Case Report

A Case of Anterior Mediastinum Paraganglioma Presented with Pericardial Effusion Two Years before Symptoms of Catecholamine Excess: First Case Report in Thailand

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Pheochromocytoma (PCC) and paraganglioma (PGL) are uncommon tumors. Clinical manifestations are mass effect or hormone secretion. The initial manifestation with pericardial effusion is rare. The author presented a case of anterior mediastinum paraganglioma presenting with pericardial effusion two years before symptoms of catecholamine excess. This is the first case reported in Thailand.

A 34 year-old female patient presented with dyspnea. There was pericardial effusion from echocardiography was diagnosed with no definite causes of pericardial effusion. After treatment with ibuprofen, pericardial effusion was absolutely resolved from repeated echocardiography. Two years later, she had headache and hypertension. Chest X-ray, there was an anterior mediastinal mass. Her 24 hours urine metanephrine was very high. By imaging, an anterior mediastinal mass was observed from CT chest without adrenal mass from CT abdomen. The result of metaiodobenzylguanidine (MIBG) scan was compatible with paraganglioma. Symptoms of headache and hypertension disappeared after surgical removal of the mass. Pericardial effusion may be the first manifestation of paraganglioma especially if the patient had hypertension or could not find the etiology. Thus, pericardial effusion should be investigated for paraganglioma. Due to long term follow-up, this indolent growing tumor may respond to NSAIDs or regress spontaneously.

Keywords: *Pheochromocytoma (PCC), Paraganglioma (PGL), Metaiodobenzylguanidine (MIBG), Nonsteroidal anti-inflammatory drugs (NSAID), Pericardial effusion*

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Paragangliomas are tumors of chromaffin cells that may secrete catecholamine outside the adrenal glands. These tumors secrete catecholamine hormone presenting triple symptoms of hypertension, palpitation and sweating. In cases of non-functioning tumor presenting with progressive mass or metastasis, the common locations of paraganglioma are the carotid body, glomus tympanicum, vagal nerve, larynx and aortico-pulmonary artery[1]. Rare locations are the rectum[2,3], urinary bladder, clauda equina, while paragangliomas in the mediastinum are usually found in the anterior mediastinum, around the base of the heart[4]. The common sites of metastasis are the lymph nodes, bones, liver, and lung. The first manifestation of paraganglioma with pericardial effusion without hypertension is rare. Only a few cases have been reported[5]. The present study reported a case of anterior mediastinum paraganglioma presenting pericardial effusion before the classic triad and regression of pericardial effusion after NSAID treatment.

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Case Report

In 2011, 34-year-old Thai female patient presented dyspnea on exertion functional class II, without chest pain or orthopnea, headache or sweating. She was healthy before. Her father had history of hypertension at age 50 and he died at age 60 from congestive heart failure. She married at age 27. She had a 6-year-old son. Physical examination revealed: Her blood pressure 110/80 mmHg, heart rate 100/m, respiratory rate 20/min, temperature 37°C. Body weight was 58 kg. Her skin was not pale, no jaundice was observed, but she had an engorged neck vein of 4 cm

at the upper sternal angle. Her chest was clear and her heart showed no left ventricular hypertrophy, faint heart sound, and she had normal S1, S2 without murmur. Other physical were normal. Investigation revealed cardiomegaly of globular shape without pulmonary infiltration from chest X-ray, normal EKG. The authors found moderate pericardial effusion, mostly in the posterior part from echocardiography as shown in Fig. 1. No evidence of cardiac temponade was found. Other investigations to find the cause of pericardial effusion included: negative ANA, ESR 19 mm/hr, CRP 0.13 mg/dL, LDH 31 U/L and normal BUN, creatinine and thyroid function test. Because most of the pericardial effusion was located in the posterior part, percardiocentesis was complicated. This patient was treated with ibuprofen 400 mg orally four times daily for two months. The clinical symptoms improved considerably and repeated echocardiography found no pericardial effusion.

In 2013, she had the symptom of throbbing headache about ten minutes off and on several times a day. She went to see a doctor at a clinic and was diagnosed with high blood pressure. She was treated with doxazocin and referred to Rajavithi Hospital. Physical examination revealed: blood pressure 114/62 mmHg, no postural hypotension, heart rate 100/min, respiratory rate 16/min and presented no Cushingoid appearance. Normal eye ground was observed and other examinations were normal. Laboratory tests showed: CBC: Hct 35.6%, WBC 6,000 cells/mcL, N 83.0%, L 12.1%, M 5.0%, platelet count 233,000/mmol, BUN 11.0 md/dL, Cr 0.6 mg/dL, Na 138.0 mEq/L, K 4.4 mEq/L, Cl 99.0 mEq/L, CO_2 24.0 mEq/L, FBS 101.0 mg/dL, Ca 8.4 mg/dL, PO_4 3.4 mg/dL and albumin of 4.0 g/dL. The EKG disclosed: normal sinus rhythm, rate 85/min, normal axis and no LVH. Her 24-hour urine metanephrine showed 547 nmol (264-1729) and urine normetanephrine 23,825 nmol (480-2424). CXR is shown in Fig. 2 and CT chest and abdomen confirmed an anterior mediastinal mass with normal adrenal gland (Fig. 3). Her MIBG SCAN (with SPECT/CT) and total body scan were conducted at 24 and 48 hours. Normal uptake in the liver and parotid gland were seen. Abnormal uptake was observed in the mass at the left side of the mediastinum. No abnormal uptake was detected in the abdomen or pelvic cavity (Fig. 4). After

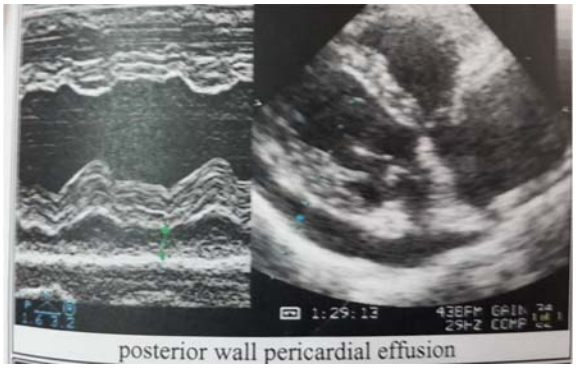

Fig. 1 Echocardiography in the patient prevailed posterior wall pericardial effusion.

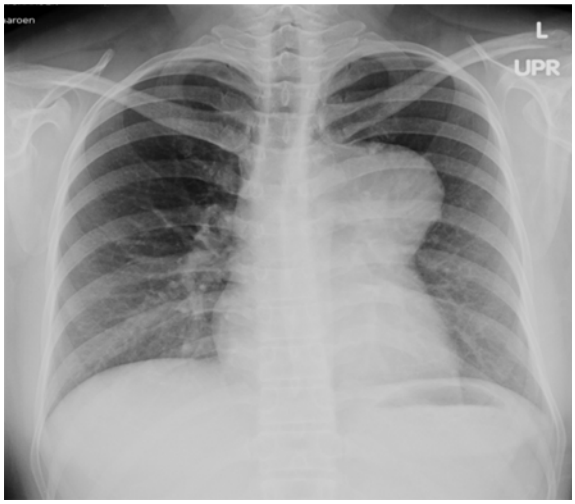

Fig. 2 CXR of this patient: Left mediastinal mass.

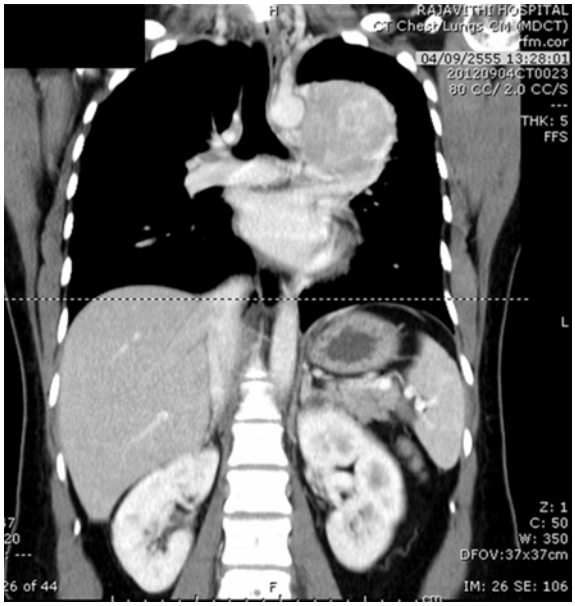

Fig. 3 CT chest and upper abdomen: Left anterior mediastinal mass with normal adrenal glands.

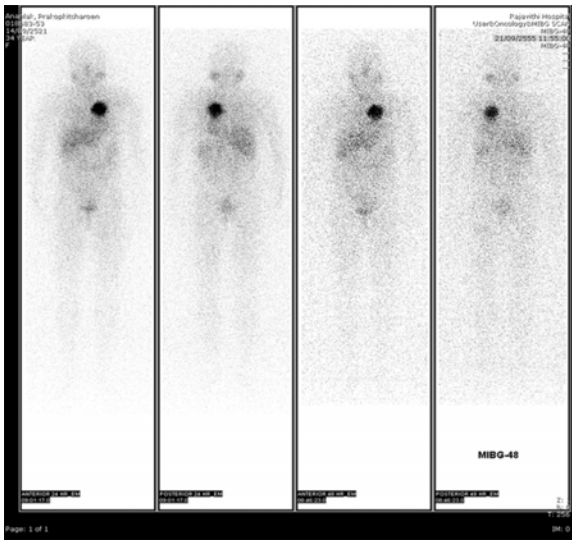

Fig. 4 MIBG of this patient, abnormal uptake is seen in the mass at left side of mediastinum. No abnormal uptake in other sites.

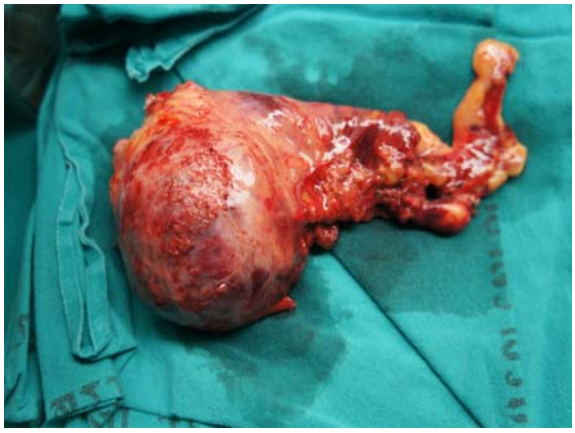

Fig. 5 Gross pathology of mediastinal paraganglioma mass.

controlling blood pressure and pre-operative evaluation, the operation removed the tumor with partial resection and reconstructed the pulmonary artery. The removed anterior mediastinal mass showed: paraganglioma 7x7x5.5 cm, presence of benign thymus and negative resected margins. Clinical headache and hypertension disappeared after removing the paraganglioma. The 24-hour urine metanephrine was repeated showing normal results. The screening for SDHB gene mutation was planned for further investigation.

Discussion

PCCs/PGLs have an estimated incidence of 2 to 8 per million[6]. PCCs/PGLs are the cause of hypertension in 0.2% to 0.6% of patients and are present in 4.0% of adrenal incidentalomas[7]. Pheochromocytomas and paragangliomas are rare endocrine tumors that can present insidiously and remained undiagnosed until death from life-threatening cardiovascular emergencies such as myocardial infarctions, cardiomyopathy, and stroke or onset of manifestations of catecholamine excess. Paraganglioma in the head and neck (HNPGL), derived from parasympathetic ganglia and are often non-secretory, and those outside the head and neck, termed extra-adrenal PGL, most often derived from sympathetic ganglia that hypersecrete catecholamines. This patient presented pericardial effusion without symptoms and signs of catecholamine excess. The investigations to find causes of pericardial effusion were negative. Pericardial effusion was resolved after NSAID treatment and two years later the patient exhibited the classic triad of catecholamine excess with anterior mediastinal mass. Even though two years after pericardial effusion and positive response to NSAID, making it unlikely to be associated with paraganglioma, a case report of a 60-year-old female presenting pericardial effusion had responded to and ibuprofen regimen temporarily and a repeat echocardiogram showed resolution. In this case, three years after presenting pericardial effusion, the doctor could detect a large intracardiac tumor causing a right ventricular outflow obstruction and finally confirmed diagnosis of paraganglioma[5]. A few cases reports of paraganglioma with spontaneous regression and regression of pheochromocytomas after initial presentation with hypertensive crises or shock have been published[8-10] as well as spontaneous regression[11]. Other tumors that have had spontaneous regression are pediatric neuroblastomas[12,13]. The hypothesized mechanisms of regression in these tumors included: biological (genetic, immunological), hormonal (such as contraceptive use), vascular (vascular insufficiency/tumor necrosis/spontaneous intratumoral vascular thrombosis) and operative mechanisms[14]. In the present case, the result of 24-hour urine metanephrine was normal but revealed an extremely high 24-hour urine normetanephrine. Phenylethanol-amine-N-methyltransferase (PNMT) is an enzyme that changes norepinephrine to epinephrine. VHL and PGL have low expressions of phenylethanolamine-N-methyltransferase (PNMT), and therefore, these tumors produce the precursor molecules normetanephrine and norepinephrine excessively, rather than the metabolites metanephrine and

epinephrine. On the other hand, tumors with RET mutations often overexpress PNMT, and therefore, have high levels of epinephrine. SDHB-associated tumors have a normetanephrine and dopamine predominance[15]. The indication for genetic testing for PCC/PGL are young patients (age lower than 50 years), positive family history, presence of syndrome features of VHL or MEN2 and multifocal or bilateral PCC/PGL or metastasis PCC/PGL[16]. This patient presented extra adrenal PGL with normetanephrine excess; the most likely genetic syndrome is SDHB mutations. A total of 13.0 to 23.0% of SDHB mutations are malignant. Therefore, in this case we plan further genetic studies with SDHB mutations.

Conclusion

Although paraganglioma is not a common cause of pericardial effusion, when the patient presents the classic triad of catecholamine excess, paraganglioma should be investigated especially in cases without specific etiology. Follow-up may be required for several years because of an indolently growing tumor.

Potential conflicts of interest

None.

References

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รายงานผู้ป่วย paraganglioma ที่ตำแหน่งในช่องอกด้านหน้าที่มีน้ำในช่องหัวใจก่อนมีอาการของฮอร์โมน catecholamine นาน 2 ปี: รายงานผู้ป่วยรายแรกในประเทศไทย

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Pheochromocytoma (PCC) และ paraganglioma (PGL) เป็นเนื้องอกที่พบไม่บ่อย ผู้ป่วยจะมีอาการของก้อนหรือการสร้างฮอร์โมน อาการแสดงที่ผู้ป่วยมาพบแพทย์ด้วยอาการน้ำในเยื่อหุ้มหัวใจเป็นอาการที่พบได้ไม่บ่อย ผู้นิพนธ์จึงเสนอรายงานผู้ป่วย paraganglioma ที่ตำแหน่งในช่องอกด้านหน้าที่มีน้ำในช่องหัวใจก่อนมีอาการของฮอร์โมน catecholamine นาน 2 ปี: รายงานผู้ป่วยรายแรกในประเทศไทย

ผู้ป่วยหญิงอายุ 34 ปี มาด้วยอาการเหนื่อยหอบ ตรวจพบว่ามีน้ำในเยื่อหุ้มหัวใจจากการตรวจ echocardiography และตรวจไม่พบสาเหตุที่ชัดเจนของน้ำในเยื่อหุ้มปอดหลังจากการได้รับการรักษาด้วยยา ibuprofen การตรวจ echocardiography ซ้ำพบว่าน้ำในเยื่อหุ้มหัวใจหายไป 2 ปีต่อมาผู้ป่วยมีปวดศีรษะ ความดันโลหิตสูง เอกซเรย์ปอดพบก้อนในทรวงอกด้านหน้าการตรวจ metaiodobenzylguanidine (MIBG) scan เข้าได้กับ paraganglioma หลังการทำผ่าตัดอาการปวดศีรษะหายไปและความดันโลหิตของผู้ป่วยกลับสู่ปกติ

อาการน้ำในเยื่อหุ้มหัวใจอาจจะเป็นอาการแสดงของ paraganglioma ถ้าผู้ป่วยมีอาการความดันโลหิตสูง และตรวจไม่พบสาเหตุที่ชัดเจนควรได้รับการตรวจหาสาเหตุของ paraganglioma และอาจจะต้องติดตามเป็นเวลานานเนื่องจากเนื้องอกกลุ่มนี้อาจจะมีการเจริญเติบโตช้าและอาจจะตอบสนองต่อยากลุ่ม NSAIDs หรืออาจจะดีขึ้นเองได้ในบางราย