CASE REPORT

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An Extra-adrenal Pheochromocytoma Presenting with Spontaneous Intracerebral Hematoma

Seong-Keun Park, M.D., Jung-Kil Lee, M.D., Jae-Hyoo Kim, M.D., Soo-Han Kim, M.D.

Department of Neurosurgery, Chonnam National University Hospital, Medical School, Gwangju, Korea

We report a 18-year-old man, who has been taking antihypertensive medication for 1month in a local clinic, presented with a sudden onset headache followed by left blindness. He experienced palpitation and chest discomfort during physical exertion since 2years before admission, but unfortunately has been ignored. Brain CT showed intracerebral hemorrhage in the left temporoparietal area, but cerebral angiogram and magnetic resonance image revealed no vascular anomaly. He was managed conservatively, and headache and visual loss were improved over time. Subsequently, on the evaluation of hypertension, he was diagnosed as having extra-adrenal pheochromocytoma on left paraaortic area from the results of endocrinological evaluations, abdominal CT scan, and ^{131}I-MIBG scintigraphy.

KEY WORDS : Spontaneous intracerebral hematoma · Extra-adrenal pheochromocytoma · Secondary hypertension.

Introduction

Pheochromocytoma is a rare but well-known cause of secondary hypertension and about 10% of pheochromocytomas in adult have been reported to develop at extra-adrenal sites[2,6,10]. Only 0.5% of hypertensive patients have pheochromocytomas, but it is imperative that the condition be diagnosed early to avoid its devastating complications. Among these complications, spontaneous intracerebral hemorrhage are unusual but fatal complication, and the incidence of cerebral hemorrhage caused by extra-adrenal pheochromocytoma is extremely rare.

We report a rare case of 18-year-old patient with spontaneous intracerebral hemorrhage with unrecognized extra-adrenal pheochromocytoma.

Case Report

Presentation

A 18-year-old man suffering from a sudden onset headache followed by blindness was brought to the emergency room. From 1month ago, he had taken antihypertensive medication in local clinic.

Examination

On admission, the patient was drowsy mental state and blood pressure was 190/100mmHg. Computed tomographic(CT) scan showed a intracerebral hemorrhage at left temporoparietal area. He was managed conservatively. Headache and visual acuity were improved day by day, but paroxysmal elevation of blood pressure. Cerebral angiogram and magnetic resonance image, obtained 1week later, revealed no vascular anomaly (Fig. 1A, B). Laboratory investigations revealed elevated urinary vanillylmandelic acid(VMA)12.5mg/day (normal $<$ 8mg/ day) and metanephrine 5.4mg/day (normal $<$ 1.2mg/ day). Abdominal CT scan demonstrated a welldefined, 3.6 $\times$ 3cm sized enhancing mass with internal cystic component in left paraaortic area (Fig. 2). ^{131}I-metaiodobenzylguanidine (MIBG) scintigraphy showed a high uptake of tracer in the same area (Fig. 3). Hypertension in the form of paroxysmal attacks was adequately controlled with alpha, beta and calcium channel blockers.

Operation

Total resection of the tumor was achieved via retroperitoneal approach with left subcostal incision in the department of Urology. Intraoperative manipulation of the mass caused ele-

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• Address for reprints : Jung-Kil Lee, M.D., Department of Neurosurgery, Chonnam National University Hospital, Medical School, 8 Hak-dong, Dong-gu, Gwangju 501-757, Korea Tel : +82.62-220-6602, Fax : +82.62-224-9865, E-mail : jklee0261@yahoo.com

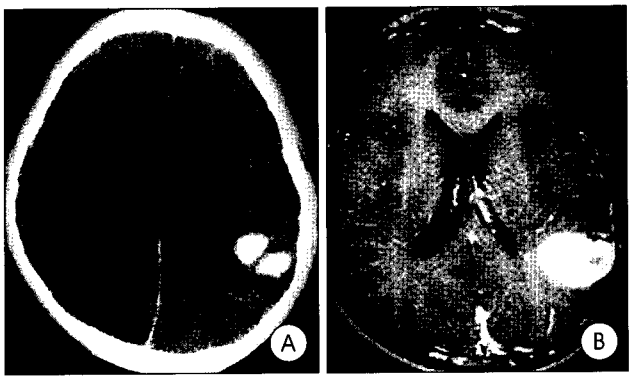

Fig. 1. A : Nonenhanced computed tomography demonstrating intracerebral hemorrhage in the left temporoparietal region, B : Magnetic resonance image(T1-weighted contrast enhanced image) showing a subacute hemorrhage in the left temporoparietal region without vascular anomaly.

Fig. 2. Contrast-enhanced abdomi-nal computed tomography showing a well-defined, 3.6°×3cm sized enhancing mass with internal cystic component in the left paraaortic area.

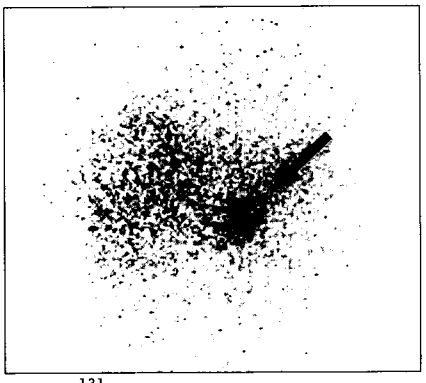

Fig. 3. ^{131}I-MIBG scintigraphy reve-aling an abnormal high uptake of tracer in the left paraaortic area.

vation of the blood pressure up to 200/110mmHg. After removal, the blood pressure promptly fell to 120/70mmHg.

Postoperative Course

Postoperatively, the patient improved rapidly and was discharged on the 7th postoperative day. One month after the abdominal surgery, the patient was free of symptoms and normotensive without medication, and urinary vanillylmandelic acid (VMA) and metanephrine level returned to normal (VMA 3.3mg/ day and metanephrine 0.2mg/ day).

Pathological examination

In gross appearance, the mass measured 5.2×3×2.7cm. The mass appeared to be well encapsulated and was reddish-brown in color, soft and rubbery in consistency. On the cut surface areas of focal hemorrhage were noted with some translucent areas and firmer yellowish ones, so that the tumor had a mottled appearance. Microscopically, the specimen discloses well defined tumor cell nest (Zellballen) bound by a delicate fibrovascular stroma. The cells vary considerably in size and shape and had a finely granular basophilic cytoplasm, and round to ovoid nuclei with prominent nucleoli. Minimal mitotic figures are noted. The capsule is intact and vascular invasion by tumor cell was not noted. Histopathologic findings of the mass proved to be a pheochromocytoma. Immunohistochemical stain showed strong immunoreactivity to chromogranin and synaptophysin (Fig. 4A, B).

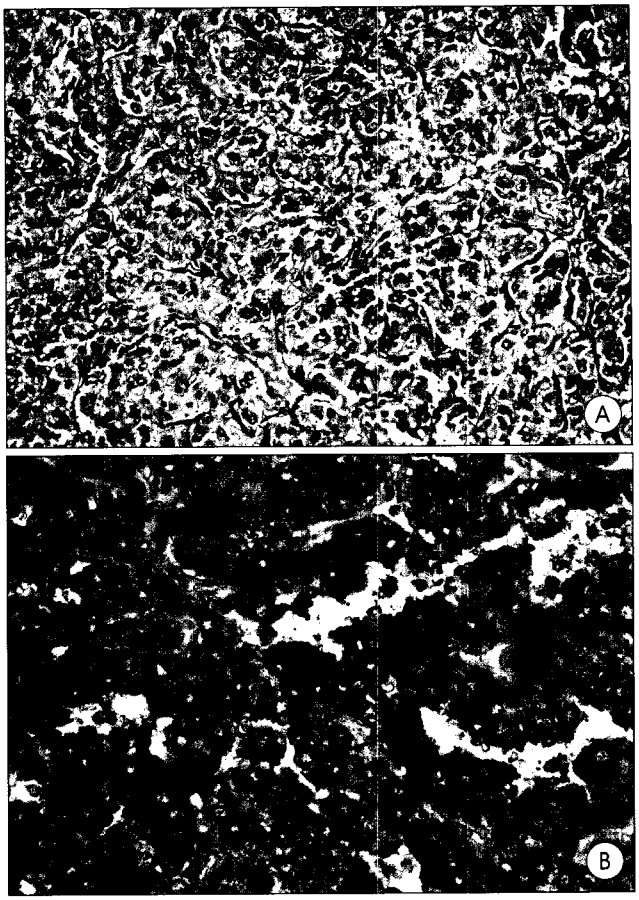

Fig. 4. Photomicrographs of tumor specimens showing well defined tumor cell nest(Zellballen) bound by a delicate fibrovascular stroma. The cells vary considerably in size and shape and had a finely granular basophilic cytoplasm, and round to ovoid nuclei with prominent nucleoli (A, H&E, ×100), and were positive for chromogranin stain (B, chromogranin stain, ×200).

Discussion

Pheochromocytomas are functionally active tumors of sympathetic nerve cells that most commonly occur in the adrenal medulla but can also develop in extra-adrenal sites. These tumors produce epinephrine and norepinephrine, and thus cause sustained or paroxysmal hypertension[3].

Their incidence in all hypertensive patients is estimated at 0.1% to 1%[9,11]. Among those diseases that are followed by secondary hypertension, pheochromocytoma is considered to often be accompanied by complications in other organs, however, cerebrovascular disease is very serious but its incidence is comparatively low. Thomas et al reported that cerebral infarction was found in 3% and cerebral hemorrhage was in 2% out of 100 studied cases[10,12,14]. Pheochromocytomas have been called 10percent tumors, since roughly 10percent are bilateral, 10percent are malignant, and 10percent are extraadrenal in location[3,11]. In the abdomen, extraadrenal chromaffin tissue is found in the paravertebral ganglia and plexuses along the aorta. The largest collection is in the organs of Zuckerkandl, located between the root of the inferior mesenteric artery and the aortic bifurcation. Failure of involution of this tissue with subsequent neoplastic transformation results in the developement of extra-aderenal phechromocytomas[6].

Pheochromocytomas are noted for its protean manifestations. Its diagnosis can be expeditiously made only in clinicians maintain a high index of suspicion. The clinical suspicion of a pheochromocytoma may be suggested by certain clinical signs and symptoms, especially hypertension with a characteristic triad : headache, diaphoresis, and palpitations. Additionally, compared with general hypertensive cerebral hemorrhage, cerebral hemorrhage due to pheochromocytoma is found more often in a comparatively younger group (24~54years old), which is similar to the range of ages where pheochromocytoma often develops[9,10]. Therefore, when cerebral hemorrhage was found in the younger group, development of this disease must be suspected[8]. The symptoms of hypertension in the patients with pheochromocytoma may be classified mainly into constant type, paroxysmal type, and normal blood pressure type[10].

The most important confirmation study is the biochemical finding of excessive catecholamine production by the tumor, and radiological studies for the localization of a suspected mass[5]. The biochemical tests for pheochromocytoma are based on detecting abnormally increased levels of several different free catecholamines or metabolites in urine or blood and are routinely used in the evaluation of hypertensive patients. They are the measurement of the 24-hr urinary excretion of free catecholamines, and the metabolites such as total metanephrines, and vanillylmandelic acid (VMA)[5]. Accurate tumor localization is an essential part of pheochromocytoma management. The three imaging techniques of choice are CT, MRI, and 131I-MIBG scan. Abdominal CT has accuracy for detection more than 90% but dose not aid in differential diagnosis from other adrenal lesion or malignancy. Abdominal MRI is accurate as CT in identifying lesion and tumor shows characteristic bright, "light bulb" image on T2WI. MRI shows excellent anatomic information of surrounding vessels. It should be initial scanning procedure in patients with biochemical finding of pheochromocytoma. MIBG scan shows anatomic and functional characterization and image of medullary tissue through catecholamine pump. It is useful in search for residual or multiple pheochromocytoma and highly sensitive and useful, especially when CT and MRI findings are negative or confusing. It has overall sensitivity 87.4%, and specificity 99%.

Macroscopically, tumors are usually encapsulated, the cut surface being dark, with hemorrhagic areas and areas of necrosis. The microscopic features are characteristic small clusters (Zellballen) separated by delicate vascular stroma. The cells had a finely granular basophilic cytoplasm with dark neurosecretory granules that contain catecholamines[2].

Complete surgical excision is the goal of treatment, but should only be carried out as an elective procedure after the most careful preoperative preparations with adrenergic blockade and meticulous intraoperative blood pressure control[11]. Hypertension persists in 10% to 35% of patients after successful resection of pheochromocytomas. However, the hypertension is relatively easy to control requiring minimal medications. Patients should be followed up for persistent hypertension apart from the possibility of tumor recurrence even after resection of apparently benign tumors[1].

Cerebral infarction and intracerebral hemorrhage are well-known but rare complications of pheochromocytoma. Intracerebral hemorrhage as a secondary complication of pheochromocytoma is occasionally reported, but compared with general hypertensive cerebral hemorrhage, this disease is found more often in a comparatively younger group. Therefore, when cerebral hemorrhage was found in the younger group or hypertensive patients with sign of sympathetic hyperactivity, phechromocytoma as a secondary cause of hypertension must be suspected[10,12].

Conclusion

We encountered a rare case of spontaneous intracerebral hemorrhage in young adult caused by a concomitant extra-adrenal pheochromcytoma. Pheochromocytoma constitutes very rare cause of secondary hypertension. However, its diagnosis is important because hypertension is usually curable by resection of the tumor, whereas it is potentially lethal if untreated and associated with long-term morbidity. Pheochromocytoma must be considered in the differential diagnosis in hypertensive patients with signs of sympathetic hyperactivity. Our case illustrates the importance

of a careful search for remedial cause of hypertension in children and young adults with spontaneous intracerebral hemorrhage.

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