

## Raymond's Syndrome Following Petrosal Sinus Sampling

H. Seyer<sup>1</sup>, J. Honegger<sup>1</sup>, W. Schott<sup>1</sup>, M. Küchle<sup>2</sup>, W. J. Huk<sup>3</sup>, R. Fahlbusch<sup>1</sup>, and H. Frisch<sup>4</sup>

<sup>1</sup>Department of Neurosurgery, <sup>2</sup>Department of Ophthalmology, <sup>3</sup>Department of Neuroradiology, University of Erlangen-Nürnberg, Erlangen, Federal Republic of Germany, and <sup>4</sup>Department of Pediatrics, University of Vienna, Vienna, Austria

### Summary

Inferior petrosal sinus sampling (IPSS) is used to evaluate the pituitary-dependency of Cushing's disease, and to predict the laterality of a microadenoma prior to transsphenoidal operation. A serious complication occurred in a 14-year-old boy: he suffered brain stem ischaemia with abducens nerve palsy and hemiparesis (Raymond's syndrome). The case prompted us to reconsider the indication for this investigation.

**Keywords:** Pituitary adenoma; Cushing's disease, inferior petrosal sinus sampling (IPSS); Raymond's syndrome.

### Introduction

In recent years, inferior petrosal sinus sampling (IPSS) has become a mainstay in the preoperative evaluation of Cushing's disease. IPSS is valuable to assure the pituitary-dependency of the disease, and may give a hint for the laterality of the microadenoma<sup>1, 3, 5, 7, 11</sup>, but this is also still under debate<sup>4</sup>. The procedure is generally considered to imply minimal morbidity<sup>6</sup>. However, in our series of 79 IPSS (6 children and 73 adults, 1987–1993), we encountered one serious complication: an abducens nerve palsy and contralateral hemiparesis developed immediately after the procedure. This, as far as we know, has not previously been reported. We present the case report of the afflicted patient and discuss the possible mechanisms.

### Case Report

A 14-year-old boy presented in January 1991 with obesity, moon-face, striae, and hirsuties. Endocrinologic assessment revealed Cushing's disease. A hypo-intense area of 3 mm was detected on the right side of the pituitary gland by magnetic resonance imaging. The patient was operated on in another neurosurgical department by a transsphenoidal approach, and a right-sided microadenoma was removed, which was confirmed by histological examination. Postoperative clinical course, however, showed further weight gain, and

endocrinological re-assessment revealed unchanged activity of Cushing's disease.

In January 1992, the patient was admitted to our department. At that time, MRI showed a suspicious but uncertain area on the left side of the sella turcica. Petrosal sinus sampling was considered appropriate to provide safer information about the side of the ACTH-source. Bilateral sampling of venous blood was performed simultaneously from the inferior petrosal sinuses. The left one was narrow, while the right one was wide, but both were easily catheterized. The tips of the catheters were flushed with heparine solution (5,000 IU/L) between the blood collections. The sampling including CRH stimulation lasted for about 30 minutes. Both catheters were withdrawn immediately thereafter. Sampling results revealed markedly higher ACTH values on the left side, suggesting a left-sided adenoma.

Immediately after the procedure, the boy experienced double vision. A complete sixth nerve palsy of the left eye developed within the following hour (Fig. 1), together with a contralateral hemiparesis. For about two days, the patient had also the feeling of hyperacusis on the left side, and a discrete asymmetry of the corners of his mouth was suspected during that time. CT revealed no haemorrhage, thus

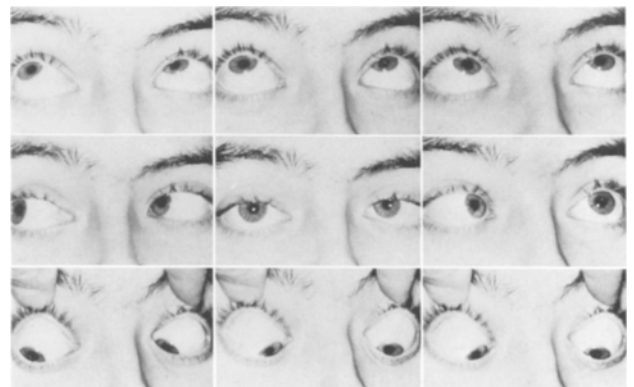


Fig. 1. Left abducens nerve palsy, documented the day after brain stem ischaemia. Extraocular eye movements in nine fields of gaze. In the middle, primary position. Upper line shows upward gaze, lower line shows downward gaze. Conjugate eye palsy is not evident

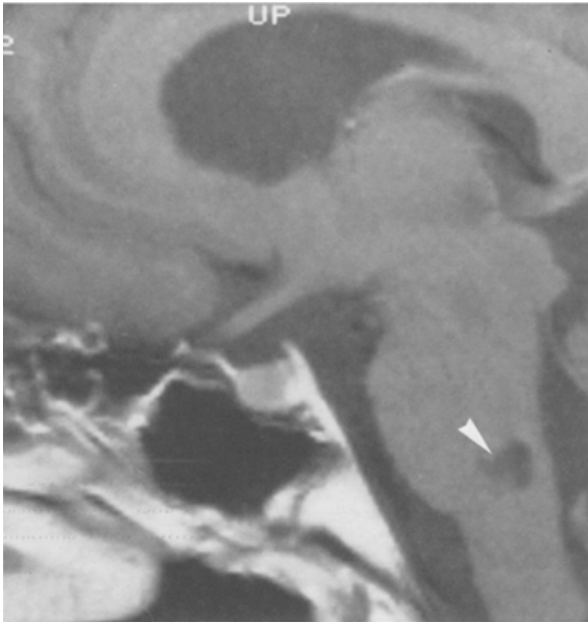


Fig. 2. T1-weighted MRI showing zone of infarction in the brain stem (sagittal view), in between the lower rear part of the pons and the medulla oblongata (arrow), supposed to involve the intrapontine abducens fascicle

anticoagulation with heparine could be commenced. While hemiparesis improved partly during the following months, abducens paralysis persisted. Therefore, transsphenoidal re-exploration was postponed. T1-weighted MRI showed a left-sided hypo-intense area in the brain stem at the level of the lower pons, which subsequently developed into a well demarcated infarction zone (Fig. 2).

Four months after the event, a left-sided adenoma was removed, and replacement therapy with hydrocortisone was required for post-operative hypocortisolism. Pituitary function was otherwise normal.

One year after the operation, hemiparesis has partly regressed, but the abducens nerve palsy shows no improvement. Therefore, extraocular muscle surgery is planned.

## Discussion

From the clinical point of view, abducens nerve palsy and contralateral hemiparesis corresponded to the syndrome described by Raymond and Cestan in 1903<sup>9</sup>.

Double vision and isolated progressive abducens nerve palsy could have been caused by thrombosis of the inferior petrosal sinus which is adjacent to the nerve and might have effected it by peripheral compression. Thrombosis of the cavernous sinus was also imaginable. But as no additional oculor-motor or trigeminal nerve palsy occurred, both mechanisms were less likely.

Hemiparesis supposed a brain stem lesion near the corticospinal tract. As hemiparesis proved to be regressive, the corticospinal tract could not have been

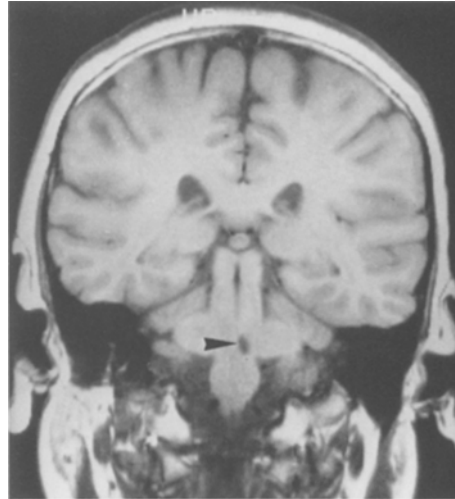


Fig. 3. Coronal view of the T1-weighted MRI shows a well demarcated lesion close to the midline of the brain stem (arrow), at the level of the fourth ventricle and the cerebellar peduncles, but evidently not involving the abducens nucleus

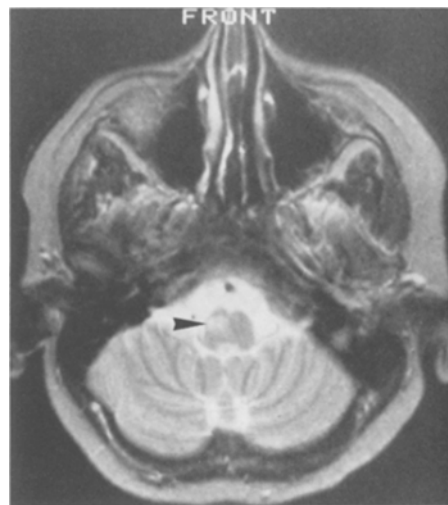


Fig. 4. Axial view of T2-weighted MRI shows an area of ischaemic lesion in the more ventral medulla oblongata, involving the corticospinal tract (arrow)

completely involved by infarction. The lesion also did not directly impair the abducens nucleus, because ipsilateral conjugate gaze palsy was not evident. The ipsilateral facial nerve might have been involved intermittently, possibly by oedema, as may be indicated by brief hyperacusis (stapedius muscle weakness).

Thus, the lesion was supposed to involve the abducens nerve fascicle, and partly include the corticospinal tract.

The often asymmetrical inferior petrosal sinuses

communicate amongst others with the basilar venous plexus<sup>10, 12</sup>, which probably drains the blood supply from the lower pons. We suppose that thrombosis of this basilar venous plexus was the most likely cause of the syndrome. As hemiparesis was regressive, thrombosis might have been only partial, or regressive, too.

The anatomical site of the lesion could be evaluated by MRI (Figs. 2–4).

Inferior petrosal sinus sampling (IPSS) in patients with Cushing's disease has become a well-established tool in the preoperative evaluation of the presence and laterality of ACTH-producing microadenomas. Findling and Oldfield<sup>2, 8</sup> perform IPSS in all patients with ACTH-dependent Cushing's syndrome on a routine basis for accurate differential diagnosis. With respect to this serious complications of brain stem insult, we advocate that in patients with Cushing's disease, IPSS should only be used if MRI shows no adenoma, or if the pituitary dependency of Cushing's syndrome is unsolved. The investigation improves the chance of a surgical cure, if no adenoma is found during systematic exploration of the pituitary, and hemihypophysectomy on the side of predominant ACTH-secretion will be required<sup>7</sup>. It has been proposed that prediction of the correct side by IPSS reduces dissection of the gland<sup>1</sup>. In our opinion, this benefit of IPSS is less significant. But in cases where no microadenoma can be found by systematic exploration, hemihypophysectomy on the side of elevated ACTH-levels provides a chance for surgical cure. However, hemihypophysectomy has been performed in only 5% of our patients. Therefore, whether IPSS is justified at all should be discussed, unless pituitary dependency of Cushing's syndrome is unclear from conventional endocrine evaluation.

### Acknowledgement

The authors thank Prof. Dr. P. Thierauf, Department of Neuropathology, University of Erlangen-Nürnberg, for reviewing the literature about venous drainage of the brain stem.

### References

- Boolell M, McNeil P, Gilford E, Cummins J, Arnott R, Alford F (1990) An overview of bilateral synchronous inferior petrosal sinus sampling (BSIPSS) in the pre-operative assessment of Cushing's disease. *Aust NZ J Med* 20: 765–770
- Findling JW, Kehoe ME, Shaker JL, Raff H (1991) Routine inferior petrosal sinus sampling in the differential diagnosis of adrenocorticotropin (ACTH)-dependent Cushing's syndrome: early recognition of the occult ectopic ACTH syndrome. *J Clin Endocrinol Metab* 73: 408–413
- Lüdecke DK (1989) Intraoperative measurement of adrenocorticotropin hormone in peripituitary blood in Cushing's disease. *Neurosurgery* 24: 201–205
- McCane DR, McIrath E, McNeill A, Gordon DS, Hadden DR, Kennedy L, Sheridan B, Atkinson B (1989) Bilateral inferior petrosal sinus sampling as a routine procedure in ACTH-dependent Cushing's syndrome. *Clin Endocrinol* 30: 157–166
- Miller DL, Doppman JL, Nieman LK, Cutler GB, Chrousos G, Loriaux DL, Oldfield ED (1990) Petrosal sinus sampling: discordant lateralization of ACTH-secreting pituitary microadenomas before and after stimulation with corticotropin-releasing hormone. *Radiology* 176: 429–431
- Miller DL, Doppman JL (1991) Petrosal sinus sampling: technique and rationale. *Radiology* 178: 37–47
- Oldfield EH, Chrousos GP, Schulte HM, Schaaf M, KcKeever PE, Krudy AG, Cutler CB, Loriaux DL, Doppman JL (1985) Preoperative lateralization of ACTH-secreting pituitary microadenomas by bilateral and simultaneous inferior petrosal sinus sampling. *N Engl J Med* 312: 100–103
- Oldfield EH, Doppman JL, Nieman LK, Chrousos GP, Miller DL, Katz DA, Cutler GB, Loriaux L (1991) Petrosal sinus sampling with and without corticotropin-releasing hormone for the differential diagnosis of Cushing's syndrome. *N Engl J Med* 325: 897–905
- Raymond A, Cestan B (1903) *Gaz Hopit Paris* 76: 829
- Shiu PC, Hanafee WN, Wilson GH, Rand RW (1968) Cavernous sinus venography. *Am J Roentgenol* 104: 57–62
- Tabarin A, Greselle JF, San-Galli F, Lepart F, Caille JM, Laptapic JL, Guerin J, Roger P (1991) Usefulness of the corticotropin-releasing hormone test during bilateral inferior petrosal sinus sampling for the diagnosis of Cushing's disease. *J Clin Endocrinol Metab* 73: 53–59
- Zovickian J, Oldfield EH, Doppman JL, Cutler GB, Loriaux DL (1988) Usefulness of inferior petrosal sinus venous endocrine markers in Cushing's disease. *J Neurosurg* 68: 205–210

Correspondence: Hendrikus Seyer, M.D., Department of Neurosurgery, University of Erlangen-Nürnberg, Schwabachanlage 6, D-91054 Erlangen, Federal Republic of Germany.