Grossly elevated plasma metanephrine levels due to midodrine, an alpha1 receptor agonist, in a patient presenting with Postural Orthostatic Tachycardia Syndrome.

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❖ Introduction:

- While phaeochromocytomas are rare tumours, their identification is essential to avoid morbidity and mortality; their biochemical identification is crucial.
- Plasma and 24 urinary metanephrines are used as first line investigations, with plasma metanephrines increasingly used first due to its simplicity and high sensitivity/specificity [1]. False positive results, however, can be as high as 20% [(1,2,3)], particularly secondary to medications; their exclusion is essential to avoid unnecessary imaging and operation.
- However, most interfering factors cause elevation of less than 4-fold above the normal range[(4)].
- In our case, we show the effect of midodrine- an alpha1 receptor agonist- in causing grossly elevated plasma, but not urinary, metanephrine.

❖ Case report:

- 41 year old lady was referred to our endocrine clinic in Oxford with a possible phaeochromocytoma. She had 6-year history of dizziness and syncope, initially diagnosed with vasovagal syncope, but latterly diagnosed with Postural Orthostatic Tachycardia Syndrome (POTS).
- Her symptoms were episodes of dizziness, shortness of breath, nausea, headaches, with or without loss of consciousness.
- Her cardiovascular investigations showed sinus tachycardia and hypotension associated with her symptoms.
- As part of investigations, plasma metanephrines were assessed and were grossly abnormal with plasma metanephrine grater than 25000pmol/l and normetanephrine of 1758 pmol/l.
- Her medications included midodrine 7.5 mg 3 hourly, bisoprolol and slow sodium. Doxazosin, an alpha1-adenoceptor antagonist, had recently been added following the above results.
- There was no relevant family history, and examination was unremarkable.
- Investigations included a repeat plasma metanephrines which showed similar results. However, 24-hour urinary metanephrines, PTH, thyroid function and pituitary profile were normal, as was adrenal CT scan.
- Midodrine was then withheld for a week, and plasma metanephrines levels returned to normal.
- Doxazosin was subsequently stopped.

❖ Investigations:

- At presentation
  P. metanephrine: >25000 pmol/l (80-510)
  P. normetanephrine: 2209 pmol/l (120-1180)
  Urinary metanephrines: Normal
- After stopping Midodrine
  P. metanephrine: 262 pmol/l
  P. normetanephrine: 910 pmol/l

❖ Discussion

- Most reported drug interference with metanephrine levels cause mild to moderate elevation, due to a variety of mechanisms.
- We highlight the massive interference in plasma, but not urine, metanephrines assay by the alpha-adrenoceptor agonist midodrine

❖ Refererence:

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Clinical Cases Pituitary/Adrenal

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