Computed tomography characteristics of adrenal ganglioneuroma: a retrospective analysis of 30 pathologically-confirmed cases

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Abstract

Objective: To investigate the computed tomography (CT) characteristics of adrenal ganglioneuromas (AGNs) and to determine the ability of CT scanning to distinguish between large (>3 cm) and small (≤3 cm) AGNs.

Methods: This retrospective study searched the electronic medical record system of a hospital between January 2008 and July 2019 in order to identify patients with pathologically-confirmed AGNs that underwent three phases of CT scanning. The CT features were compared between large and small AGNs.

Results: A total of 30 patients with pathologically-confirmed AGNs were included in the study. The majority of patients (76.7%; 23 of 30) were asymptomatic and there were nonspecific symptoms in seven patients. The 'pointed peach' sign appeared in more than half of the patients (53.3%; 16 of 30). The CT value of the arterial phase, progressive enhancement, morphology and calcification in the CT images were found to be significantly different between large and small AGNs. Progressive enhancement was more likely to occur in small AGNs. Most large AGNs had...
irregular shapes, while small AGNs were likely to be round or oval with a smooth border. Calcifications were noted in large AGNs (42.9%; six of 14).

**Conclusion:** CT scanning can show many of the key imaging characteristics of AGNs used to distinguish between large and small AGNs.

**Keywords**
Adrenal ganglioneuroma, computed tomography, adrenal neoplasm

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**Introduction**

Ganglioneuromas (GNs) are rare, benign entities that originate from the sympathetic nervous system.\(^1\)\(^2\) GNs may occur anywhere in the body that contains sympathetic nerves, from the base of the skull to the pelvic cavity, but the two most common sites are the retroperitoneum and posterior mediastinum.\(^2\)\(^–\)\(^5\) GNs in the adrenal gland are more uncommon, accounting for 21% of the disease entity.\(^6\) Little is known about the computed tomography (CT) characteristics of adrenal GNs (AGNs) due to their rarity. Only sporadic case reports or small patient populations have been reported.\(^7\)\(^–\)\(^10\) Reports on the CT features of AGNs show wide variations and it can be difficult to differentiate AGNs from other adrenal neoplasms including adrenal adenoma, adrenocortical carcinoma and pheochromocytoma.\(^9\)\(^\)\(^11\) Hence, it is a challenge for radiologists to achieve a precise diagnosis of AGNs ahead of any planned surgery. In addition, it is generally believed that large adrenal tumours (>3cm) are usually functional and heterogeneous compared with small adrenal tumours.\(^12\)

This study aimed to retrospectively investigate the CT characteristics of AGNs and to determine whether there were any significant differences between large AGNs (>3 cm) and small AGNs (≤3 cm) with a relatively large sample size.

**Patients and methods**

**Patient population**

This retrospective study searched the electronic medical record system of Tongde Hospital of Zhejiang Province, Hangzhou, Zhejiang Province, China between January 2008 and July 2019 in order to identify patients that fulfilled the following inclusion criteria: (i) the histopathological pattern was AGN; (ii) contrast-enhanced CT images and clinical data were available; (iii) the surgery was performed after the CT examination had been undertaken.

This retrospective study was approved by the Institutional Review Board and Ethics Committee of Tongde Hospital of Zhejiang Province, Hangzhou, Zhejiang Province, China (no. KTSC2017004) and all the participants provided written informed consent.

**CT examinations**

All of the data from the CT scans including unenhanced and contrast-enhanced CT were obtained by one of the following three multi-detector CT scanners: a 16 multidetector-row CT scanner (Siemens Definition AS or SOMATOM Definition Flash; Siemens Healthcare, Erlangen, Germany) or a LightSpeed VCT (GE Healthcare, Milwaukee, WI, USA).
The scanning protocol was as follows: 0.625–1.2 mm collimation; 1.0 pitch; kVp/effective mA 120/100–300; 3–5 mm thickness. After finishing the unenhanced CT, a peripheral intravenous dose of 120 ml of non-ionic iodinated contrast agent was given to the patients at the rate of 3–4 ml/s. CT scans of the arterial and venous phases were initiated 30s and 60s after the onset of contrast injection, respectively. All of the CT images were collected during an inspiratory breath hold.

**CT image analysis**

Abdominal CT image reading was performed by two skilled attending physicians (S.C. & Y.J.) with 9 and 11 years of experience that reached a consensus. Both physicians were blinded to the pathological results when evaluating the CT images. The CT characteristics of the AGNs were qualitatively compared with regard to their location, morphology, number, enhancement degree (ED), long diameter (LD), short diameter (SD), enhancement potentiality (EP), absolute percentage washout (APW), relative percentage washout (RPW), preoperative CT diagnosis, progressive enhancement, cystic degeneration, haemorrhage, calcification, ‘pointed peach’ sign and relapse. The locations were classified as left and right. Morphologies were divided into round, oval and irregular. Enhancement degree (none, mild, moderate) of the lesions was determined: none referred to the difference between the maximum and minimum CT values of the lesions being <10 Hounsfield units (HUs); while mild and moderate enhancement were defined as the difference between the maximum and minimum CT values of the lesions being ≤20 HUs or >20 HUs, respectively. Progressive enhancement referred to the CT value of the portal venous phase (CTV) being higher than that in the arterial phase (CTA) and the value of the CTA was higher than the CT of the unenhanced (CTU). Cystic degeneration was defined as CT attenuation values varying from −20 HUs to 20 HUs. Calcification referred to when the CT attenuation values were as high as cortical bone on unenhanced CT images. In additional, the longest diameter and shortest diameter of the tumour were obtained on axial images. The mean diameter (MD) was defined as (LD + SD)/2. All participants were divided into a large AGN group and a small AGN group according to the size of the MD (>3 cm versus ≤3 cm, respectively). Clinical data and CT characteristics of the large and small lesions were compared.

**Statistical analyses**

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk $W$-test was used to test for a normal distribution of all continuous variables. Statistical comparisons between continuous data from the large AGN and small AGN groups were undertaken using an independent two-sample $t$-test or the Mann–Whitney $U$-test based on data normality. As for categorical variables, $\chi^2$-test or Fisher’s exact test was used. A $P$-value <0.05 was considered statistically significant.

**Results**

A total of 30 patients were enrolled in this study. The participants consisted of 16 females and 14 males, with a mean ± SD age of 41.1 ± 12.4 years (range, 16–74 years). The interval between the CT scans and abdominal surgery was less than 30 days (mean: 14 days). Of the 30 patients, 23 (76.7%) were asymptomatic; and non-specific symptoms consisted of abdominal pain ($n = 3$, 10.0%), hypertension ($n = 3$, 10.0%) and hyperglycaemia ($n = 1$, 3.3%).
No significant differences were found in age, sex, clinical symptoms and abnormal endocrine/experimental examinations between the two groups. Detailed demographic and clinical characteristics are summarized in Table 1.

The CT findings of the AGNs are summarized in Table 2. The mean size of the lesions was 35.7 mm (mean diameter; range, 15–112 mm), which included 14 large lesions and 16 small lesions. Plain CT scans showed that the AGNs had a mean density of 32 HU (range, 23–43 HU) and the mean post-contrast attenuation on the arterial phase was 37 HU (range, 24–50 HU). The mean density of the AGNs was 45 HU (range, 28–70 HU) on the venous-phase with 63.3% (19 of 30) of which presenting with progressive enhancement. The CTA value was significantly lower in the large AGNs compared with the small AGNs ($P < 0.05$), while the CTU and CTV values were not significantly different between the two groups. The differences in DEAP, DEPP, ED, EP, APW and RPW were not significantly different between the two groups. Progressive enhancement was frequently found in small AGNs (81.2%; 13 of 16), but rarely in large lesions (42.9%; six of 14) ($P < 0.05$). Figure 1 shows the CT scans for a 36-year-old female with a small right adrenal tumour (a mean diameter of 19 mm) that shows a progressive enhancement pattern.

No significant differences were found in age, sex, clinical symptoms and abnormal endocrine/experimental examinations between the two groups. Detailed demographic and clinical characteristics are summarized in Table 1.

| Characteristic                | All patients n = 30 | Large lesions >3 cm n = 14 | Small lesions ≤3 cm n = 16 |
|------------------------------|--------------------|-----------------------------|---------------------------|
| Age, years                   | 41.1 ± 12.4        | 42.2 ± 14.3                 | 40.0 ± 10.8               |
| Sex, male/female             | 14/16              | 7/7                         | 7/9                       |
| Nonspecific symptoms         |                    |                             |                           |
| Hypertension                 | 3 (10.0)           | 0 (0.0)                     | 3 (18.8)                  |
| Abdominal Pain               | 3 (10.0)           | 2 (14.3)                    | 1 (6.3)                   |
| Hyperglycaemia               | 1 (3.3)            | 0 (0.0)                     | 1 (6.3)                   |
| Abnormal endocrine and       |                    |                             |                           |
| experimental examinations    | Cortisol           | 4 (13.3)                    | 1 (7.1)                   | 3 (18.8) |
| PRA                          | 2 (6.7)            | 0 (0.0)                     | 2 (12.5)                  |
| PAC                          | 2 (6.7)            | 0 (0.0)                     | 2 (12.5)                  |
| CEA                          | 2 (6.7)            | 2 (14.3)                    | 0 (0.0)                   |
| PSA                          | 1 (3.3)            | 1 (7.1)                     | 0 (0.0)                   |
| Ferritin                     | 4 (13.3)           | 2 (14.3)                    | 2 (12.5)                  |

Data presented as mean SD or n of patients (%).

No significant between-group significant differences ($P \geq 0.05$); continuous data were compared using an independent two-sample t-test or the Mann–Whitney U-test based on data normality; categorical data were compared using $\chi^2$-test or Fisher’s exact test.

PRA, plasma renin activity; PAC, plasma aldosterone concentration; CEA, carcinoembryonic antigen; PSA, prostate specific antigen.
Table 2. Computed tomography (CT) findings of patients \( (n = 30) \) with adrenal ganglioneuromas (AGN) that were included in a study to investigate the CT characteristics of the lesions.

| Characteristic | All patients \( n = 30 \) | Large lesions \( > 3 \text{ cm} \) \( n = 14 \) | Small lesions \( \leq 3 \text{ cm} \) \( n = 16 \) | Statistical analyses\(^a\) |
|---------------|---------------------------|-----------------|-----------------|-------------------|
| CT values, HU |                           |                 |                 |                   |
| CTU           | 33                        | 32              | 34              | NS                |
| CTA           | 37                        | 34              | 40              | \( P = 0.049 \)   |
| CTV           | 45                        | 41              | 48              | NS                |
| DEAP          | 4                         | 2               | 6               | NS                |
| DEPP          | 12                        | 9               | 14              | NS                |
| Enhancement degree |                   |                 |                 |                   |
| None          | 7 (23.3)                  | 4 (28.6)        | 3 (18.8)        |                   |
| Mild enhancement | 18 (60.0)                | 8 (57.1)        | 10 (62.5)       |                   |
| Moderate enhancement | 5 (16.7)                 | 2 (14.3)        | 3 (18.8)        |                   |
| Enhancement potentiality | 0.4                    | 0.3             | 0.4             | NS                |
| APW, %        | 212                       | –291            | 786             | NS                |
| RPW, %        | 21                        | –21             | –21             | NS                |
| Progressive enhancement | 19 (63.3)               | 6 (42.9)        | 13 (81.3)       | \( P = 0.029 \)   |
| LD, mm        | 40.5                      | 59.1            | 24.2            | –                 |
| SD, mm        | 30.9                      | 45.2            | 18.5            | –                 |
| Mean D, mm    | 35.7                      | 52.1            | 21.3            | –                 |
| Location      |                           |                 |                 |                   |
| Left/right    | 12 (40.0)                 | 7 (50.0)        | 5 (31.3)        |                   |
| Right         | 18 (60.0)                 | 7 (50.0)        | 11 (68.8)       |                   |
| Morphology    |                           |                 |                 | \( P = 0.001 \)   |
| Round         | 3 (10.0)                  | 0 (0.0)         | 3 (18.8)        |                   |
| Oval          | 16 (53.3)                 | 4 (28.6)        | 12 (75.0)       |                   |
| Irregular     | 11 (36.7)                 | 10 (71.4)       | 1 (6.3)         |                   |
| Number of lesions |                     |                 |                 | NS                |
| Single        | 28 (93.3)                 | 13 (92.9)       | 15 (93.8)       |                   |
| Multiple \( \geq 2 \) | 2 (6.7)                  | 1 (7.1)         | 1 (6.3)         |                   |
| Preoperative CT diagnosis |               |                 |                 | NS                |
| AGN           | 17 (56.7)                 | 10 (71.4)       | 7 (43.8)        |                   |
| Adenoma       | 10 (33.3)                 | 2 (14.3)        | 8 (50.0)        |                   |
| Benign tumour | 3 (10.0)                  | 2 (14.3)        | 1 (6.3)         |                   |
| Cystic degeneration | 1 (3.3)                 | 1 (7.1)         | 0 (0.0)         | NS                |
| Haemorrhage   | 1 (3.3)                   | 1 (7.1)         | 0 (0.0)         | NS                |
| Calcification | 6 (20.0)                  | 6 (42.9)        | 0 (0.0)         | \( P = 0.003 \)   |
| ‘Pointed peach’ sign | 16 (53.3)               | 8 (57.1)        | 8 (50.0)        | NS                |
| Relapse       | 2 (6.7)                   | 2 (14.3)        | 0 (0.0)         | NS                |

Data presented as mean SD or \( n \) of patients (%).

\(^a\)Continuous data were compared using an independent two-sample \( t \)-test or the Mann–Whitney \( U \)-test based on data normality; categorical data were compared using \( \chi^2 \)-test or Fisher’s exact test.

CTU, CT value of unenhanced; CTA, CT value of arterial phase; CTV, CT value of venous phase; DEAP, degree of enhancement in arterial phase; DEPP, degree of enhancement in portal venous phase; APW, absolute percentage washout; RPW, relative percentage washout; LD, long diameter; SD, short diameter; NS, no significant between-group difference \( (P \geq 0.05) \).
irregular mass, while 75.0% (12 of 16) small AGNs manifested as oval masses. Figure 2 shows the CT scans for a 32-year-old female with a large adrenal tumour (a mean diameter of 112 mm) that had an irregular shape. Of the 30 patients, the majority of AGNs (93.3%; 28 of 30) had a single lesion. Only two patients had two lesions with an equal distribution between the large and small AGNs. Figure 3 shows the CT scans for a 52-year-old male with two well-defined lesions in the left adrenal area. The accuracy of the CT diagnosis of the AGNs before the surgery was undertaken was 71.4% (10 of 14) in large AGNs and 43.8% (seven of 16) in small AGNs. Half of the small AGNs (50%; eight of 16) were diagnosed as adrenal adenomas. The presence of calcification was significantly different between the two groups; 42.9% (six of 14) of the large AGNs demonstrated multiple punctate calcifications, whereas none of the small AGNs exhibited calcifications ($P < 0.05$). Figure 4 shows the CT scans for a 28-year-old male with an oval tumour that had multiple punctate calcifications. The presence of haemorrhage, ‘pointed peach’ sign and relapse were not significantly different between the two groups. The ‘pointed peach’ sign appeared frequently in both large AGNs (57.1%; eight of 14) and small AGNs (50.0%; eight of 16). Figure 5 shows
the CT scans for a 16-year-old male with an oval, well-defined tumour that had a typical ‘pointed peach’ sign. Among the entire cohort, two patients in the large AGN group had recurrences at 5 months and 1 year after excision during a mean follow-up of 50 months.

Discussion
To the best of our knowledge, the present report describes the largest series of AGNs in which the CT characteristics have been described in detail. These current results show that this disease appears to occur in women and men equally, which is similar to previous reports of AGNs.\textsuperscript{14–16} Unlike previous reports that demonstrated that AGNs mostly occur in older children and young adults,\textsuperscript{6,17} the mean ± SD age in this current retrospective study was 41.1 ± 12.4 years (range, 16–74 years). As shown in other case reports on AGNs, 63–93\% of patients were asymptomatic.\textsuperscript{9,18} In the current study, asymptomatic patients accounted for 76.7\% (23 of 30) and the remainder showed nonspecific symptoms such as abdominal pain, hypertension and hyperglycaemia. It was not clear whether these nonspecific symptoms were helpful in terms of making a diagnosis of AGN. Typically, AGNs are clinically silent and asymptomatic even when they are large because they do not usually excrete excessive levels of catecholamines or steroid hormones.\textsuperscript{17} The clinical features for the

![Figure 2. Representative computed tomography (CT) scans of a 32-year-old female with pathologically-confirmed adrenal ganglioneuroma. (a) A plain CT scan showed an irregular-shaped and heterogeneous tumour with a mean diameter of 112 mm (white arrow); (b and c) dynamic enhanced CT scans showed the peripheral pancreas and right kidney were pushed by this large adrenal tumour. Note the blood vessels (black arrows) crossed the lesion without invasion. The preoperative CT diagnosis was adrenal ganglioneuroma.](image)
diagnosis of AGNs are described as inadequate. A definite diagnosis of AGNs is based on the typical pathological features that are found in the adrenal tumour specimen.\textsuperscript{15,19} In this current study, the surgical procedures provided ample tissue for a definite pathological diagnosis.

It has been reported that adrenal tumours that are larger than 3 cm are likely to be functional, while those that are less than 3 cm are not.\textsuperscript{12} In addition, tumour size is a crucial decisive factor for the prognosis of adrenal tumours.\textsuperscript{7} Hence, this current study analysed the AGNs based on their tumour size using a cut-off medium diameter of 3 cm. The current results demonstrated that there was no difference in location between large and small AGNs, which was consistent with a previous report.\textsuperscript{15} In this current study, the CTU, CTA and CTV values in the small AGNs were larger than those of the large AGNs, but only CTA was significantly different ($P < 0.05$). Meanwhile, DEAP, DEPP, ED and EP were not significantly different between the two groups. These current results are consistent with previous observations that the CTU of AGNs varied from 20 to 46 HU.\textsuperscript{9,10,20–22} Compared with large AGNs, small AGNs were more likely to have progressive enhancement ($P < 0.05$). A possible mechanism for this progressive enhancement is that the contrast agent accumulates in the extracellular space due

![Figure 3. Representative computed tomography (CT) scans of a surgery-confirmed adrenal ganglioneuroma in a 52-year-old male. (a) A plain CT scan depicted two well-defined lesions in the left adrenal area without local necrosis and haemorrhage (arrows); (b and c) dynamic enhanced CT scans showed homogeneous and non-obvious enhancement. The CT values of the unenhanced, arterial and venous phases were 32, 32 and 36 Hounsfield units, respectively. The two lesions were regarded as benign tumours following preoperative CT.](image-url)
to the appearance of profuse myxoid matrix. These findings suggest that small AGNs have a larger amount of homogeneous myxoid matrix than large AGNs since large AGNs tend to develop cystic degeneration, haemorrhage and calcification.

In this current study, the majority of the large AGNs (71.4%; 10 of 14) were of an irregular shape, whereas the majority of the small AGNs (93.8%; 15 of 16) were round or oval (*P* <0.05). Round, oval shapes are regarded as a benign appearance, while the irregular shape is associated with a malignant phenotype. It is our opinion that small AGNs usually have a round and homogenous morphology that is similar to adrenal adenomas. This was consistent with the current findings that half of the small AGNs were misdiagnosed as adrenal adenomas prior to surgery. Usually, adrenal adenomas are less than 5 cm in diameter and have a rapid washout of more than 50% after contrast. In contrast, large AGNs are typically large, heterogeneous and can mimic adrenocortical carcinomas. As was the finding in most of the current patients, the majority of small and large AGNs consisted of single lesions and no significant difference was detected between the two groups. In this current study, 7.1% (one of 14) of the large AGNs had cystic degeneration and haemorrhage, but none of the small AGNs had these pathological features. Previous

![Representative computed tomography (CT) scans of a 28-year-old male that had a slightly higher than normal carcinoembryonic antigen level. (a) A plain CT scan revealed an oval tumour with heterogeneous attenuation in the left adrenal gland and multiple punctate calcifications (arrow); (b and c) dynamic enhanced CT scans showed heterogeneous enhancement. The preoperative CT diagnosis was adrenal adenoma.](image)
Reports demonstrated rates of calcification in AGNs of 30–60%. Of the 30 patients, six large AGNs (42.9%) had calcifications on CT, but none was observed in the small AGNs ($P < 0.05$). The presence of calcifications has been reported to be a characteristic feature for the diagnosis of AGNs. Microscopically, AGNs are characterized by the irregular proliferation of spindle-shaped cells and sporadically dystrophic calcifications due to ganglion cells. The ‘pointed peach’ sign means the tumour is embedded along the space of the surrounding organs and the blood vessels, but does not invade the vascular wall and vascular cavity, which is another characteristic of AGNs. In this current study, 57.1% (eight of 14) of the large AGNs and 50.0% (eight of 16) of the small AGNs displayed the ‘pointed peach’ sign. The outcomes of AGNs after surgical resection were excellent in the current study, with only two patients in the large AGN group experiencing recurrences at 5 months and 1 year after excision during a mean follow-up of 50 months.

This retrospective study had several limitations. First, the retrospective nature of the study was a limitation due to the risk of selection bias, but it is the only study design that is viable for a tumour that is as rare as AGN. Secondly, the CT images were acquired using three different CT scanners and this may have influenced the findings. Although this current study included a relatively large number of patients, more samples are needed to support these CT findings.

Figure 5. Representative computed tomography (CT) scans of a 16-year-old male with an adrenal ganglioneuroma. (a) A plain CT scan depicted an oval, well-defined tumour with homogeneous density in the left adrenal gland and a typical ‘pointed peach’ sign was observed (white arrow); (b and c) dynamic enhanced CT scans displayed good homogeneous enhancement. The tumour was embedded along the space of the surrounding organs and the blood vessels, but did not invade the vascular wall and vascular cavity (black arrow). The preoperative CT diagnosis was consistent with the final pathological diagnosis.
In conclusion, the present study reports on the largest series of CT features in AGNs to date. AGNs are rare tumours that seldom present with any clinical symptoms. Most AGNs occur in adults with an equal incidence in females and males. The CT scan imaging characteristics of AGNs are helpful in distinguishing between large and small AGNs. Small AGNs have a higher CTA value than large AGNs. Progressive enhancement is more likely in small AGNs. Large AGNs usually have an irregular shape, while small AGNs are round and oval. The presence of calcification might support a diagnosis of a large AGN. The ‘pointed peach’ sign is another characteristic that might help in the diagnosis of AGNs. The outcomes of AGNs were excellent after surgical excision.

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