

# Patient with a Pituitary Adenoma Haemorrhage and Total Ophthalmoplegia under Treatment with ASS and Plavix as a Secondary Stroke Prophylaxis

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## Abstract

In our case report, we discuss a patient, who underwent a dual antiplatelet therapy as a secondary prevention of stroke. To our knowledge, there are no other cases in the literature reviews about pituitary haemorrhage on dual antiplatelet therapy. The 7<sup>th</sup> most common reason for intrapituitary haemorrhage is aspirin. However, the risk for bleeding was not considered when a dual therapy was administered.

The patients, who have suffered a stroke, need a suitable secondary stroke prophylaxis. The dual therapy has shown advantages over the monotherapy with aspirin or with clopidogrel. The personal approach to every patient, who has suffered a stroke, has to be taken. The pituitary adenoma can increase the risk for intracranial bleeding, when a dual therapy is used as a second stroke prophylaxis.

**Keywords:** Pituitary adenoma haemorrhage • Aspirin and clopidogrel • Secondary prevention of stroke • Pituitary bleeding • Therapy with aspirin and clopidogrel

## Introduction

Patients with pituitary adenomas are at risk either for necrosis or for haemorrhage. In the literature review, around 10% of the patients present themselves with haemorrhage or with necrosis into hypophyse with acute onset of the symptoms. In our case report, we discuss a patient, who underwent a dual antiplatelet therapy as a secondary prevention of stroke. To our knowledge, there are no other cases in the literature reviews about pituitary haemorrhage on dual antiplatelet therapy [1].

A 66-old patient presents herself with an acute onset of partial ophthalmoplegia on the left side. The patient was diagnosed with pituitary adenoma one year before the onset of the symptoms. In the beginning of 2017, she developed a stroke and therefore a dual antiplatelet therapy was necessary as a secondary prevention. On the day of the onset of the symptoms, she developed acute holocephalgie, nausea and partial ophthalmoplegia on the left side. On the CT scan in our emergency room, there were not any signs of an intracranial bleeding or new stroke. The hypophyseal adenoma seemed unchanged. The patient was admitted at the stroke unit at our hospital for further evaluation and therapy. On the following day a MRI scan was carried out, where a haemorrhage into the hypophyse

was observed. An emergency operation was carried out because of the progress of the neurological deficit. Post operatively the patient showed an improvement in n. abducens and n. oculomotorius [2].

## Case Presentation

### Pathophysiology

Understanding the mechanism leading to acute onset of ophthalmoplegia in patients with haemorrhage into the hypophyse improves the indications for surgery. Although there are several case reports on spontaneous recovery after pituitary hemorrhage, the general understanding is that an urgent surgery up to 6 hours after the onset of the symptoms will provide an improvement in the neurological status. Haemorrhage with or without infarction occurs in a pituitary tumour and destroys most of the solid tumour, leading to the clinical syndrome of pituitary apoplexy. Once infarction occurs, a large portion of the adenoma or even the entire tumour becomes a haemorrhagic mass that swells rapidly and produces acute compression of the neighbouring structures. It may not only compress the carotid mechanically but it may also induce local vasospasm by irritation. Some blood may escape from it into the

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**Received:** 10 February, 2020; Manuscript No. JCDE-23-5183; **Editor assigned:** 13 February, 2020; Pre QC No. P-5183; **Reviewed:** 28 February, 2020; QC No. Q-5183; **Revised:** 13 July, 2020; Manuscript No. R-5183; **Published:** 10 August, 2023; DOI: 10.37421/2165-7920.2023.13.1571

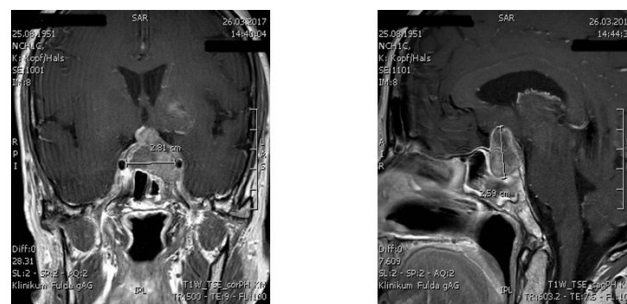
basilar sub-arachnoid space or it may set up an inflammatory reaction in the basilar cisterns [3].

## History of the patient

In December 2016, the patient was admitted at our hospital because of new neurological deficit. She developed suddenly motor aphasia and facial palsy on the left side. By the admission at our hospital, an emergency CT scan was carried out where no infarct demarcation was observed. The angiographic studies have shown a clot in M1 segment on the left side. According to the guidelines for thrombolysis, in this case thrombolytic therapy was not indicated because of the uncertain time of onset of the neurological deficit. Subsequently was a MRI scan carried out where the patient was diagnosed with infarct in the basal ganglia region [4]. On the MRI scan was a mass in the pituitary region observed. This mass had the characteristics of macroadenom in pituitary region. The prolactin levels were 2 times elevated (44 µg/l). At this time, the levels of FT3, TSH and ACTH were elevated as well. We consulted the patient and we set the indication for surgery for decompression in suprasellar region. After the information consent, the patient denied any surgical intervention for the time being. According to the guidelines for Prevention of Stroke, a therapy with ASS 100 (life-time therapy) and clopidogrel 75 (3 months therapy) was indicated. 1 week later, the patient was discharged and the neurological deficit showed an improvement. Three months later the patient presented herself one more time in our emergency room. The patient reported general weakness, nausea, headache and diplopia, beginning symptoms of pituitary apoplexy. The symptoms had a rapid onset. In our emergency room a CT scan was carried out, where no acute neither haemorrhage nor new infarct was seen. The patient was admitted at the neurological department for further examinations. On the following day, a MRI scan was carried out, where a haemorrhage in the region of the hypophyse was observed [5,6].

## MRI scan

The DWI sequences show no diffusion disturbance in supra- and infratentorial brain regions and offer no evidence for an ischemic triggering of the newly occurred left sided occipital motor palsy. In the high-resolution T1-weighted sequences before and after contrast application, a slight degree of size progression of the left-pituitary is seen compared to the pre-examination of 12/16 from formerly 2.4 × 2.2 to 2.8 × 2.6 cm. Significant susceptibility artefacts within the tumour formation are seen in the T2 FFE sequences/T2\* sequences. These artefacts are due to the paramagnetic effect of deoxy/methaemoglobin and provide the image morphological correlate of a given haemorrhage within the tumour formation [7]. The size progression is thus based on acute intratumoral hemorrhage with mechanical affection of the left-sided nervus oculomotorius in the course of the left sinus cavernosus. Due to the hypointense signal characteristics in the T2-weighted sequences and a still missing hyperintense signal development in the native T1-w sequences, the time of the bleeding event can be limited to a period of 6 hours to 3 days (Figure 1).



**Figure 1.** Coronal view, haemorrhage within the tumour formation and sagittal view, haemorrhage within the tumour formation.

## Surgery

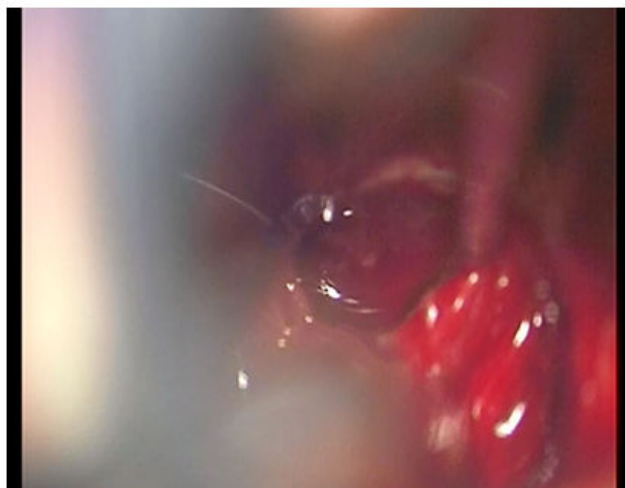
At the time of the consultation of the patient, she had already developed a total ophthalmoplegie on the left side by sinus cavernosus syndrome. The patient was informed about the emergency surgery indication to decompress the cranial nerves. To our knowledge, there is no study, which observed the improvement of the cranial nerve palsies after decompression in the pituitary region. The general understanding is made up on observation in the traumatic cranial nerves palsies, where a decompression, carried out sooner, brings a better and faster improvement of the cranial nerve palsies [8].

After the information consent, the patient agreed to the operation. Here two things had to be considered. First, the patient is on therapy with aspirin. The effects of Aspirin are connected to the irreversible inhibition of prostaglandin-H2-synthase. This enzyme is required for the enzyme required for prostaglandin and thromboxane synthesis. Aspirin acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the PTGS enzyme. This makes aspirin different from other NSAIDs, such as diclofenac and ibuprofen), which are reversible inhibitors (Suicide inhibition) [9,10].

The blocking of thromboxane A2 is the reason for the inhibitory effects of the platelet aggression for the lifetime of the platelets. The information consent of the patient was obtained and she was informed, that the risk for a post-operative haemorrhage is substantial.

Nevertheless, the patient agreed with the operation. We performed a transsphenoidal/endonasal approach for the removal of the tumour. The patient was put in a Mayfield. Perioperatively 7 ampules of desmopression (minirin) were administered. The effects of the Minirin are connected to the increase of factor of von willebrand and factor VIII, thus activation and aggregation of platelets is promoted [11,12].

After the dural opening, a hard part of the tumour was observed together with liquid parts with blood. The tumour was partially removed due to the heavy bleeding (intraoperatively were 2 platelet concentrates, PPSB and fibrinogen administered to control the bleeding). With this bleeding problem, it is unthinkable to violate the wall of sinus cavernosus, thus we decide to leave a part of the tumour, which is attached to the wall of the sinus. (Figure 1).



**Figure 2.** Intra-op view, sinus cavernosus wall.

Post operatively the patient showed a tendency to improve, diplopia was observed in all directions (all 3 nerves showed improvement tendency) and the patient could open her eye up to 20 degrees. 3 months after the operation, the patient presented herself for the follow-up check and the patient had recovered almost completely. A slight n. oculomotorius palsy remained [13,14].

## Results and Discussion

To our knowledge, there are no cases on the literature review, where a spontaneous bleeding in the pineal region with therapy with aspirin and clopidogrel was observed. The clinical significance of the case incorporates the risk-benefit problems with patients with tumours and the need of anti-aggregate therapy. According to bleeding risk with long-term low-dose aspirin: A systematic review of observational studies, the risk for possible intracranial haemorrhage is around 1.4%. Aspirin was associated with increased bleeding risks when combined with non-steroidal anti-inflammatory drugs, clopidogrel and selective serotonin reuptake inhibitors compared with monotherapy.

The therapy with aspirin and clopidogrel is dangerous for the patients with tumours. The risk-benefit ratio has to be extremely good rated and the possible negative effects have to be discussed with the patients. It is proven that the dual therapy as a secondary stroke prophylaxis benefits the patients who had a history of stroke. However, the risk of bleeding needs to be taken under consideration [15].

## Conclusion

Three months later the patient presented herself one more time in our emergency room. The patient reported general weakness, nausea, headache and diplopia, beginning symptoms of pituitary apoplexy. The symptoms had a rapid onset. In our emergency room a CT scan was carried out, where no acute neither haemorrhage nor

new infarct was seen. The patient was admitted at the neurological department for further examinations.

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**How to cite this article:** Pavlov, Orlin, Mirchev Nikolay, Obersheimer Jens and Behr Robert. "Patient with a Pituitary Adenoma Haemorrhage and Total Ophthalmoplegia under Treatment with ASS and Plavix as a Secondary Stroke Prophylaxis." *J Clin Case Rep* 13 (2023): 1571.