

Pheochromocytoma: reporting of two cases with a brief review

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Abstract

Pheochromocytoma arise from the chromaffin cells of adrenal gland or cells of sympathetic ganglion. The tumors secrete excessive adrenaline and nor-adrenaline and may cause severe elevation of blood pressure. Cardinal symptoms of pheochromocytoms are headache, diaphoresis, palpitation and high blood pressure which may be paroxysmal in nature.

However, 10% of pheochromocytomas are only incidentally discovered during investigation of the patient for other reasons not related to suprarenal disease. We have reported here two cases of suprarenal tumors (pheochromocytoma), one of which is incidentally found while investigating her chest and epigastric pains.

Keyword: Pheochromocytoma, incidentaloma, paroxysmal hypertension, hypotension.

Introduction

Frankel made the first description of a patient with pheochromocytoma in 1886. However, it was Ludwig Pick, a pathologist who was first to coin the term pheochromocytoma in 1912. Pheochromocytoma was successfully removed by Roux of Switzerland and by Mayo in U.S.A. (1926).

Exact pathology in the genesis of pheochromocytoma is not known but recent study has demonstrated that mutation of succinate

dehydrogenase (SDH) gene which is a major component of mitochondrial complex II may be responsible for abdominal paraganglioma and cancer of pheochromocytoma. It has been observed that SDH (B) gene mutation takes place in 40%-50% cases of pheochromocytoma. Pheochromocytoma arises from the chromaffin cells of adrenal medulla or cells of sympathetic ganglion, so they may also be called chromaffinoma or paraganglioma. The tumor cells secrete excess of adrenaline and causes severe elevation of blood pressure. Cardinal symptoms of active

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pheochromocytoma are headache, diaphoresis and palpitation in presence of high blood pressure.

In adult 80% of pheochromocytomas are unilateral and solitary, 10% are bilateral.

Although 97% of pheochromocytoma occur in the abdomen, rest may occur in thorax (10%), ureter, urinary bladder (1%) and sympathetic nerve chain in the neck (3%). Extra-adrenal pheochromocytomas are less than 5 cm in diameter, mostly located inside abdomen in association with coeliac, superior mesenteric and inferior mesenteric ganglia.

Pheochromocytomas are often referred to as "Ten percent tumor" for the following reasons: -

1. 10% of pheochromocytomas are said to be malignant
2. 10% tumors are bi-lateral
3. 10% are extra-abdominal
4. 10% may occur in children
5. 10% are associated with MEN syndrome
6. 10% may be familial
7. 10% may recur after surgery
8. 10% of pheochromocytomas are incidentally found during C.T. or MRI investigations for other reasons

Surgery is the mainstay of treatment. Laparoscopic operation is advisable by those experienced in that field. Intra abdominal adrenalectomy is otherwise satisfactory and done in most centers.

Case report

Case No 1.

A 53 years male, from Lumbini, Rupandehi, Butowal presented with pain in the right lumbar region for past 3 days, pain was acute in onset and radiated to epigastric and right lumbar region. There were no relieving factors for pain except slight relief with analgesic. He also complained of non-projectile type of yellow colored vomiting about 15-20 episodes in the last couple of days. Patient was restless since last one day with throbbing headache, palpitation, blurring of vision, dizziness and excessive sweating. There was no history of fever, diarrhoea, or chest pain. He gave history of severe abdominal pain about a year back and was diagnosed as acute pancreatitis at U.S.G. examination with oedematous pancreas. He is a known hypertensive and diabetic since last 2 years and was under irregular medication. There is no relevant family history. He drinks alcohol 2-3 glasses every day and a smoker both for last 33 years.

On exam: Appearance is ill-looking, with average build and poor nutrition. Weight at admission is 50kg. There is no anemia, icterus or lymphadenopathy. No visible neck veins.

Vitals

Pulse 108/min regular, bounding, Temp- 98.6° F, Resp-rate 26/min, Abdomino-thoracic, BP-180/110 mm of Hg (upper extremity) and 178/112 mm of Hg. (In the lower extremity)

Symtemic exam

Abdomen- there was an ill-defined small non-tender mass in right lumbar region and moderately enlarged and tender liver with epigastric tenderness, No other abnormality was detected in any systemic examination.

Prov. Diagnosis

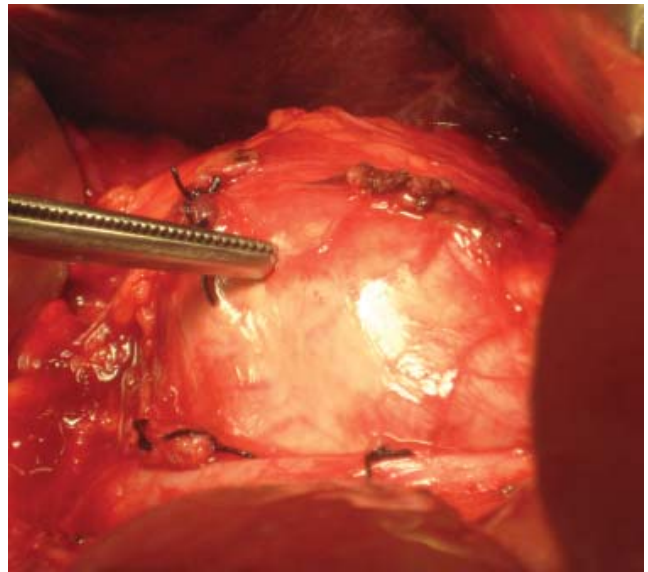
1. Renal tumor
2. Pancreatitis (alcoholic)
3. Acute hepatitis

Patient was subjected to the following routine and special investigations. Blood-Hb 11gm%, ESR-24mm, TC-9500, DLC-N83, LY-12, E-4, M-01, ESR-5mm, Random blood sugar-200 mg, Urea-45 mg%, Creatinine -1.5 mg %/ , Potassium 3.5 mg, Sodium 137mg, Serum amylase normal, Serum bilirubin 1.27mg%, VMA 120mg / day(normal,3-90mg/day) Urine(routine) -NAD,ECG-sinus rhythm, USG (abdomen),- a rt adrenal mass approx 3×5cms ? pheochromocytoma , CT- A homogenous enhancing well defined mass lesion in the rt. supra-renal area measuring approx 7.5×5.5cm in size. The plane of the mass with superior pole of rt. Kidney is maintained. No calcification noted Impression-right adrenal mass.

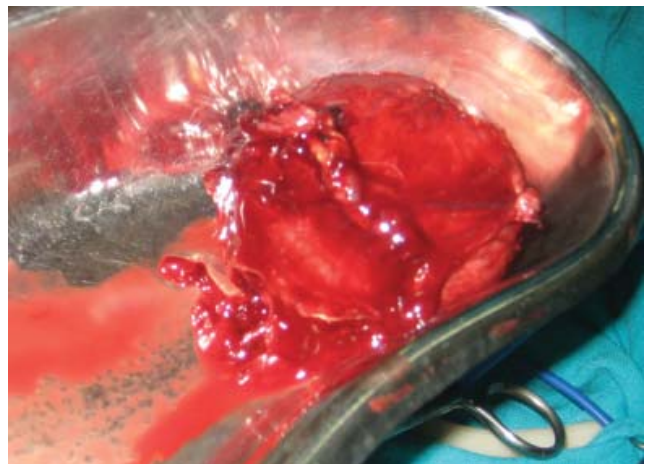
Patient was treated with phenoxybenzamin 10 mg bd for 2 weeks, Amlodipin 5 mg bd and Alprozolam 0.25mg HS. Patients was subjected to right adrenalectomy under GA. At operation the adrenal mass was found to be firm in consistency. There

was approx 200-250 ml blood loss. During manipulation of the tumor, B.P. went up to 350/190 mm Hg and operation had to be temporarily stopped for a brief period.

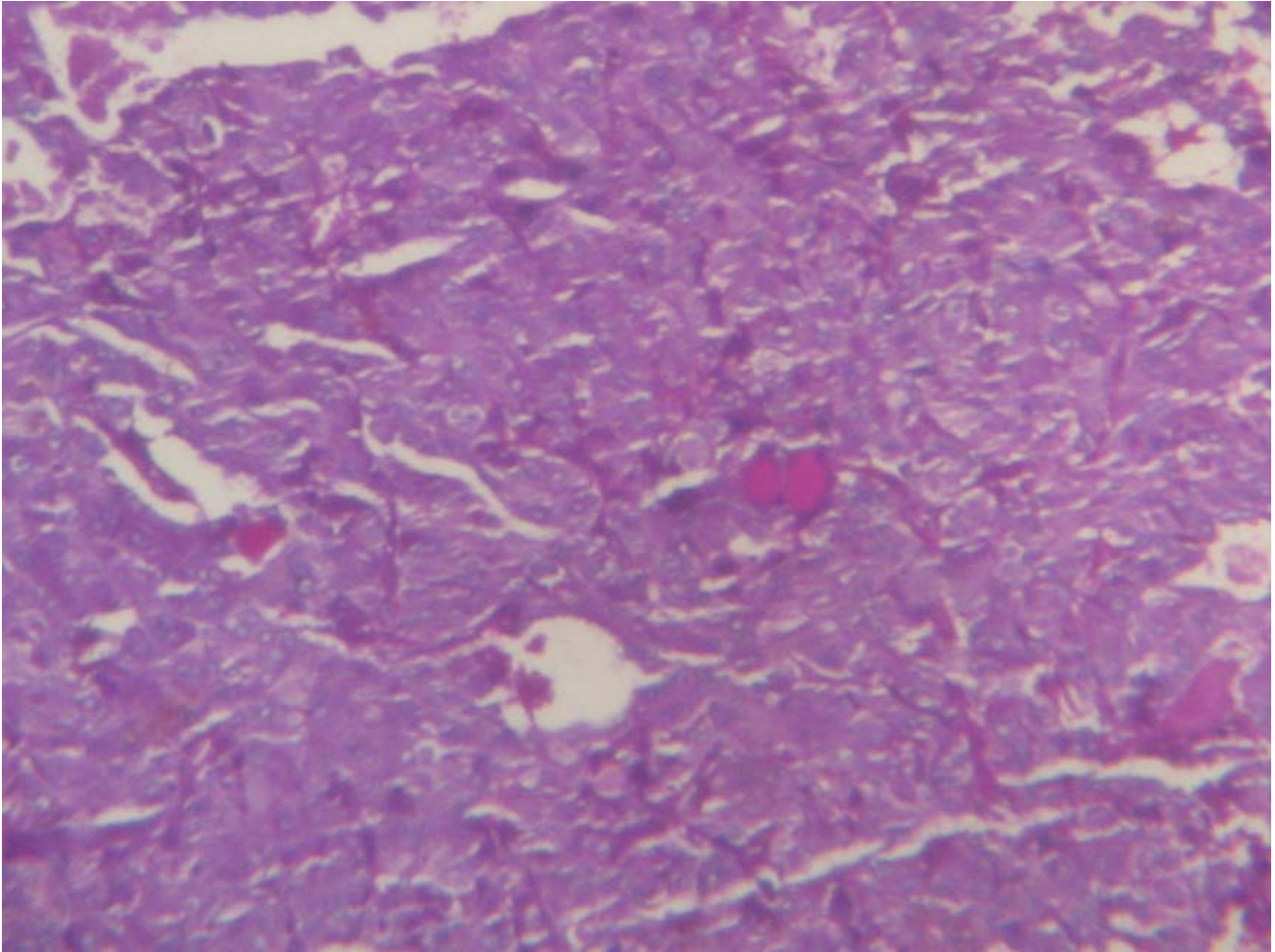
Rt. Adrenalectomy was successfully performed and except transitory hypotension within an hour of operation which is controlled by dopamine, rest of the post-operative period was uneventful.



Case No. 1 (a) – at operation



Case No. 1 (b) – after excision



Case No.1 (c) – microscopic picture

Case no 2

A 37 year old Hindu female, house-wife by occupation from Makawanpur district of Nepal presented with occasional palpitation and headache since about a year. As her complaints were not of serious nature and were only occasional she ignored it except taking some pain killer for headache. But presently when she had experienced continuous dull aching central chest and epigastric pain she reported to our Institution. She said that she was very much apprehensive as if something serious was going to happen to her suddenly. She was a

pre-menopausal woman with regular menstrual cycle. There was no history of fever, sweating, vomiting or diarrhoea. She had no history of any surgical ailment or medical problems of importance. She is non-diabetic and non-hypertensive. On exam- Average built, moderately nourished young lady with all her vitals within normal limit. Pulse-80/min, regular, normal vol. and character, all peripheral arterial – pulsations are equal. B.P. normal CVS- Heart rate 80/min, regular, normal intensity. No adventitious sounds. B.P. in both upper extremities are almost equal, Rt side 120/80 and 116/80 on the left side.

No visible neck veins or abnormal pulsations in the neck.

Abdomen: on deep palpation a vague intra-abdominal mass with ill-defined margins could be felt in the right loin which was non-tender and did not move with respiration. Other systemic examination revealed no other relevant findings Patient was subjected to the following routine as well as special investigations.

Hb-12.3 gm/dl, ESR-40 mm T.C. 10.9 /dl D.L.C.- N-75, L-21, M-2,B-0,Band cell-0;E-2, Random blood sugar-116.8 mg/dl, Urea-26.7mg%, Creatinine 0.9 mg/dl, K⁺ 4.6 µeq, Na_{+135mg %}

Urine- N.A.D

Special Investigations

ECG:normal Sinus rhythm.

UGI endoscopy: normal.

Serum amylase:normal

Urinary amylase :normal

TSH :normal limit

Urinary vinyl mandalic acid :normal level (9mg/24hours)

USG abdomen: Large well defined echogenic SOL in right supra-renal area measuring 95×92mm containing multiple hypoechoic areas within. The

mass is compressing the postero-medial aspect of rt. liver and IVC. The upper pole of right kidney is also compressed.

C.T. Scan: Tumor size is 9.2 cm×9.5 cm and pre-contrast density is 30 HU and post – contrast density is 45 HU. There is compression of IVC

Impression: Rt. Supra-renal mass (?) pheochromocytoma

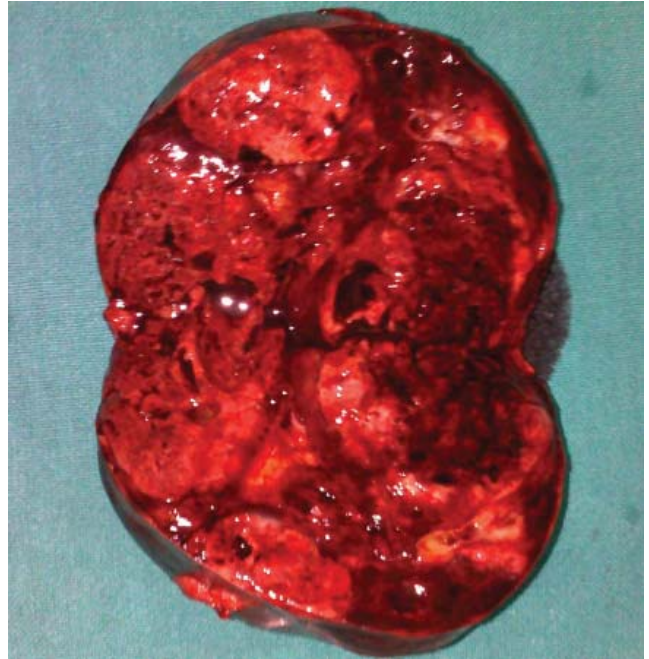
The patient was subjected to rt, adrenalectomy under GA. Her intra-operative period was eventful.



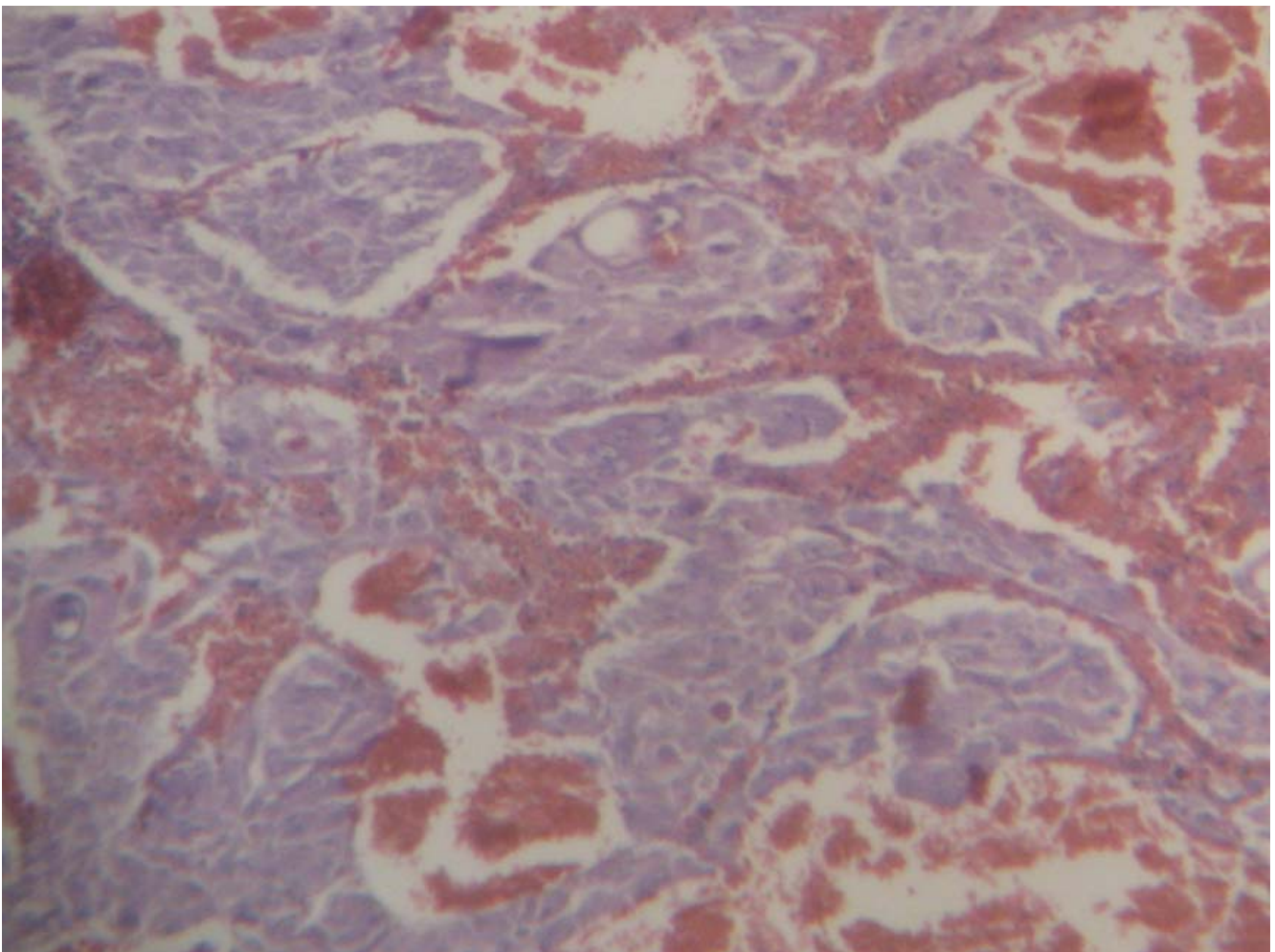
Case No. 2 (a)



Case No. 2 (b) – pheochromocytoma after



Case No. 2 (c) – cut section of the tumor



Case No. 2 (d) – Microscopic picture

Discussion

Since 2008 June we came across two cases of pheochromocytoma- one of which (case no

1) was clinically, radiologically and biochemically proven while the other (case no2) was sub-clinical in nature.

Pheochromocytoma is a neuro-endocrine tumor of the medulla of adrenal gland that originate from the chromaffin cells or extra-adrenal chromaffin tissue that failed to involute after birth and secrete excessive amount of catecholamines, usually adrenaline (epinephrine) if in the adrenal gland and not extra-adrenal, and nor-adrenaline (nor-epinephrine).⁽¹⁾ Extra-adrenal tumors, also called paraganglioma may be found at sites of sympathetic ganglia in organ of Zuckerkandl, neck, mediastinum, abdomen and pelvis.² Extra-adrenal pheochromocytomas are known as paraganglioma and comprises 15-18% of all pheochromocytomas. Location of paraganglioma may be at any site where paraganglia are present.³ Pheochromocytoma, unlike normal adrenal medulla, are not innervated and catecholamine release is not initiated by neural impulses. Changes in direct flow, pressure, chemicals, drugs and angiotension II may initiate release of the hormone into the circulation.⁴

Reported incidence of pheochromocytoma is approximately 1:100,000 individuals with 20% cases occurring in children and adolescents. Children have a higher frequency of bilateral tumors than adults (20%vs 5-10%) but lower rate of malignancy.⁴

Pheochromocytomas can occur at any age with a peak incidence in the 4th and 5th decades of life,

are mostly benign and have no gender predilection, although may occur more frequently in female children.² There are reports of pheochromocytoma occurring in babies as young as 5 days old and in adult of 92 years.⁴ 84% of all multifocal tumors (including bilateral tumors) and 59% of pheochromocytomas with onset at the age of 18 years or younger were found to be hereditary.⁵ A small minority (about 10-20% of pheochromocytoma arise because the person has an inherited susceptibility to them⁴ The incidence of malignancy in pheochromocytoma varies between 2.5% and 13% according to literature.⁶ Malignant tumors are found to be associated with familial variety and associated with MEN type II a and type II b.⁷ The malignant diagnosis occurs according to whether metastasis or invasion exists. The malignant pheochromocytoma usually metastasizes to bone, lung, kidney and lymph nodes⁶ 10 - 20% of tumors are bi-lateral and familial. Hypertension is present in most cases which may be either persistent or paroxysmal, may be precipitated by any strain or during anaesthesia or at operation, may also be precipitated by anti-depressant or opiate group of drugs.⁷

All pheochromocytomas do not produce clinical symptoms. 10% of pheochromocytomas are diagnosed incidentally while doing abdominal screening by C.T. MRI or during laparotomy for other reasons without prior suspicion of adrenal pathology. These are known as Incidentaloma. Incidental tumors less than 1cm have no clinical symptoms and rarely even large tumors do not show clinical symptoms.⁸ In our case no 2, the tumor size is 9.2cm ×9.5cm and pre-contrast density is 30 HU

and post contrast density is 45HU but there were no obvious clinical symptoms, which is rather rare. We also observed that there is no relation of malignancy with the tumor size although it is reported in some studies that tumor size of 4-20 HU are suspicious, density more than 20HU are rated as malignant and carcinoma prevalence is 25% if the mass is bigger than 6cm.⁸ Both our cases are bigger than 6cm without any radiological or histopathological evidence of malignancy. While we had no difficulty in correctly diagnosing our first case as a symptomatic pheochromocytoma with classical triad of symptoms like paroxysmal elevated blood pressure, palpitation and trunkal sweating along with positive radiological and biochemical investigations. (USG, CT scan and VMA), our second case, in absence of typical clinical symptomatology, negative biochemical test that are available in our hospital and doubtful C.T. scan report it was not easy to clinically label the case as pheochromocytoma.

One of the important signs of silent pheochromocytoma is the occurrence of hypertensive attack during induction of anaesthesia and / or manipulating the mass at operation (a confirmatory test of silent pheochromocytoma).⁹ During operation in our 2nd case, not only the blood pressure went high, but also there were frequent ventricular ectopics which was controlled by the anaesthetist by giving Na-nitropruside and á-blocker. About 25-50% of hospital death in patients with pheochromocytoma occur during induction of anaesthesia or operative procedure for other causes due to hypertensive crisis and myocardial dysfunction.¹⁰

Pheochromocytomas are diagnosed by testing 24 hour catecholamines and their metabolites in urine and plasma which provide 95% of the evidence of the disease. ⁽¹¹⁾ We did adrenalectomy in our case no 2 because of the tumor size, which was subsequently diagnosed to be so, after histopathological examination only. We therefore label this case as a silent pheochromocytoma – a benign Incidentaloma.

Conclusion

While our case No 1 was diagnosed beyond any doubt as pheochromocytoma by history, clinical examination and investigations, our case No 2, a young lady with complaints of occasional mild headache and dull aching central chest and epigastric pain having all laboratory findings within normal limit, we were not aware of the existence of a pheochromocytoma till the USG study and C-T scan revealed a supra-renal mass suggestive of a (?) pheochromocytoma. We were pretty sure of its existence only during giving anaesthesia and at operation. We therefore, are inclined to conclude that the second case may be regarded as an incidental pheochromocytoma from the right supra-renal gland.

Reference

1. Wikipedia, the free encyclopedia.
2. Schwartz principal of surgery, Ninth edition, chapter 38 page-1399 F. Charles Brunnicordi, Dana K. Anderson, Joenothy R. Billior et. al.

3. The internal journal of surgery, 2006, Vol-8, No2 " large Asymptomatic adrenal incidentaloma" Satyendra K, Tewary MS, Manish K. Singh, R.C. Sukla MD et.al.
4. Pheochromocytoma: eMedicine Pediatrics: General Medicine > oncology Patricia, M.V. Deptt of endocrinology, Albert Einstein college of medicine. Updated: 27 August 2009.
5. Germ line mutation in non-symptomatic Pheochromocytoma *New Eng. J. Med.* 2002; **346**: 1459-66 (May 9, 2002) Hartmut P.H. Newmann MD, Birke Bansch, Sarah R. Mcwhinney, BA, Barnhard U. Bender MD et al.
6. Metastatic Pheochromocytoma of the Thoracic spinal extradural space – case report and review of literature. *Kobe. J. Med Sci.* 2005; **51**(4): 49-53. Alaattin Yurt, M.Nuri Arda and Enver Vardar.
7. Gaint malignant pheochromocytoma of adrenal gland: Biologic time bomb. V.Yagnik MS, FAMS, J. Rathod MBBS MS, R. Bhatt MBBS, MS " Internal journal of oncology, 2009;**6**: No 2.
8. Mesut Ozkaya, Mehmet Fatih Yubasioglu, Ertan Bulbuloglu, Sevgi Bakaris et.al. *Cases J.*2008; **1**:10 May 25
9. Incidental pheochromocytoma presenting with sub-laboratory findings [http : /ukpmc.ac.uk/articles/ PMC 2438313](http://ukpmc.ac.uk/articles/PMC2438313)
10. Masui, 2010;**59** (7): 883-6" Pheochromocytoma" (article in Japanese) surgical center, yamanashi university hospital, chuou 409-3898 Masamune T, Matsukawa T.
11. Incidental pheochromocytoma presenting with sub-laboratory findings in asymptomatic mass: A case report, *Cases J.*2008, **1**: 10 published on line 2008; 25.doi: 10:1186/1757-1626-1-10 Mesut Ozkaya, Mehmet Fatih Yuzbasioglu, Ertan Bul Buloglu et.al.