Role of bilateral inferior petrosal sinus sampling (BIPSS) in the diagnosis of Cushing's disease in a patient with double superior vena cava

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ABSTRACT
Cushing's syndrome is known to have a wide spectrum of clinical presentation with debilitating consequences and morbidity if not diagnosed and treated in time. Sometimes the diagnosis of Cushing's syndrome can be challenging to the endocrinologist, especially when the usual battery of biochemical tests and advanced cross-sectional imaging is negative or inconclusive. We described a case in which the use of bilateral inferior petrosal sinus sampling (BIPSS) was conclusive albeit being technically challenging (due to a rare incidental finding of double superior vena cava) and invasive in nature.

CASE REPORT
A 52-year-old Chinese woman presented to the endocrinology department with a series of medical complaints. She had progressive weight gain (with central obesity) despite having a rigorous exercise regimen, poorly controlled diabetes mellitus with easy bruisability and patchy hair-loss. She was also diagnosed with osteoporosis with dual-energy x-ray absorptiometry (DEXA) bone mineral densitometry (BMD) demonstrating a T-Score below -2.5. The attending endocrinologist performed a series of biochemical tests including urinary free cortisol (UFC) levels and dexamethasone-corticotropin-releasing hormone test, all of which were inconclusive. A computed tomography (CT) of the adrenal glands along with a magnetic resonance imaging (MRI) of the pituitary gland also failed to reveal an adrenal mass or a pituitary adenoma. Given the strong clinical suspicion of Cushing's disease and inconclusive work-up, after discussion with the treating endocrinologist and the patient, a unanimous decision was made to perform a bilateral inferior petrosal sinus sampling (BIPSS) to confirm the diagnosis of Cushing's disease.

Before the procedure, the patient fasted overnight. Informed consent was also obtained prior to the procedure after explanation of the procedure, possible risks and complications. BIPSS was then performed after obtaining intravenous access via the bilateral common femoral veins (CFVs) using Seldinger technique with a 6 French Terumo Vascular Sheath (Terumo Corporation, Tokyo). The right femoral sheath was intended for the right jugular catheterization and the same for the left to prevent confusion during the sample collection. A 5 French Torcon NB Advantage Beacon tip catheter with DAV tip configuration (Cook Medical, Bloomington, Indiana) and a 0.035-inch hydrophilic straight Terumo guidewire (Terumo Corporation, Tokyo) was used for catheterization of the internal jugular veins (IJVs). Under fluoroscopic guidance, the inferior vena cava, right atrium and superior vena cava (SVC) were crossed. The catheter was then manipulated into the right brachiocephalic vein and finally the right IJV. About 10 ml of Iohexol (Omnipaque 350; GE Healthcare) was hand injected at the level of the superior bulb of the right IJV to opacify its tributaries, namely the inferior petrosal sinus (IPS) (Fig. 1). A
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roadmap to mark the ostium of the IPS was also obtained at this stage. A 2.5 French Cantata super-selective microcatheter (Cook Medical, Bloomington, Indiana) was then introduced coaxially through the 5 French catheter; with its tip parked at the level of the IPS ostium. With the help of the microwire, the IPS was then entered followed by the microcatheter. A gentle venogram was performed through the microcatheter after removal of the microwire with a 2 ml Luer lock syringe. Demonstrating the reflux of contrast media into the ipsilateral cavernous sinus indicates a correct position of the microcatheter within the IPS.

After we experienced difficulties in entering and crossing the left brachiocephalic vein, a venogram was performed. It revealed a small rudimentary left brachiocephalic vein and a persistent left SVC draining into the coronary sinus (Fig. 2). The left-sided IPS was therefore entered via the right atrium, coronary sinus, persistent left SVC and the left IJV (Figs. 3 and 4).

Once the microcatheters were in position (Fig. 5), simultaneous venous blood samples were obtained from each sites, including the both inferior petrosal sinuses and the peripheral sites (which were obtained via the vascular sheaths). Once the baseline samples (usually two sets of baseline samples) were obtained, corticotropin-releasing hormone (CRH) was injected peripherally as a slow bolus at 1 mcg/kg (maximum 100 mcg). The post-CRH samples were obtained from each port at 2, 5, 10, and 15 minutes. Post sampling, the catheters and sheaths were removed, and manual pressure was applied at the bilateral groin sites until venous hemostasis was achieved. In our index case, the procedure was uneventful and the patient was discharged the next day.

Subsequently the BIPSS results in our index case not only confirmed the diagnosis of Cushing's disease but also localized the hormonally active microadenoma in the right side of her pituitary gland.

**DISCUSSION**

Efforts to measure the pituitary venous effluent was first reported by Corrigan and colleagues in 1977 [1]. Since then, the technique has been refined and standardized by various investigators and currently it is a very useful tool used by the endocrinologist for the evaluation of Cushing's syndrome, especially when the usual battery of biochemical tests and cross-sectional imaging are negative or inconclusive.

**Etiology & Demographics**

**Cushing's syndrome:**

Although the most common cause of Cushing's syndrome is exogenous intake of glucocorticoid, we shall be discussing only about the endogenous causes of Cushing's syndrome; which may be due to adrenocorticotrophic hormone (ACTH) dependent causes like excessive ACTH production from a pituitary microadenoma (Cushing's disease), ectopic ACTH secretion by a non-pituitary tumor, or ACTH independent excessive autonomous secretion of cortisol from a hyperfunctioning adrenocortical tumor [2].

Cushing's syndrome is a very rare entity with an annual incidence of 2 to 4 cases per million [3]. Cushing's disease is the most frequent cause of Cushing's syndrome, with an annual incidence of between 1.2 to 2.4 cases per million. It is also 3-8 times higher in women than in men [3].

**Double superior vena cava:**

Double SVC is a rare congenital venous anomaly with a reported frequency of about 0.3 to 0.5% in the general population and about 4% of patients with congenital heart disease. Normally the right anterior cardinal and common cardinal veins form the SVC, and the left anterior cardinal vein regresses during fetal development. In case of double SVC, the left anterior cardinal vein fails to regress and persists. On the other hand, the regression of the normally persistent right cardinal vein would result in the formation of a left SVC [4].

**Clinical & Imaging findings**

**Cushing's syndrome:**

Cushing's syndrome can present with a myriad of non-specific symptoms and signs such as weakness, lethargy, weight gain, menstrual irregularities, depression, loss of libido, acne, purplish skin striae, hyperpigmentation, thinning of skin and easy bruising. It can also present with more suggestive features like proximal myopathy, new onset or worsening of diabetes mellitus or hypertension (despite measures to control them), osteoporosis and hirsutism. Cushing's disease may also cause symptoms related to mass effect from the tumor such as headache or visual disturbances, namely bitemporal hemianopia (due to compression of the optic chiasm).

Clinicians heavily rely on biochemical testing to narrow down their differential diagnosis of Cushing's syndrome, after which a targeted cross-sectional imaging of either the pituitary or adrenals glands is performed. Since adrenocorticotrophic hormone (ACTH) dependent Cushing's syndrome is secondary to a pituitary microadenoma (Cushing's disease) in about 90% of patients, the pretest probability of Cushing's disease is also about 90% [2,5]. Therefore, pituitary imaging is commonly utilized to detect and localize the position of a pituitary microadenoma. It is also used as a guide for surgical exploration. A contrast-enhanced MR is favored over CT, due to the poor sensitivity (reported to be about 47%) of the latter for the detection of pituitary microadenomas [3]. The quoted sensitivity of MRI in some series ranged between 69 to 90% [5]. Dynamic contrast-enhanced thin section T1-weighted MR is ideally performed for the detection of microadenomas, as they usually display a hypointense signal intensity due to failure to rapidly enhance in relation to the avidly enhancing pituitary gland. However, approximately 5% of these pituitary microadenomas will also rapidly take up the gadolinium contrast media, thus giving an isointense signal on MRI with resultant failure to visualize these lesions [6]. This is further compounded by the fact that detection of a pituitary microadenoma on MR does not confirm its functionality, since 10% of the general population harbors non-functioning incidentalomas [2,3].
Therefore, bilateral inferior petrosal sinus sampling (BIPSS) has a role in differentiating between Cushing’s disease and the other causes of Cushing’s syndrome with confidence. The reported sensitivities and specificities are 95% and 100%, respectively, without CRH stimulation and 100% and 100%, respectively, after CRH stimulation for BIPSS [7]. It can also be used for lateralizing small hormone-producing adenomas within the pituitary gland, as in approximately 60% of individuals, pituitary venous drainage is symmetrical with most of the venous effluent from each side of the pituitary draining into the ipsilateral IPS [8].

**Double superior vena cava**

In the absence of congenital heart disease, double SVC or duplication of SVC is usually detected incidentally on either cross-sectional imaging or on radiograph, when traversed by a left-sided central venous catheter or during the introduction of cardiac pacemaker and defibrillator wires; where it courses along the left side of mediastinum towards the heart. In these cases, the left component of the duplicated SVC almost always drains into the coronary sinus [4] with no physiologic impact on circulation. This finding in our index case is also incidental and has no known association with Cushing’s disease.

**Anatomy of the inferior petrosal sinus**

The inferior petrosal sinus (IPS) connects the posteroinferior part of the cavernous sinus to the superior bulb of the internal jugular vein (IJV) via the petroclival fissure. Various patterns of confluence with the IJV are described in the literature. In majority, the IPS narrows down to a single vein (about 2 mm in diameter), draining into the ipsilateral IJV. In about 25%, the IPS "forms plexiform channels" that drains into the IJV [9] and in about 1%, there is no connection between the IPS and the IJV making standard sampling impossible [8,10]. The latter information needs to be relayed to the patient during consent taking.

**Techniques & Complications of BIPSS**

The entry into the left IJV is often described as difficult as opposed to the right IJV, due to the presence of a valve at the junction of the left IJV and left subclavian vein. In our case, this problem was rather circumvented, as the patient was incidentally found to have a double SVC, which imposed another technical challenge, as the coronary sinus draining into the right atrium needed to be catheterized to get access to the left IJV and left IPS.

After accessing the IPS, a gentle venogram should be performed not only to confirm the position of the microcatheter within the IPS but also to check for communication with ipsilateral cavernous sinus. The position of the microcatheter should also be well within the IPS to prevent its dislodgement.

In the rare event of absent communication between the IPS and IJV, the catheters can be placed at the C1-2 levels for sampling. However, sampling at this level may be associated with false results due to contamination from the transverse or sigmoid sinuses.

Deep catheterization or entry into the cavernous sinus is not required or recommended, as cavernous sinus sampling has no superior diagnostic accuracy compared to IPS sampling. It is also technologically more challenging with increased risk of complications. Some authors [8,9] advocate the infusion of intravenous heparin after the IPS is accessed by the microcatheters, but this can be avoided as in our case with periodic gentle flushes of saline via the microcatheter to maintain its patency and prevent clot formation around the catheter tip.

Larger sized vascular sheaths should be used when accessing the venous system as they help in the simultaneous collection of peripheral venous blood samples during the BIPSS.

Teamwork is a crucial element especially at the stage of collecting the venous samples, as each member should know the timing and the site/side of the venous samples obtained. The samples must also be placed immediately into properly labeled purple/lavender-top EDTA-containing tubes and stored on ice (for serum ACTH levels).

The most common complication during the BIPSS procedure is groin hematoma, seen in about 3-4% of the patients [8,9]. The incidence of serious complications like cerebrovascular accident (usually pontocerebellar junction stroke) is very low at 2 per 1000 cases when performed by an experienced intervention radiologist [11]. The cause of this complication is not clearly understood but is presumed to be due to localized venous hypertension [11].

Therefore, during the entire procedure the patient must be closely monitored to look for signs of brain stem stroke: slurred speech, hemifacial paresthesia, perioral tingling sensation, and labile hypertension. The procedure should be immediately terminated, in the event the patient develops such signs. So only light sedation and anxiolysis is recommended for this procedure. Very rarely deep venous thrombosis, pulmonary embolism, transient cranial nerve palsies, and venous subarachnoid hemorrhage with obstructive hydrocephalus have been reported [9].

**Results in our index case**

The BIPSS results (table 4) obtained from our index case confirmed the clinical suspicion of Cushing’s disease. The results revealed a high petrosal sinus to peripheral vein ACTH ratio, exceeding 3:1, confirming a pituitary source of ACTH excess. It also revealed a right petrosal sinus to left petrosal sinus ACTH lateralization ratio of 5.2, successfully localizing the ACTH excess to be from the right side of the patient’s pituitary gland. The criterion for lateralization is a side-to-side gradient $\geq 1.4$ post-CRH stimulation. A gradient $< 1.4$ indicates a midline lesion with an approximate accuracy of 70% [7]. The prolactin levels were taken as a control to indicate the correct cannulation of the petrosal sinuses, as they corresponded with the ACTH levels in the respective sites.
Treatment & Prognosis

The treatment of choice for Cushing’s disease is transsphenoidal selective adenomectomy with a remission rate ranging from 69 to 98% (simple average 79%), recurrence rate from 3 to 17% (simple average 10%), and the acute surgical mortality rate from 0 to 1.9% [12].

Medical therapy is also employed non-concurrently or as an adjuvant to radiation therapy for patients who are either poor surgical candidates or those with failed surgery. It is also used as a temporizing measure preoperatively. Numerous drugs with various mechanism of actions, such as neuromodulation to limit ACTH levels, adrenal enzyme inhibition, and glucocorticoid receptor antagonism are used with varying results and side-effects [13].

Differential Diagnoses

Although Cushing’s disease is the most common cause of endogenous Cushing’s syndrome, differentiating it from the other causes is of paramount importance as their treatments are radically different [2].

A cortisol-secreting adrenal tumor, usually an adenoma, needs to be excluded in the diagnostic workup of Cushing’s syndrome. Dedicated CT or MR can be used to detect and characterize an adrenal adenoma. Adrenal adenomas are well-defined nodules with an average attenuation of less than 10 Hounsfield unit (HU) for a lipid-rich adenoma and more than 10HU for a lipid-poor adenoma on unenhanced CT. Since an adenoma enhances rapidly with intravenous contrast media and washes out the agent rapidly also, a dynamic contrast-enhanced CT or MR should show a wash-out value of more than 50% [14]. Its T1-weighted and T2-weighted signals on MR is variable but in case of lipid-rich adenomas, chemical shift imaging can be used to demonstrate a signal ‘drop out’ in the out-of-phase images, i.e., appearing hypointense than the in-phase images [14]. Since a unilaterial cortisol-secreting adrenal tumor will result in suppression of ACTH secretion, the remaining ipsilateral and contralateral adrenal gland may be atrophic in appearance [2].

Various non-pituitary tumors are known for causing ectopic secretion of ACTH. Small-cell lung cancer and bronchial carcinoid tumors are the most common sources, but cases of medullary thyroid carcinoma, pancreatic carcinoid tumor, thymic carcinoid tumor and disseminated carcinoid are also documented to be ectopic sources of ACTH. Although dedicated imaging of these organs or sites can be performed for detection and further characterization, many carcinoid tumors, small-cell lung cancers, and medullary thyroid carcinoma have been found to express high numbers of somatostatin receptors [15]. Therefore, with the recent advent of somatostatin receptor imaging, these lesions can be identified with a higher degree of sensitivity and specificity [16].

In patients with a clinical suspicion of Cushing’s disease without a suggestive pituitary lesion on magnetic resonance imaging (MRI), bilateral inferior petrosal sinus sampling (BIPSS) provides excellent specificity and higher sensitivity than the other currently available biochemical testing strategies and despite its invasive nature, the complication rates are low when performed by a trained interventionist. Double superior vena cava (SVC) has no known association with Cushing's disease, but the presence of such congenital venous anomaly makes the procedure of bilateral inferior petrosal sinus sampling (BIPSS) technically more challenging, therefore having a sound anatomical knowledge of such rare venous anomaly is paramount for the procedure to be performed safely and successfully.

REFERENCES


Interventional Radiology: Role of bilateral inferior petrosal sinus sampling (BIPSS) in the diagnosis of Cushing's disease in a patient with double superior vena cava

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FIGURES

Figure 1 (left): 52-year-old female patient with Cushing's disease and double superior vena cava. FINDINGS: Digital subtraction venogram of the right internal jugular vein (IJV) obtained in the anteroposterior view shows the opacification of the bilateral cavernous sinuses (thin solid arrows) and the inferior petrosal sinuses (thin dotted arrows). TECHNIQUE: Venogram of the right internal jugular vein. Siemens AXIOM Artis zee, 70 kV. 10 ml of Iohexol (Omnipaque 350; GE Healthcare) by hand injection. It was performed via a 5 French Torcon NB Advantage Beacon tip catheter (thick arrow) with DAV tip configuration (Cook Medical, Bloomington, Indiana) introduced via a 6 French Terumo Vascular Sheath (Terumo Corporation, Tokyo) inserted in the left common femoral vein (CFV). The other vascular catheter (thin solid arrow) inserted via the right CFV is left in-situ in the right internal jugular vein.

Figure 2: 52-year-old female patient with Cushing's disease and double superior vena cava. FINDINGS: Digital subtraction venogram in the anteroposterior view demonstrates a small rudimentary left brachiocephalic vein (thick dotted arrow) draining into the persistent left superior vena cava (SVC) (thick solid arrow) which then drains into the coronary sinus (*) of the heart. TECHNIQUE: Venogram of the left brachiocephalic vein. Siemens AXIOM Artis zee, 70 kV. 10 ml of Iohexol (Omnipaque 350; GE Healthcare) by hand injection. The venogram was obtained with another 5 French Torcon NB Advantage Beacon tip catheter (thin dotted arrow) with DAV tip configuration (Cook Medical, Bloomington, Indiana) introduced via a 6 French Terumo Vascular Sheath (Terumo Corporation, Tokyo) inserted in the left common femoral vein (CFV). The other vascular catheter (thin solid arrow) inserted via the right CFV is left in-situ in the right internal jugular vein.
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Figure 3: 52-year-old female patient with Cushing's disease and double superior vena cava.
FINDINGS: Fluoroscopic spot radiograph in the anteroposterior view shows the guide wire (arrowhead) in the left internal jugular vein (IJV) with the tip of the catheter (dotted arrow) following this guidewire in the persistent left superior vena cava (SVC). Note the other vascular catheter (solid arrow) in-situ in the right IJV.
TECHNIQUE: Fluoroscopic spot radiograph of the mediastinum. Siemens AXIOM Artis zee, 70 kV. Under fluoroscopic guidance a 0.035-inch hydrophilic straight Terumo guidewire (Terumo Corporation, Tokyo) was manipulated into the coronary sinus (*) via the right atrium to access the persistent left superior vena cava. The guide wire was followed by a 3 French Torcon NB Advantage Beacon tip catheter with DAV tip configuration (Cook Medical, Bloomington, Indiana).

Figure 4: 52-year-old female patient with Cushing's disease and double superior vena cava.
FINDINGS: Digital subtraction venogram performed in the anteroposterior view via the second 5 French vascular catheter (thin arrow) parked in the left internal jugular vein (IJV). It demonstrates the contrast opacification of the left IJV, its confluence with the left subclavian vein (arrowhead) and the persistent left superior vena cava (thick arrow) draining into the cavernous sinus (*).
TECHNIQUE: Venogram of the left internal jugular vein. Siemens AXIOM Artis zee, 70 kV. 10 ml of Iohexol (Omnipaque 350; GE Healthcare) by hand injection.
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Figure 5: 52-year-old female patient with Cushing’s disease and double superior vena cava.

FINDINGS: (a): Digital subtraction venogram obtained in the anteroposterior view shows the tip of the microcatheter (thick solid arrow) within the inferior petrosal sinus (thin dotted arrow), just beneath the cavernous sinus (thin solid arrow).

(b): Fluoroscopic spot radiograph in the anteroposterior view obtained to confirm the positions of the bilateral microcatheters (thick solid arrows), before the commencement of the bilateral inferior petrosal sinus sampling.

TECHNIQUE: (a): Venogram of the right inferior petrosal sinus. Siemens AXIOM Artis zee, 70 kV. 2 ml of Iohexol (Omnipaque 350; GE Healthcare) by gentle hand injection. Two 2.5 French Cantata super-selective microcatheters (Cook Medical, Bloomington, Indiana) are introduced coaxially through the bilateral 5 French catheters.

(b): Fluoroscopic spot radiograph of the skull. Siemens AXIOM Artis zee, 70 kV.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Excessive ACTH production from a pituitary microadenoma.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>1.2 to 2.4 cases per million.</td>
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<tr>
<td>Gender ratio</td>
<td>3-8 times higher in women than in men.</td>
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<tr>
<td>Age predilection</td>
<td>None.</td>
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<tr>
<td>Risk factors</td>
<td>None.</td>
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<td>Treatment</td>
<td>Surgery with transphenoidal selective adenomectomy.</td>
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<td></td>
<td>Medical and radiation therapy are reserved for patients</td>
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<tr>
<td></td>
<td>who are not surgical candidates or has failed surgery.</td>
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<tr>
<td>Prognosis</td>
<td>Surgery has remission rate ranging from 69 to 98% (simple</td>
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<td>average 79%), recurrence rate from 3 to 17% (simple</td>
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<td>average 10%), and the acute surgical mortality rate from</td>
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<td></td>
<td>0 to 1.9%.</td>
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<td>Findings on imaging</td>
<td>Hypodense or hypointense lesion on dynamic contrast-</td>
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<td>enhanced CT or MR. CT has a low</td>
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<td></td>
<td>sensitivity of about 47%. Sensitivity for MRI</td>
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<td></td>
<td>ranged between 69 to 90%.</td>
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<td></td>
<td>Positive BIPSS results for radiologically occult hormonally</td>
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<td></td>
<td>active pituitary microadenomas.</td>
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Table 1: Summary table for Cushing’s disease.
Etiology: Unknown.

Incidence: 0.3 to 0.5% of the general population.

Gender ratio: None.

Age predilection: Congenital lesion.

Risk factors: None.

Treatment: Not required as there is no physiologic impact on circulation.

Prognosis: Good.

Findings on imaging: Usually found incidentally on either cross-sectional imaging or on radiograph, when traversed by a central venous catheter or during the introduction of cardiac pacemaker and defibrillator wires; where it courses along the left side of mediastinum towards the heart.

Table 2: Summary table for double superior vena cava.

<table>
<thead>
<tr>
<th>Differential</th>
<th>Imaging findings</th>
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<tbody>
<tr>
<td>Cushing’s disease.</td>
<td>• Lesions are hypodense or hypointense on dynamic contrast-enhanced CT or MR respectively.</td>
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<td></td>
<td>• Positive BIPSS results for radiologically occult hormonally active pituitary microadenomas.</td>
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<tr>
<td>Adrenal adenoma</td>
<td>• Well-defined nodules with an average attenuation of less than 10 HU for a lipid-rich adenoma and more than 10 HU for a lipid-poor adenoma on unenhanced CT.</td>
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<td></td>
<td>• Wash-out value of more than 50% on a dynamic contrast enhanced CT or MR.</td>
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<td></td>
<td>• Signal “drop out” in the out-of-phase MR sequences for a lipid-rich adenoma.</td>
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<td>• In case of unilateral hormonally active adrenal adenoma, the remaining ipsilateral and contralateral adrenal gland may be atrophic in appearance.</td>
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<tr>
<td>Ectopic secretion of ACTH, from small-cell lung cancer, bronchial carcinoid tumors, medullary thyroid carcinoma, pancreatic carcinoid tumor, thymic carcinoid tumor and disseminated carcinoid.</td>
<td>• Dedicated US, CT and MR of these organs sites can be performed for their detection.</td>
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<td>• Positive uptake of radiotracer in somatostatin receptor imaging.</td>
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Table 3: Differential diagnosis table for Cushing’s disease.
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<table>
<thead>
<tr>
<th>Minutes after administration of human CRH</th>
<th>-5</th>
<th>-1</th>
<th>+2</th>
<th>+5</th>
<th>+10</th>
<th>+15</th>
<th>+30</th>
<th>+45</th>
<th>+60</th>
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<td>ACTH (purple tube)</td>
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<td>Right inferior petrosal sinus</td>
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<td>152.2</td>
<td>238.9</td>
<td>&gt;1522.0</td>
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<td>&gt;1522.0</td>
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<tr>
<td>Left inferior petrosal sinus</td>
<td>25.3</td>
<td>20.4</td>
<td>293</td>
<td>73.1</td>
<td>44.2</td>
<td>47.9</td>
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<tr>
<td>Peripheral</td>
<td>19.7</td>
<td>17.7</td>
<td>21.2</td>
<td>32.2</td>
<td>37.2</td>
<td>43.5</td>
<td>40.3</td>
<td>36.1</td>
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<td>Prolactin (yellow tube)</td>
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<td>7632.0</td>
<td>6408.0</td>
<td>6316.0</td>
<td>5461.0</td>
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<tr>
<td>Left inferior petrosal sinus</td>
<td>259.6</td>
<td>1293</td>
<td>261.4</td>
<td>257.4</td>
<td></td>
<td></td>
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<tr>
<td>Peripheral</td>
<td>261.1</td>
<td>260.5</td>
<td>264.2</td>
<td>261.9</td>
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<td>Cortisol (yellow tube)</td>
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<tr>
<td>Peripheral</td>
<td>305.0</td>
<td>289.0</td>
<td>506.0</td>
<td>673.0</td>
<td>629.0</td>
<td>676.0</td>
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</table>

Table 4: BIPSS result in our index case after administration of 80µg of human corticotropin-releasing hormone (CRH) (1µg/kg) slow intravenous (peripherally) bolus over 1 minute.

ABBREVIATIONS

ACTH=Adrenocorticotropic hormone
BIPSS = Bilateral inferior petrosal sinus sampling
BMD= Bone mineral densitometry
CRH = Corticotropin-releasing hormone
CT = Computed tomography
DEXA= Dual-energy x-ray absorptiometry
IJV = Internal jugular vein
IPS = Inferior petrosal sinus
MRI= Magnetic resonance imaging
SVC = Superior vena cava
UFC= Urinary free cortisol

KEYWORDS

Bilateral inferior petrosal sinus sampling; BIPSS; Cushing's disease; Double superior vena cava; Inferior petrosal sinus; Pituitary gland; Pituitary microadenoma

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