No signs of increased intracranial pressure were detectable. No cerebral venous or arterial obstructions were evident. Haemodynamic assessment by transthoracic echocardiography showed normal left ventricular ejection fraction (60%). Inferior vena cava diameter was 10 mm (our reference values are between 15 and 20 mm) and cardiac index estimation was 2.2 L/min/m² (our reference values are between 2.8 and 4.2 at rest). These findings were consistent with low cardiac output related to hypovolaemia.

The serum lactate level was 5 mmol/L (normal value <2 mmol/L).

Kidney function tests were normal but creatinine clearance calculation obtained from a 24 h urine sample collection showed a high clearance value (180 mL/min) reflecting glomerular hyperfiltration. Renal sodium excretion was also high (150 mmol/L) despite a low serum sodium level (133 mmol/L).

In the presence of documented hypovolaemia as noted above, these renal findings indicated renal salt wasting.

Blood glucose and liver function tests were within normal range.

DIFFERENTIAL DIAGNOSIS

Acute arterial hypertensive response—cushing reflex—related to increased intracranial pressure was the main differential diagnosis.

This diagnosis was unlikely because of the absence of any sign of brain oedema or hydrocephalus on brain CT. In addition our patient had no neurological sequelae or cerebral vascular damage.

TREATMENT

Haemodynamic management consisted of adequate blood volume resuscitation by 3500 mL of crystalloid solution infusion followed by continuous

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α -blocker vasodilator infusion to achieve an inferior vena cava diameter of between 15 and 20 mm and a target mean arterial blood pressure between 65 and 75 mm Hg, respectively. Pneumococcal meningitis was treated with an intravenous dose of amoxicillin 200 mg/kg/day for 14 days in association with intravenous dexamethasone 10 mg every 6 h during the first 4 days.

OUTCOME AND FOLLOW-UP

Blood lactate normalised rapidly and skin livedo disappeared within 30 min once adequate blood volume and lower arterial blood pressure have been achieved. Moreover, features of renal salt wasting disappeared and urine output fell to 1.5 mL/kg/h within few hours.

No catecholamines support was needed.

Vasodilator therapy was gradually tapered to maintain a target mean arterial blood pressure between 65 and 75 mm Hg, then stopped on the fourth day after admission.

Neurological outcome was favourable with no need for mechanical ventilation; the patient had no neurological sequelae and was discharged within 15 days after admission.

DISCUSSION

Management of acute arterial hypertension in the critical care setting has been discussed but it concerned only surgical patients in the postoperative period and more than 30 years ago acute arterial hypertension has been recognised as a source of complications in the postoperative period.^{5 6} Recent reviews about management of acute hypertensive crisis did not mention acute arterial hypertension management in the setting of sepsis or critical illness.^{4 7}

However, this phenomenon might be quite common. In one recent study, high levels of arterial blood pressure were associated with glomerular hyperfiltration in the critical care setting⁸ suggesting arterial hypertension and glomerular hyperfiltration might coexist in the critically ill. Owing to the association between the two entities, one might suppose acute arterial hypertension to induce glomerular hyperfiltration and to some extent some degree of renal salt wasting resulting in hypovolaemia. Hypovolaemia related to renal salt wasting could then stimulate the renin-angiotensin system and sustain arterial hypertension thus creating a vicious circle resulting in *hypertensive hypovolemic circulatory failure*. Recognition of this type of circulatory failure might have several implications: First of all, it would be necessary to find a consensus based on clinical trials for managing this type of circulatory failure. This could be of great importance since one might assume that vasodilators by lowering peripheral vascular resistance would be beneficial for organ perfusion by reducing renal fluid loss and reversing sepsis-related microcirculatory dysfunction. This beneficial effect of vasodilators therapy on microcirculation during sepsis was recently emphasised.⁹ On the contrary, one might assume that early vasodilator therapy during sepsis could be responsible for an increase in norepinephrine load if secondary hypotension was to occur. Increased norepinephrine load has been recently associated with increased mortality during septic shock.¹⁰ Finally, some recent data suggest that cerebral ischaemia¹¹ is a common finding during sepsis. This might be due to sepsis-related loss of cerebral blood flow autoregulation.¹² Thus, the acute hypertensive response occurring during sepsis might be a neurally mediated protective mechanism against cerebral ischaemia. If this scenario was true, lowering arterial blood pressure could be deleterious for cerebral perfusion.

Thus, during acute sepsis, the immediate deleterious effect of unnecessary high level of arterial blood pressure might be renal salt wasting and low cardiac output as reported here.

However, we recently reported sepsis-related renal salt wasting in the absence of sepsis-related hypertensive response.¹³

These findings point out the difficulty to define a 'high blood pressure value' in the context of acute sepsis and underline the complex interaction between systemic and renal circulations.

Clinical and biological criteria might be helpful to define this upper limit until the sepsis management guidelines recognise arterial hypertension as a real challenge during the resuscitation of patients with sepsis.

Learning points

- ▶ Sepsis-related circulatory failure is usually but not always manifested by low arterial blood pressure.
- ▶ Acute arterial hypertensive response occurring during sepsis could be a common condition masked by the use of anaesthetic drugs having hypotensive properties.
- ▶ This hypertensive response could lower cardiac output and induce organ failure.
- ▶ Acute hypertensive response might also be a defense mechanism against sepsis-related cerebral ischaemia.
- ▶ Sepsis management guidelines should include the management of 'hypertensive hypovolemic circulatory failure' in the management strategy of severe sepsis.

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Competing interests None.

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