CLINICAL PRACTICE ARTICLE

Functional and non-functional types of adrenal tumors: a case series [version 1; peer review: 1 not approved]

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Abstract

Adrenal gland masses could be classified into functional, malignant, or benign. An adrenal cortical adenoma is one of the most common incidentalomas found with either functional or non-functional type. Pheochromocytoma is a neural crest cell origin tumor associated with catecholamine production. A classic triad of headache, sudden episodic perspiration, and tachycardia marked a pheochromocytoma. We report three patients with adrenal tumors. First, a 52-year-old woman with complaints of pain in the left flank suggests a left kidney tumor. The patient has an increased blood pressure intraoperatively. Adrenal cortical adenoma was found postoperatively. The second case is an Indonesian male 27-year-old with pain in the upper right abdomen. Intraoperative, the patient also has an escalation in blood pressure. Antihypertensive drugs are also used in this patient. Postoperatively, a pathology result of pheochromocytoma was revealed from this patient. The third case, adrenal myelolipoma, was suspected in a 48-year-old male and underwent surgery because of tumor growth. Later, a histopathological examination revealed myelolipoma of the adrenal. Management of adrenal tumor should be done individually based on each patient. In the first and second cases, blood pressure was unstable intraoperatively and was managed using several drugs, and was stable at follow-up. In the third case was no hemodynamic problem. In the case of an adrenal tumor, management tailoring should be based on the individual patient.

Keywords

Adrenal cortical adenoma, adrenal tumor, pheochromocytoma, adrenal myelolipoma

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version 1 28 Jul 2021	✗ view

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: Indrawan DH: Conceptualization, Data Curation, Formal Analysis, Methodology, Project Administration, Writing – Original Draft Preparation; **Prapiska FF**: Conceptualization, Data Curation, Formal Analysis, Methodology, Project Administration, Resources, Supervision, Writing – Review & Editing; **Warli SM**: Supervision, Validation, Visualization; **Sihombing B**: Supervision, Validation, Visualization; **Siregar GP**: Supervision, Validation, Visualization

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Introductions

The adrenal gland is a unique retroperitoneal endocrine organ that is different if compared with other retroperitoneal structures in embryological, anatomical, and their role in homeostasis. Tumors of the adrenal gland can be classified as functional or non-functional. The tumors may arise from the adrenal gland or could be secondary lesions. They may be benign or malignant.[1,2] Tumors of the adrenal gland are relatively common. The prevalence of adrenal gland tumors is three to ten percent of the human population.[3] Adrenal tumor sometimes found as an incidentaloma, which means the tumor more than 1 cm in size was found during an imaging study with indications other than the adrenal condition, but this excludes the patients who were done an imaging study during cancer work-up. Adrenal tumors are known to be one of the most commonly found incidentaloma.[4–8]

Adrenal masses could be classified into functional, malignant, or benign masses. In functional terms, adenoma causing Conn's of Cushing's syndrome, pheochromocytoma, aldosteronoma, and adrenal carcinoma were included. While malignant were comes from metastases, carcinoma, lymphoma, or neuroblastoma. Last but not least, benign masses consisted of non-functioning adenoma, angiomyolipoma, cysts, and hemorrhage.[9] Pheochromocytomas are neural crest cell tumors and linked with catecholamine production.[10] The initial examination, usually using ultrasound as the diagnostic modality, could be detected in 90% of cases as an enlargement of the adrenal gland.[11] The founding could be variable from solid to mixed cystic and solid to cystic.[12] Pheochromocytomas patients often present with hypertension, tachycardia, headaches, palpitations, diaphoresis, chest pain, anxiety, and even weight loss. Around 10% of the patients do not have hypertension as their primary symptom.[13]

An adrenal cortical adenoma is one of the most common incidentalomas found.[13] An adenoma mass should be grouped into functioning and non-functioning adrenal adenomas. It should be noted that functioning and non-functioning adenomas could not be classified using imaging techniques.[14] Adenomas show a uniform hypoechoic mass relative to the fat. Adenomas are relatively small mass made them be difficult to be found during an ultrasound examination.[9]

The treatment for adrenal tumor requiring surgery usually because of the treatment failure in functional adrenal masses or a malignant tumor for either primary adrenal cortical carcinoma or solitary metastasis from nonadrenal sources, such as lungs, breasts, kidneys, and melanomas.[15] Today, laparoscopic adrenalectomy is the first choice for adrenal disorder surgical procedures. But, there are some conditions that are requiring open adrenalectomies, such as patients with adrenal carcinoma, large pheochromocytoma with blood pressure that may be hard to control, and patients that are requiring a simultaneous abdominal procedure.[16] But the absolute contraindications for adrenalectomy are extensive metastatic disease, uncorrected coagulopathy, and severe cardiopulmonary disease that precludes anesthesia.[14] The authors report two cases of adrenal glands tumors requiring open adrenalectomy. This study was conducted with surgical CARE checklist guideline as a guidance.[15]

Case 1

A 52-year-old Indonesian female presented with pain on the left flank. Pain has been felt for six months. Hematuria was found. History of diabetes was found with the highest fasting glucose reported was 159 mg/dL, hypertension was found with a regular blood pressure of about 170/100 mmHg—patient with a history of percutaneous cardiac intervention four months ago. The patient was referred to our Regional Referral Hospital with a left adrenal tumor. The patient also has depression diagnosed by a psychiatrist having 23-score in Beck Depression Inventory-II (BDI II) questionnaire. It has been experienced by the patient two years ago, initiated by the death of her husband. The patient also felt a problem in her marriage, as she never felt intimate with her husband from the first day of their marriage. The patient was diagnosed with an adrenal tumor for the last five years, and since then, she has felt useless in her life. From the radiologic examination, we found a mass from the suprarenal organ, suggestive of an adrenal tumor as a conclusion (Figure 1). Thus, we used the left adrenal tumor as a working diagnosis.

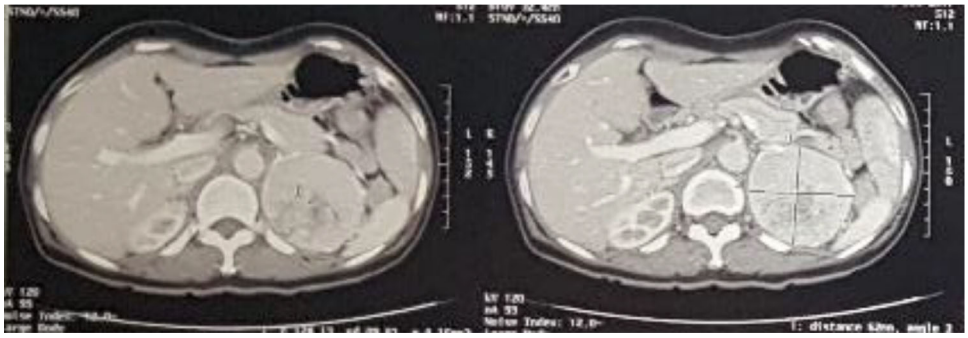

Figure 1. CT Scan showed a left mass suggestive adrenal tumor.

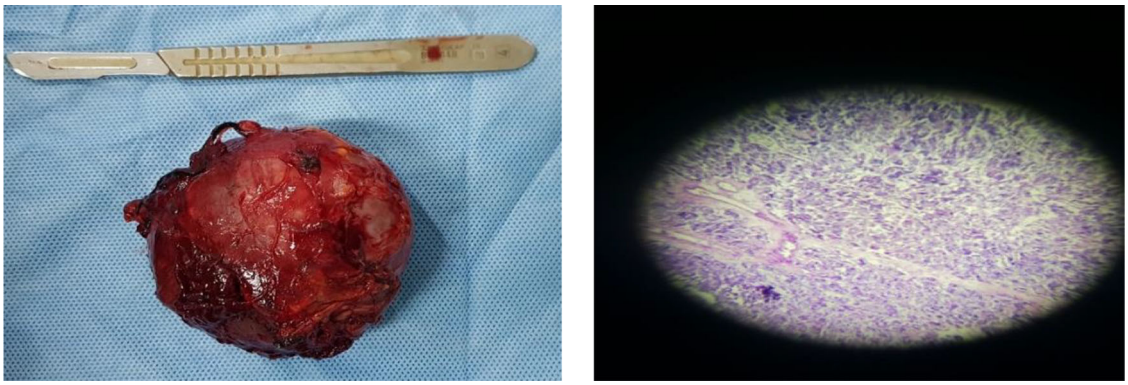

Figure 2. Macroscopic and microscopic tumor.

Adrenalectomy was performed for the left adrenal tumor. During the operation, unstable blood pressure was noted and could increase over 200 mmHg. Then the anesthesiologist used several medications to lower the blood pressure immediately. The problems with her blood pressure did not persist after the surgery. The highest blood pressure after adrenalectomy was 130/80 mmHg. Post adrenalectomy mass was sent to the pathology department in order to perform a pathology examination (Figure 2). The result came within one week after the procedures and revealed a picture of tumor cells forming nests is largely separated by fibrous fibers by an invasion of blood vessels. Tumor cells with rounded and oval nuclei are enlarged, rough chromatin, protruding nuclei, cytoplasm partly eosinophilic, partly clear, and bubbly. Abnormal mitosis is easy to find. The stroma consists of infiltrated fibrous connective tissue, with a conclusion of adrenal cortical adenoma.

During the follow-up, the patient shows a normal condition, with normal blood pressure (maximum 125/80 mmHg) but the fasting glucose still not yet within the normal value.

Case 2

We were reporting an Indonesian male 27-year-old with pain in the upper right abdomen. The pain has been experienced by the patient since one month ago and aggravating within this week. A mass was felt by the patient on the upper right abdomen. No hematuria was reported, no passing stone, no history of hypertension and diabetes. From physical diagnosis, we found a positive ballottement test on the right flank. Other physical examinations were within normal limits.

During the preoperative preparation, blood pressure was within the normal limit. An initial complete blood test showed normal hemoglobin (12.3 g/dL), white blood cells (9,800/μL), and thrombocyte (319,000/μL). Normal glucose analysis was found, different from our first case.

The radiological examination found an adrenal tumor (Figure 3). Based on the radiological examination, the right adrenal tumor was suspected as our diagnosis.

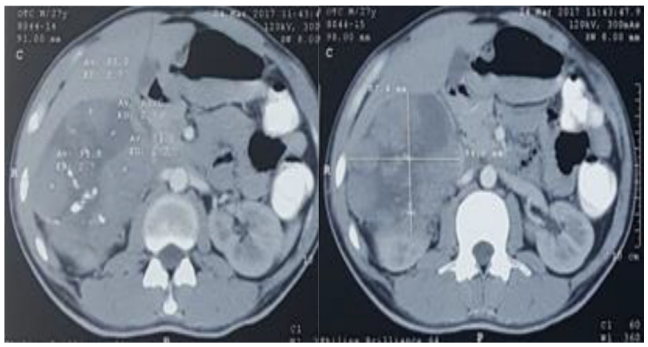

Figure 3. CT Scan showed a left mass suggestive adrenal tumor.

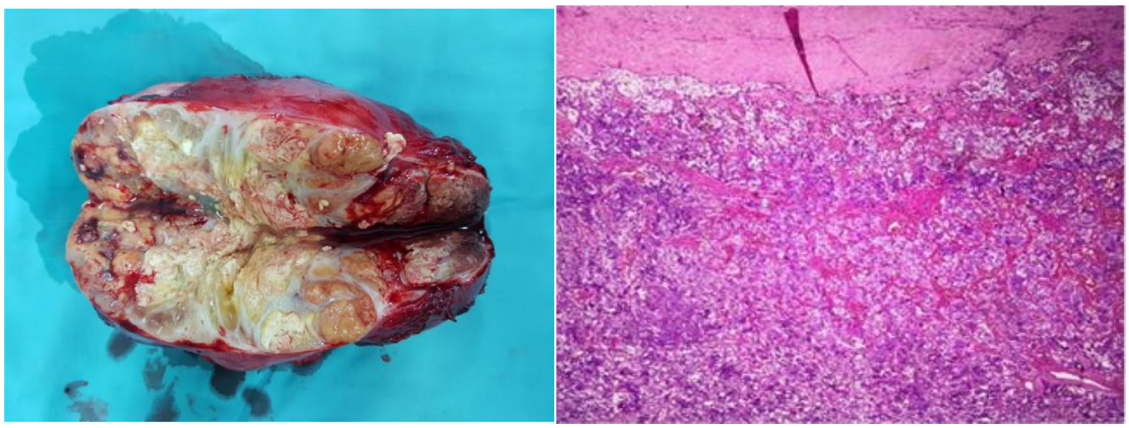

Figure 4. Macroscopic and microscopic tumor (HE).

Right adrenalectomy was performed on December, 7th 2017. We found a bulging mass from the posterior. Then we opened the white line of Toldt. The next step was releasing the mass from lateral, superior, inferior, and the last, media. Anterior pedicels and branches from the vena cava and aorta towards the right adrenal were then ligated and cut. Intraoperatively, several antihypertensive drugs were used by the anesthesiologist to maintain the blood pressure at a lower level. Normal blood pressure was preserved after removal of the adrenal gland.

The mass on the right upper abdomen was inspected by the pathology department on December, 8th 2017, and after the next five days, a result was reported, which was a pheochromocytoma (Figure 4). The follow-up was done, and the patient did not show any problem with the blood pressure, blood glucose, and the complete blood count was normal.

Case 3

We were reporting a 48-year-old male who came to urology clonic referred from digestive surgery consultant with an intraabdominal tumor suspected with adrenal myelolipoma. The mass was felt to increase in size for the last one month. No pain on palpation, no history of hematuria, cloudy urine, or passing stone. The patient also complained of fatigue and shortness of breath. On examination, hemodynamic was within normal limits. On urological examination, ballotement was found on the right flank without any tenderness. From computed tomography scan, an upper right abdomen mass was found, pushing liver to the superior and kidney to the inferior (Figure 5). The mass sized $12.8 \times 10 \times 10$ cm, suspected of adrenal myelolipoma.

We performed a tumor removal for this patient (Figure 6). Intraoperatively, the hemodynamic remained stable. Based on this finding, we could rule out pheochromocytoma. Later, a histopathological examination revealed adrenal preparations appear to be the proliferation of mature fat cells with a round, oval, eccentric, smooth chromatin nucleus, numerous cytoplasm and clear, between groups of fat cells appear to group hematopoietic cells, at certain focus looks interstitial bleeding (Figure 7). No signs of malignancy were found in this preparation, the impression of Myelolipoma of Adrenal.

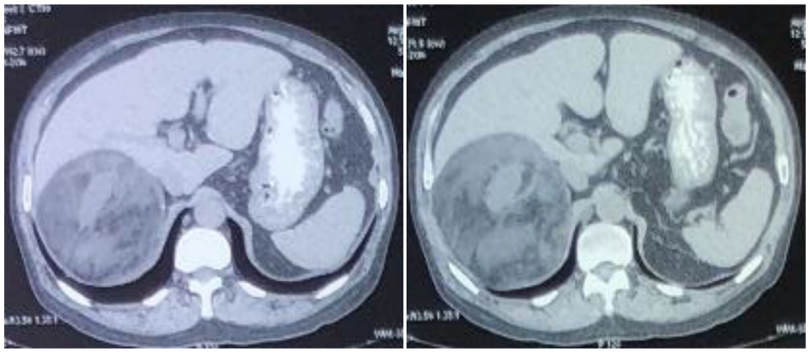

Figure 5. CT Scan examinaton showed an upper right abdomen mass.

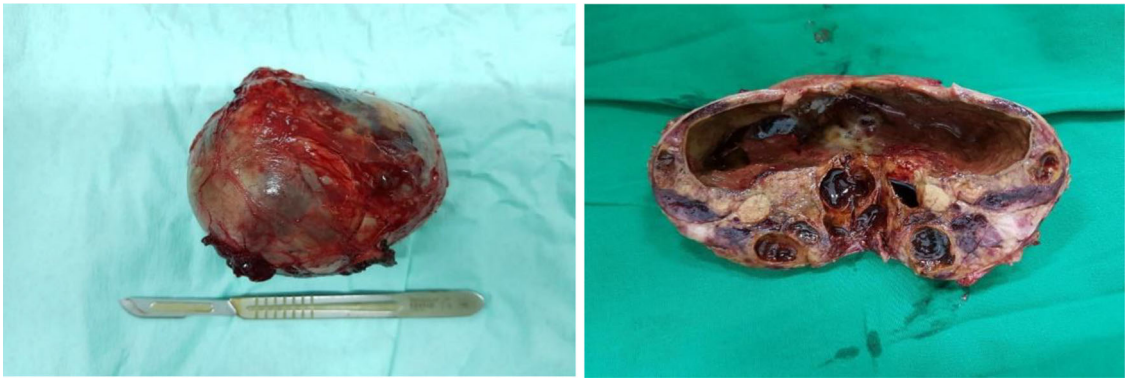

Figure 6. Macroscopic tumor after adrenelectomy.

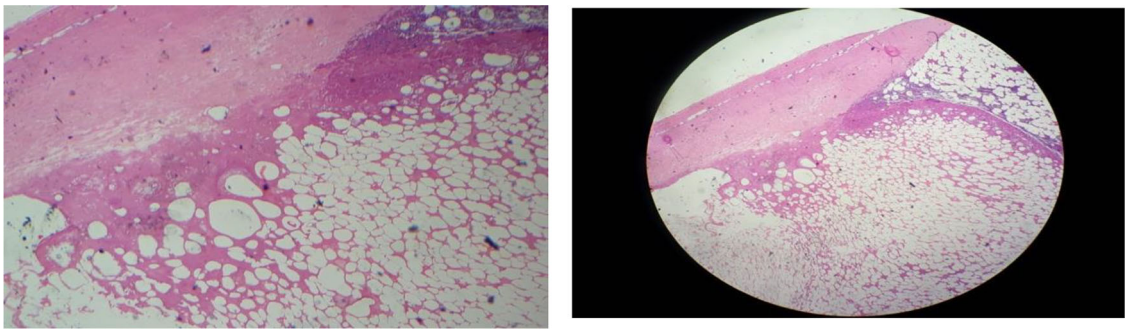

Figure 7. Microscopic of tumor.

Discussion

From this case series, we reported two cases of adrenal tumors, with one case of adrenal cortical adenoma and one case of pheochromocytoma. Adenomas are the most common benign tumors from the adrenal gland. From our first case, an adrenal cortical adenoma was found associated with diabetes, hypertension, and depression. This case is suggestive of a functional adrenal cortical adenoma. The glucocorticoids' production from the adenoma could increase hypercortisolism, or known as Cushing syndrome.[17]

Cortisol production from benign adenomas often results from a unilateral hyperplastic mass, although a bilateral one might also happen. Systemic manifestations from hypercortisolism are central obesity, dyslipidemia, or hypertension.[17] In our patient, we found hypertension without dyslipidemia or central obesity. On the other hand, one patient may come to clinical practice with a high blood glucose level, and when screened for hypercortisolism, he/she may have a subclinical Cushing syndrome.[18] In our patient, we have a high blood glucose level, which becomes normal after adrenalectomy. Similar results were stated by Midorikawa and Mitchel. They found that an adrenalectomy procedure may improve glucose control together with hypertension.[19,20] Cushing syndrome may also be related to depression. Labeur *et al.* also stated this manifestation in their study.[21]

Pheochromocytoma is a tumor of the catecholamine-producing cells of the adrenal medulla. The classic presenting sign of pheochromocytoma patients is paroxysmal hypertension, while the other could demonstrate persistent high blood pressure and normotensive.[17] There is a classic hallmark triad of pheochromocytoma, headache, sudden episodic perspiration, and tachycardia.[22] In our case, we failed to find any clinical manifestation, which has been stated earlier. Our patient has normal blood pressure without headache, perspiration, or even tachycardia. This might be similar to a study from Adler *et al*. They said as many as 20% of pheochromocytoma patients could present with no symptom at all.[23]

Intraoperatively, both of our cases showed similar symptoms with a spike in blood pressure. This manifestation has also been reported by Kakoki *et al.*[24] However, after the adrenalectomy procedure, the patients did not sustain any elevated blood pressure. This also happened during the follow-up.

Adrenal myelolipoma is a rare, non-functional, and benign neoplasm of the adrenal gland.[25] Because of the rarity, in the past adrenal myelolipomas, were found during the autopsy. Nowadays, because of radiological studies such as

ultrasonography, computed tomography, and magnetic resonance imaging, incidentaloma has become more commonly found.[26] The management of this tumor is usually conservative because most of them are asymptomatic. However, surgical intervention is suggested in a large tumor (larger than six cm).[27] So, the management is based on the size and the symptoms of the tumor.[28]

Conclusions

We report a case series with three cases of adrenal tumor. The first case is an adrenal cortical adenoma suggestive a functional type. The second case is a pheochromocytoma without the classic hallmark. Both cases have unstable intraoperative blood pressure and have to be stabilized using several medications. During the follow-up, normotensive was achieved in both patients. The third cases have no hemodynamic disturbance in preoperative, intraoperative, and postoperative. In case of adrenal tumor, management tailoring should be based on individual patient.

Acknowledgement

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Consent

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patients.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

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✗

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In the article by Indrawan et al. the authors describe a case series of three patients with adrenal masses. In particular, they describe a case with adrenal cortical adenoma, a second case with pheochromocytoma and a third with an adrenal myelolipoma.

I regret to say, that the article should not be approved for indexing. The article has scientific misinformation. For instance, the authors indicate that the usual examination for the pheochromocytoma is the ultrasound or that only 10% of patients with pheochromocytoma do not present hypertension, whereas the truth is that many patients with pheochromocytoma have normal blood pressure levels (see reference list and attached document for examples) and the diagnostic imaging of choice after the biochemical confirmation of a pheochromocytoma is the CT (or MRI in certain cases). Another example is the part where the authors indicate that adrenalectomy is totally contradicted in cases of synchronous metastatic disease. That is also misleading. In many cases disease debulking has been associated with better survival for some patients.

The authors do not describe in detail the physical examination, or the diagnostic procedures followed in daily routine care for adrenal lesions (e.g., concentrations of plasma or urinary metanephrines, steroids, dexamethasone suppression test, assays used for the metabolites, upper cut offs of reference intervals). The discussion does not include information or conclusions based on findings that could add to our understanding of the disease processes, diagnosis or treatment.

The article will require copy editing. In addition, the article adds little on what is already known in the literature and lacks novelty.

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Is the background of the cases' history and progression described in sufficient detail?
No

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
No

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
No

Is the conclusion balanced and justified on the basis of the findings?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Adrenal diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 09 May 2022

Fauriski F Prapiska, Faculty of Medicine Universitas Sumatera Utara - H. Adam Malik General Hospital, Medan, Indonesia

Thank you for your thoughtful remarks. We appreciate the time and effort that you have dedicated to provide feedback on our manuscript and are grateful for the comments on our paper. We would like to address a few topics that have been raised.

1. We thank the reviewer for pointing this out. USG is utilized as an initial diagnostic technique, not as a gold standard. According to Campbell-Walsh-Wein Urology, Computerized Tomography Scan is the gold standard in adrenal imaging.

2. We appreciate the reviewers insightful suggestion. However, as stated by Zuber, Kantorovich, and Pack in the metabolism Clinics of North America Journal, roughly 5% to 15% of pheochromocytoma patients have normal blood pressure.

Once again, we thank you for the time you put in reviewing our paper.

Best regards,

Fauriski F Prapiska (Corresponding author)

Competing Interests: No commenting interest were disclosed