Author's response to reviews

Title: Ganglioneuroma; A rare cause of adrenal incidentaloma: a case report

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Author's response to reviews: see over
Response to Reviewer 1:
Reviewer: Theodossis S. Papavramidis

Section Abstract:
1- “Adrenal gland location can be seen rarely.” What does the authors mean?

In this sentence we want to mention that adrenal ganglion is a rare location of ganglioneuroma. We changed the sentence to GN can rarely placed in adrenal gland (reference 7,10)

2- “This tumor is usually asymptomatic and majority of cases are detected incidentally.” According to the most recent review this is not true (see Papavramidis et al South Med J 2009)

According to this literature major symptom was pain in retroperitoneal ganglioneuroma. But in our manuscript the topic is incidental lesion. However, in our case the onset symptom of the case was right lower quadrant pain, the lesion was on the other side. The mass was detected incidentally. Incidental lesion has not get symptoms.

Section Introduction:
1- “Adrenal gland location can be seen rarely” what does the authors mean by this?

In this sentence we want to mention that adrenal ganglion is a rare location of ganglioneuroma. We changed the sentence to GN can rarely placed in adrenal gland.

2- “This tumor is usually asymptomatic and majority of cases are detected incidentally.” According to the most recent review this is not true (see Papavramidis et al South Med J 2009). Two thirds of the patients have symptoms…

According to this literature major symptom was pain in retroperitoneal ganglioneuroma. But in our manuscript the topic is incidental lesion. However, in our case the onset symptom of the case was right lower quadrant pain, the lesion
was on the other side. The mass was detected incidentally. Incidental lesion has not get symptoms.

3- “Although adrenal ganglioneuroma (AG) is usually hormonally silent and therefore asymptomatic,” the last two words should be removed

Last two words were removed.

**Section Case Report:**

1- Why did the patient had MRI following the CT that showed a well-defined mass?

Although the mass was a well-defined mass on CT, MRI was performed because of the bigger size (≥6cm) and calcification.

2- Why did the patient did a PET?

PET was performed because of the malignancy suspicious on MRI. On T1A-weighted MR images the tumor was shown as slightly hypointense mass, whereas slightly hyperintense on T2A-weighted MRI. After intravenous injection of gadolinium, the mass showed a progressive, heterogeneous and delayed enhancement. Due to the tumor size and with consideration of the differential diagnosis of malignant lesion we performed $^{18}$F-2-Fluoro-deoxy-D-glucose-positron emission tomography (PET) scan.

3- It would be nice to have a figure of the surgical specimen

We add a figure of the surgical specimen.

4- The functional testing performed should also be mentioned

We mentioned functional test on the second paragraph of case report section. Owing to the normal levels of all endocrine test, we didn’t give the results. If the editor and reviewer want to see the results insistedly, we will mention the results.

5- Why didn’t they remove the tumor laparoscopically?

According to our institution surgical strategy, we prefer open surgery if the tumor size is bigger than 6 cm and suspicious findings for malignancy.

**Section Discussion:**

1- “In this manuscript, the case was purely silent and asymptomatic.” This is not the case… the patient had symptomatology on presentation…he came to the department for pain.

The case was changed to patients on the text. The patient had symptomatology on presentation, but unfortunately on the other side. Patient’s symptom was not related with the ganglioneuroma.
2- The authors should discuss the treatment options

We discuss the treatment options on the last part of the discussion section. According to our knowledge surgical resection is the only treatment methods for these masses.
**Response to Reviewer 2:**

**Reviewer:** Nickolaos Michalopulos

1. Major grammar and editing revisions should be made. I suggest the manuscript to be revised by someone that English is his native language. Many words that are used are unsound.

The author that English is his native language revised manuscript.

2. Abbreviations should be spell out in their first appearance in the manuscript. Do not use abbreviations in the abstract.

Abbreviations were removed from the abstract and used in their first appearance.

3. The authors should briefly report others adrenal lesions that are preoperatively diagnosed as incidentalomas.

We mentioned other adrenal lesions in discussion section (yellow print)

4. The authors perform a PET scan to evaluate the potency of malignancy of the tumor. According to the CT scan images that are provided the tumor dislocate the surrounding tissues without infiltrate them. The authors must justify their decision to perform a PET scan. Is PET scan an integral imaging tool in pre-operative evaluation of adrenal tumors?

However on CT image showed well defined mass, tumor size larger than 5 cm, heterogeneity and calcification were suggested malignancy. The curious point of this manuscript is the SUV levels in PET CT. It was reported that all ACC cases showed a SUV of 3.0 or higher, and that the sensitivity and specificity to distinguish ACC from adenoma were 100% and 98%, respectively (reference 14,15). The SUV of 4.1 in the present case was not within these ranges, also it suggested to ACC.

5. Have laparoscopic or endoscopic procedures a role in the management of these tumors? Why they did not performed a minimally invasive procedure?

According to our institution surgical strategy, we prefer open surgery if the tumor size is bigger than 6 cm and suspicious findings for malignancy.

6. Is ganglioneuromas purely benign tumors? The authors should clarify the potency of malignancy of these tumors and add the corresponding literature

According to our knowledge ganglioneuromas are purely benign tumors. GN belongs to neurogenic tumors group with ganglioblastoma and neuroblastoma. The differential point of GN from the other neurogenic tumors is benign potential (Reference 7).
7. What are the main risk factors for recurrence and malignancy of ganglioneuromas?

We could not find any study about recurrence and malignancy of ganglioneuromas. In the literature there was only few study about recurrence of neurogenic tumors. But these recurrences are generally malign masses.

8. The authors should discuss the management of recurrence disease.

In the literature papavramidis et al suggest that the tumor’s good prognosis and slow growth may contribute to the increased age of appearance. We could not find any findings about recurrence for ganglioneuroma.

9. The authors should briefly discuss the differences between adrenal ganglioneuromas, paragangliomas and pheochromocytomas.

This topic was added to discussion. (yellow print)

10. Are any differences in the management of ganglioneuromas according to their location (adrenal, retroperitoneal)? (Corresponding literature: Papavramidis et al. Retroperitoneal Ganglioneuroma in an Adult Patient: A Case Report and Literature Review of the Last Decade. Southern Medical Journal 2009.)

The topic was mentioned in manuscript according to this literature. (yellow print)


The topic was mentioned in manuscript.

12. The images legends should be display in the end of the manuscript and not in the manuscript.

It was done.