Endocr (2009) 35:293–296
DOI 10.1007/s12020-009-9180-4

CASE REPORT

Adrenal ganglioneuroma: report of a new case

Cihangir Erem · Ozge Ucuncu · Irfan Nuhoglu · Akif Cinel · Umit Cobanoglu · Adem Demirel · Ekrem Koc · Mustafa Kocak · Gulname Fındık Guvendi

Received: 17 November 2008 / Accepted: 24 March 2009 / Published online: 15 April 2009

Abstract Although adrenal ganglioneuroma (GN) is a rare tumor originating from the neural crest tissue of the sympathetic nervous system, detection of this tumor has increased, as imaging procedures such as ultrasonography (US) and computed tomography (CT) have become prevalent. The clinical presentation for most patients is asymptomatic, and most of those tumors are hormone silent. We describe a case of adrenal GN incidentally diagnosed in a 68-year-old female patient. Physical examination, routine laboratory studies, and hormonal tests were within normal ranges. Abdominal CT and magnetic resonance imaging showed a solid oval tumor approximately 6 × 4 cm in the left adrenal gland without remarkable signs of malignancy. Left adrenalectomy was performed for treatment purposes. Histological diagnosis of the tumor was a ganglioneuroma originating from the adrenal medulla. Adrenal GN occurs rarely in adults and preoperative diagnosis is difficult, especially in asymptomatic cases. It needs careful evaluation and surgical treatment. According to our knowledge, this is the fifth case of adrenal GN in an adult patient from Turkey in English literature.

Keywords Adrenal gland · Ganglioneuroma · Incidentaloma

C. Erem · O. Ucuncu · I. Nuhoglu · A. Demirel · M. Kocak
Department of Internal Medicine, Karadeniz Technical University, Trabzon, Turkey

A. Cinel · E. Koc
Department of General Surgery, Karadeniz Technical University, Trabzon, Turkey

U. Cobanoglu · G. F. Guvendi
Department of Patology, Karadeniz Technical University, Trabzon, Turkey

C. Erem (✉)
K.T.Ü. Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Endokrinoloji ve Metabolizma Hastalıkları Bilim Dalı, 61080 Trabzon, Turkey
e-mail: cihangirerem@hotmail.com

Introduction

Ganglioneuroma (GN) is a rare benign, differentiated, slow-growing neoplasm arising from neural crest tissue and is composed of mature ganglion cells and Schwann's cells in a fibrous stroma [1–3]. The incidence of ganglioneuromas is unknown. They may arise anywhere along the paravertebral sympathetic plexus [3]. Their localization is the retroperitoneal (32–52%), mediastinal (39–43%), or cervical region (8–9%) [3–5]. Only a small proportion of GNs are of adrenal origin and occur most commonly in children and young adults [2].

Characteristically, ganglioneuromas do not secrete excess catecholamines or steroid hormones. They are often clinically silent and asymptomatic tumors even if they are large [3]. As imaging procedures such as ultrasonography (US) and computed tomography (CT) have become more widely performed, the number of GNs found incidentally has increased [6, 7]. However, it is difficult to diagnose these tumors precisely as GN preoperatively. Definitive diagnosis is done by histological examination. Assessment and management of the adrenal GNs are similar to those of other adrenal tumors [8, 9]. We present an adult case report of adrenal GN incidentally diagnosed in a 68-year-old female patient. Histopathological examination of the adrenal mass confirmed the diagnosis.

Case report

A 68-year-old female, who presented with nausea and vomiting, was diagnosed as having antral gastritis by upper gastrointestinal endoscopy. During investigation of this disease, a heterogenous, hypoechogenic left adrenal solid mass, measuring 63 × 40 × 28 mm, was incidentally detected of abdominal US (Fig. 1), and he was referred to our clinic for further examination. Blood pressure was normal. Physical examination demonstrated no significant finding. Tension Holter monitoring revealed normal blood pressure. Routine laboratory tests were normal. Endocrine tests, including plasma aldosteron concentration (PAC), plasma renin activity (PRA), PAC/PRA ratio, intact parathyroid hormone (iPTH), serum calcitonin, cortisol and adrenocorticotropin hormone (ACTH) levels, diurnal cortisol rhythms, 24-h urinary free cortisol, androgen hormones, 24-h urinary catecholamines, and their metabolites were within normal ranges.

Abdominal CT showed a well-demarcated, homogenous, hypodense left adrenal solid mass (60 × 50 × 30 mm) with faint calcifications, and a slightly lobular edge. On T_1-weighted abdominal magnetic resonance imaging (MRI), the tumor was visualized as a heterogenous mass (60 × 45 mm) with a low signal intensity (hypointense) below that of the liver, but predominantly greater than that of muscle, located in the left adrenal gland (Fig. 2a). T_2-weighted MRI revealed a heterogenous hyperintense mass measuring 60 × 45 mm with calcification in central of tumor, located in left adrenal gland (Fig. 2b). Out-of-phase MRI did not show significant signal loss in the lesion when compared with in-phase MRI (Fig. 2c).

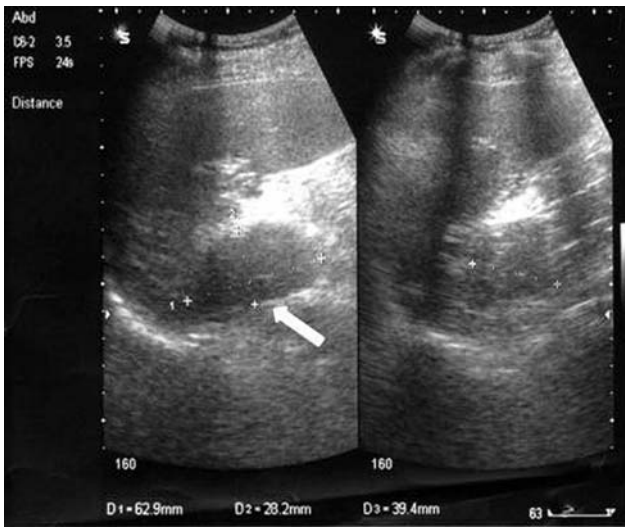

Fig. 1 Abdominal US shows a heterogeneous hypoechogenic left adrenal solid mass measuring 63 × 40 × 28 mm (*arrow*)

Characteristics on MRI were not in favor of the diagnosis of adrenocortical adenoma. A ^{131}Iodine-metaiodobenzylguanidine (^{131}I-MIBG) scan could not be performed.

From these findings, we suspected the tumor to be a GN as a higher probability or carcinoma as a lower probability arising from the left adrenal gland. Left adrenalectomy was performed by the transabdominal route under general anesthesia. The resected tumor was well circumscribed, measured 75 × 60 × 30 mm in dimension, and it was encapsulated. The cut surface of the tumor was solid with whitish gray color without evidence of hemorrhage or necrosis. Microscopically, the sections showed irregular proliferation by spindle-shaped cells and occasionally scattered mature ganglionic cells with dystrophic calcification and focal lymphocytic infiltration (Fig. 3a, b). Spindle-shaped cells were strongly stained with monoclonal antibody to S-100 protein, and ganglionic cells were stained with monoclonal antibody to neuron-specific enolase, synaptophysin, and chromogranin-A (Fig. 4a, b). The specimen did not show any evidence of malignant degeneration histologically. The histological diagnosis was adrenal GN. Eight weeks after the operation, she was well and had no tumor recurrence.

Discussion

GNs are rare and well-differentiated tumors in the neuroblastoma series of tumors [6, 10]. They should be distinguished from the other groups because they are considered benign and constituted by mature sympathetic ganglion cells [10, 11]. They usually occur in older children and young adults and are the most common sympathetic nervous system tumor in adults [8, 12]. Most GNs are located in the posterior mediastinum and retroperitoneum [8]. The GN occurs only rarely in the adrenal medulla [1, 6–9, 12–14]. To our knowledge, our case is a fifth report that describes adrenal GN from Turkey in the English literature

The clinical presentation of the most patients with adrenal GN is asymptomatic, and most of these tumors are hormone silent [7] as in the present case. Although GNs are generally considered to be non-secretory, some GNs are endocrinologically active [1, 8, 15, 16].

Corcerning the imaging characteristics of adrenal GN, US shows a homogenous, hypoechogenic solid mass with well-defined borders. However, US is not useful for determining the quality of the adrenal mass [6, 17, 18]. On CT, this tumor commonly appears as a well circumscribed with an oval shape and tends to partially or completely surround major blood vessels [6, 17]. The tumor is usually a homogenous, hypodense mass. Adrenal GN is homogenous mass with a signal intensity less than that of liver on T_2-weighted MRI and as a hetorogenous mass with a

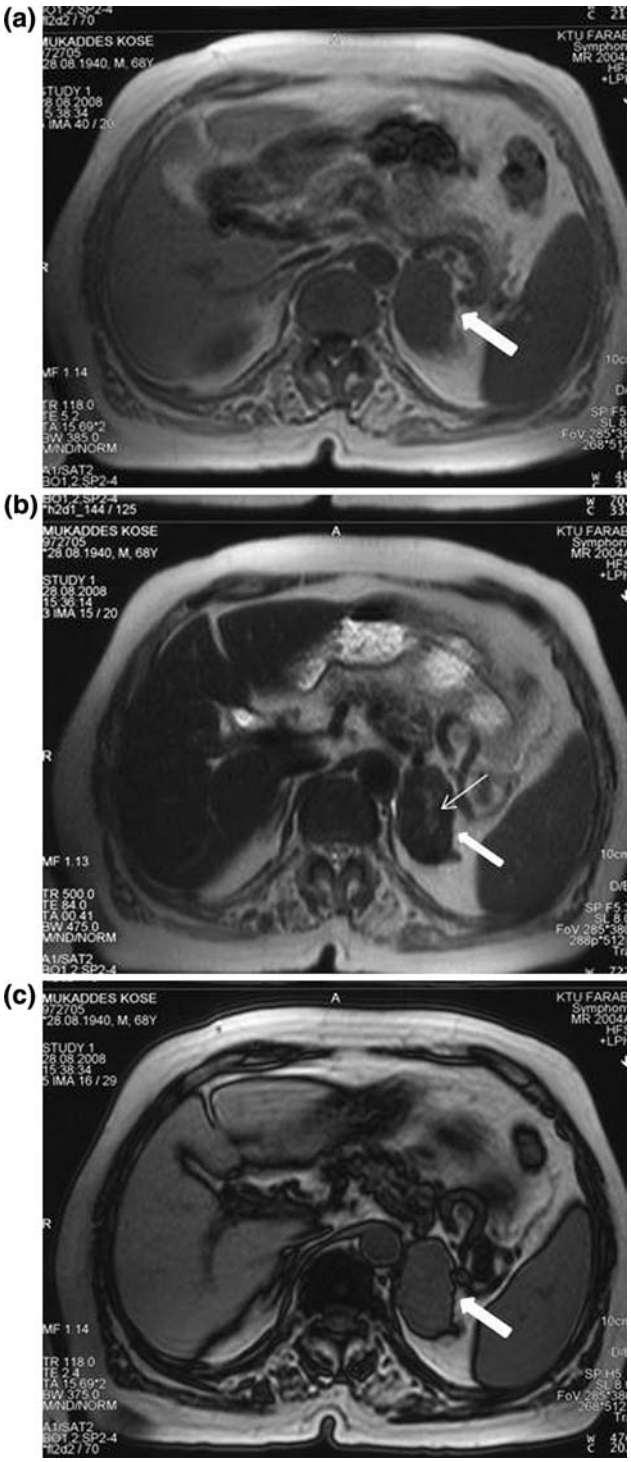

Fig. 2 **a** Transverse T1-weighted MRI shows an oval, slightly lobulated left adrenal mass that measures 60 × 45 mm (*arrow*). The mass is homogeneous, with signal intensity less than that of liver (hypointense). **b** Transverse T_2-weighted MRI scan demonstrating oval heterogeneous mass (*thick arrow*) with slightly high signal intensity greater than that of liver and with central crescent-shaped calcifications in adrenal mass (slightly hyperintensity) (*thin arrow*). **c** Out-of-phase MRI not showing significant signal loss in the lesion when compared with in-phase MRI (*arrow*)

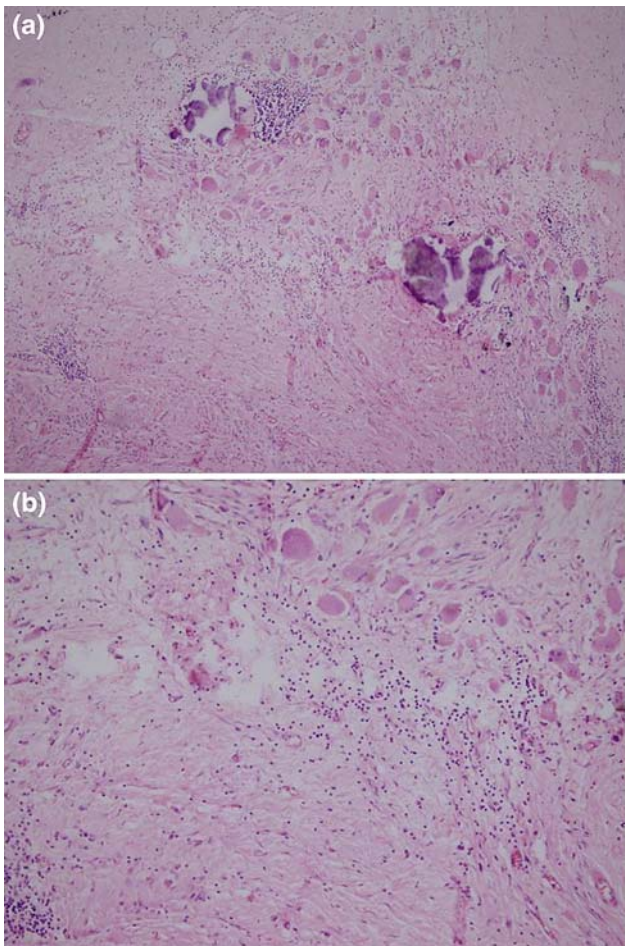

Fig. 3 **a** The tumor showing multiple mature ganglion cells in Schwannian cell dominant stroma with focal lymphocytic infiltration (hematoxylin and eosin staining, original magnification ×100), **b** Microscopic findings show scattered mature ganglionic cells in background of spindle shaped cells (Schwann cells), (hematoxylin and eosin staining, original magnification ×400)

predominant high signal intensity on T_2-weighted MR images as in the present case [6, 17]. It reveals no absolute change in signal intensity on chemical shift imaging (Fig. 2c). It has been suggested that heterogeneity may help distinguish GN from other adrenal masses that have high signal intensity on T_2-weighted images [19].

The indication of laparoscopic surgery for adrenal mass is somewhat doubtful. Because the likehood of adrenal cancer has been revealed to increase in adrenal lesions with a diameter greater than 6 cm, a recent National Institutes at Health State-of-the-Science Statement recommended that non-secretory adrenal incidentalomas larger than 6 cm or with suspicious features of malignancy on imaging procedures should be treated using adrenalectomy because of the increased prevalence of malignancy [6]. In the present case, open left adrenalectomy was preferred, because laparoscopic surgery increases the risk of tumor recurrence.

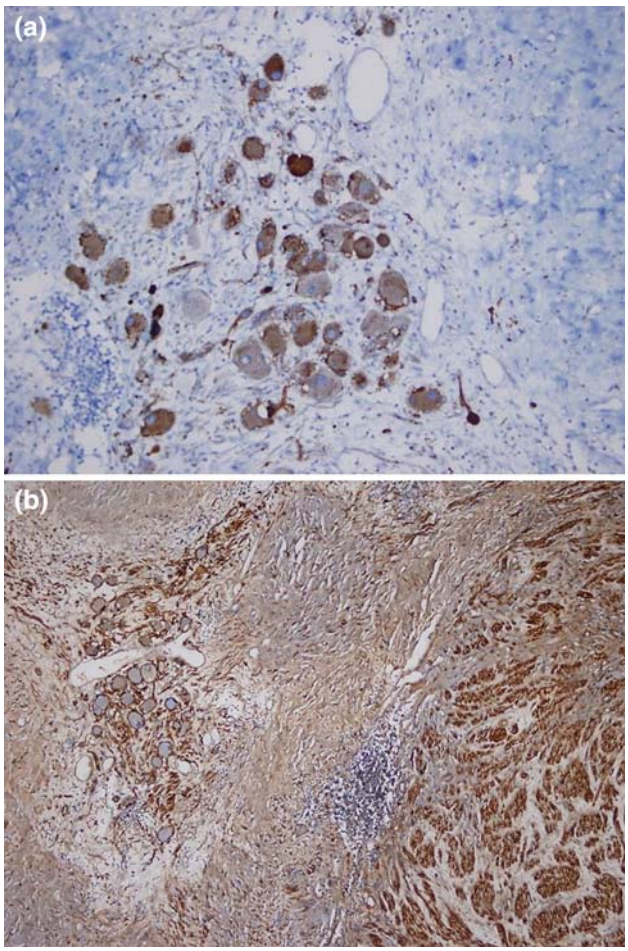

Fig. 4 **a** Neoplastic ganglionic cells were positive for synaptophysin (immunoperoxidase staining, ×200), **b** Spindle-shaped sustentacular cells (Schwann cells) stained brown for S-100 protein (immunoperoxidase staining, ×100)

Grossly, GNs are large, encapsulated masses of firm consistency with a homogenous, solid, grayish-white cut surface. Microscopically, they are of two subtypes. The mature subtype consists of a spindle cell tumor resembling a neuroblastoma but has fascicles composed of neuritic processes, Schwann cells, and perineural cells and shows numerous ganglion cells [14]. The maturing subtype has a similar stroma but with ganglion cells of differing maturation, from fully mature ones to neuroblasts. On immunohistochemical analysis, they are characterized by reactivity with S-100 and neuronal markers such as NSE and synaptophysin [20]. The present case was concordant with the mature subtype of GN.

In conclusion, adrenal GN occurs rarely in adults and preoperative diagnosis is difficult, especially in asymptomatic cases. It needs careful evaluation and surgical treatment. According to our knowledge, this is a rare case of non-functioning GN presenting as an incidental adrenal mass in an adult patient.

References

1. C. Erem, M. Kocak, A. Cinel, H.O. Ersoz, A. Reis, Dopamine-secreting adrenal ganglioneuroma presenting with paroxysmal hypertension attacks. Saudi. Med. J. **29**, 122–125 (2008)
2. F. Arredondo Martínez, M. Soto Delgado, A. Benavente Fernández, B. Basquero González, A. Zurera Cosano, R. Linares Armada, Adrenal ganglioneuroma. Report of a new case. Actas. Urol. Esp. **27**, 221–225 (2003)
3. G.N. Zografos, K. Kothonidis, C. Ageli, N. Kopanakis, K. Dimitriou, E. Papaliodi, G. Kaltsas, M. Pagoni, G. Papastratis, Laparoscopic resection of large adrenal ganglioneuroma. JSLS **11**, 487–492 (2007)
4. T. Ichikawa, A. Koyama, H. Fujimoto, M. Honma, T. Saiga, N. Matsubara, Y. Ozeki, N. Arimizu, Retroperitoneal ganglioneuroma extending across the midline: MR features. Clin. Imaging **17**, 19–21 (1993)
5. S.E. Rha, J.Y. Byun, S.E. Jung, H.J. Chun, H.G. Lee, J.M. Lee, Neurogenic tumors in the abdomen: tumor types and imaging characteristics. Radiographics **23**, 29–43 (2003)
6. K. Yamaguchi, I. Hara, M. Takeda, K. Tanaka, Y. Yamada, M. Fujisawa, G. Kawabata, Two cases of ganglioneuroma. Urology **67**, 622.e1–622.e4 (2006)
7. C.L. Chen, S.T. Huang, P.L. Chang, K.F. Ng, Adrenal ganglioneuroma: report of five cases. Chang. Gung. Med. J. **23**, 550–554 (2000)
8. V. Çelik, G. Ünal, R. Özgültekin, S. Göksel, H. Ünal, A. Çerçel, Adrenal ganglioneuroma. Br. J. Surg. **83**, 263 (1996)
9. R. Gupta, A.K. Dinda, Ganglioneuroma of the adrenal gland: a rare case. Indian J. Pathol. Microbiol. **50**, 782–784 (2007)
10. G. Cerullo, D. Marrelli, B. Rampone, C. Miracco, S. Caruso, M. Di Martino, M.A. Mazzei, F. Roviello, Presacral ganglioneuroma: a case report and review of literature. World J. Gastroenterol. **13**, 2129–2131 (2007)
11. V.S. Ghali, J.E. Gold, R.A. Vincent, J.M. Cosgrove, Malignant peripheral nerve sheath tumor arising spontaneously from retroperitoneal ganglioneuroma: a case report, review of the literature, and immunohistochemical study. Hum. Pathol. **23**, 72–75 (1992)
12. J.R. Leavitt, D.L. Harold, R.B. Robinson, Adrenal ganglioneuroma: a familial case. Urology **56**, 508 (2000)
13. C.A. Koch, F.M. Brouwers, K. Rosenblatt, K.D. Burman, M.M. Davis, A.O. Vortmeyer, K. Pacak, Adrenal ganglioneuroma in a patient presenting with severe hypertension and diarrhea. Endocr. Relat. Cancer **10**, 99–107 (2003)
14. M. Gültekin, P. Dursun, C. Salman, O. Ozyüncü, A. Saglam, T. Küçükali, A. Ayhan, Ganglioneuroma mimicking ovarian tumor: a report of a case and review of the ganglioneuromas. Arch. Gynecol. Obstet. **271**, 66–68 (2005)
15. A. Tosaka, M. Ando, C. Arisawa, T. Okano, Endocrinologically active retroperitoneal ganglioneuroma with positive iodine-131-metaiodobenzylguanidine scintigraphy. Int. J. Urol. **6**, 471–474 (1999)
16. K. Lucas, M.J. Gula, A.S. Knisely, M.A. Virgi, M. Wollman, J. Blatt, Catecholamine metabolites in ganglioneuroma. Med. Pediatr. Oncol. **22**, 240–243 (1994)
17. R. Radin, C.L. David, H. Goldfarb, I.R. Francis, Adrenal and extra-adrenal retroperitoneal ganglioneuroma: imaging findings in 13 adults. Radiology **202**, 703–707 (1997)
18. G.J. Lonergan, C.M. Schwab, E.S. Suarez, C.L. Carlson, Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma: radiologic–pathologic correlation. Radiographics **22**, 911–934 (2002)
19. A.D. Serra, R.B. Rafal, J.A. Markisz, MRI characteristics of two cases of adrenal ganglioneuromas. Clin. Imaging **16**, 37–39 (1992)
20. P. Kleihues, W.K. Cavenee, *Classification of Tumors, Pathology and Genetics of Tumors of the Nervous System*, (World Health Organization, Lyon, 2000), pp. 153–161