Pituitary apoplexy in residual pituitary adenoma following surgical treatment in the follow-up period: management strategy

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Abstract: Pituitary apoplexy is a rare clinical event, used to occur spontaneously. Although, some predisposing factors for pituitary apoplexy is reported ie. head injury, digital cerebral angiography, bromocriptine therapy, coughing, lumbar puncture for CSF drainage, pneumoventriculography, even during surgery, in the immediate postoperative period and raised intracranial tension. Although pituitary apoplexy occurring following radiotherapy as primary treatment modality is reported, however, apoplexy occurring in residual adenoma following surgery, receiving adjuvant radiation therapy for residual adenoma is not reported in the literature. Authors reports two-cases of pituitary apoplexy, which occurred in the residual pituitary adenoma after a varying period in the follow-up period. These patients were previously operated by transcranial approach for decompression of the pituitary adenoma. The pituitary apoplexy occurred in one case after an interval of one and half years following surgical intervention for pituitary adenoma decompression and next case developed after five years. Both the cases had also received radiotherapy in the postoperative period for residual pituitary adenoma.

Key words: Pituitary apoplexy, residual pituitary adenoma, transsphenoidal surgery

Introduction

Pituitary apoplexy is clinical syndrome characterized by sudden onset of headache, commonly associated with vomiting, meningeal irritability, and often ophthalmoplegia or visual deterioration (13, 17-19). Apoplexy mostly occurs spontaneously, although in some cases may have predisposing factors including head endocrine manipulation, trauma, cerebral angiography, bromocriptine therapy, radiation therapy of pituitary adenoma lumbar puncture, and in the immediate postoperative period. (5, 6, 7, 8, 11) We are reporting two cases of pituitary apoplexy, which was encountered in patients, who were operated

for pituitary adenoma and also received radiation therapy for residual many years prior to current occurrence of apoplexy.

Illustrated Case I

A 42- year- old male presented to our neurosurgical services with a history of sudden onset headache, vomiting and rapidly progressive decline in the visual acuity for the last 15 days. He was operated for a pituitary adenoma four year back by transsphenoidal approach. (Figures 1, 2, 3) The histopathology revealed chromophobe pituitary adenoma. He also received radiotherapy in, for residual adenoma. General examination was normal, with stable vitals. Neurological examination revealed visual acuity of 6/9 and 6/24 respectively in the right and the left eye. He had bitemporal field defect. Fundi revealed bilateral primary optic atrophy. He also had right seventh cranial nerve upper motor-neuron paresis. The rest of the neurological examination was normal. The haematological and biochemical profiles were normal. However, urinary specific gravity ranged from 1008-1014. Hormonal profile showed Growth hormone - 2 (normal upto-5ng/ml), serum cortisol (8 am) - 0.8 µ g / dl (normal 5 -18), serum prolactin 12 ng /ml (normal 1.3-24), TSH- 2.8 µ IU /dl (normal 0.4- 4.6), free T3- 1.4 pg/ml (2.2- 5) and, free T4- 0.3 ng /dl (0.7- 1.8). X-ray chest was normal. Cranial CT scan revealed a pituitary macro-adenoma, showing fair enhancement with contrast agent. MRI sagittal view showed large sellar mass with suprasellar extension having heterogeneous hyperintense signal on T1 weighted image (Figure 4), and coronal T1 weighted image (Figures 5, 6) suggestive of apoplectic bleed in the residual pituitary adenoma with further decent into sphenoid sinus due to deficient sellar floor, caused by previous surgery. There was associated mild hydrocephalus. He underwent decompression of pituitary adenoma through sub-labaial transsphenoidal approach. Intra-operatively a large cyst containing fluid with evidence of old hemorrhage was encountered. Histopathology revealed chromophobe pituitary adenoma with evidence of haemorrhage. Immunohistochemistry morphological work-up was negative prolactin and growth hormones. He showed unremarkable recovery in the postoperative period. His vision was 6/9and 6/12 in the right and left eye respectively at the time of discharge from hospital on fourth postoperative day. He was kept on cortisol and thyroxin as maintenance therapy. He was well at last follow-up 3 year after second surgery and follow-up CT scan revealed no residual.

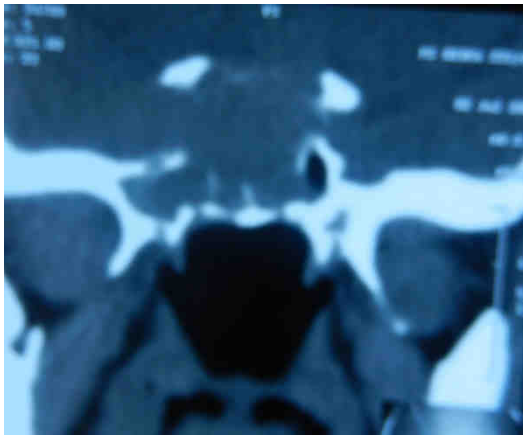

Figure 1 - Contrast enhanced cranial CT, coronal view showing large enhancing sellar suprasellar mass with a right parasellar extension (pre- op)

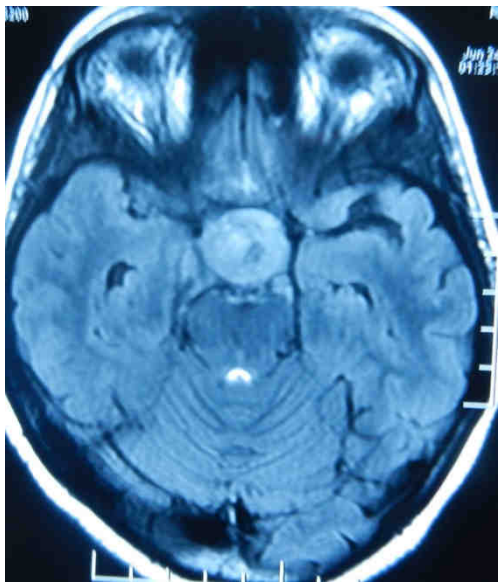

Figure 2 - MRI brain, T!WI mage sowing homogeneous hyperintense mass (pre- op)

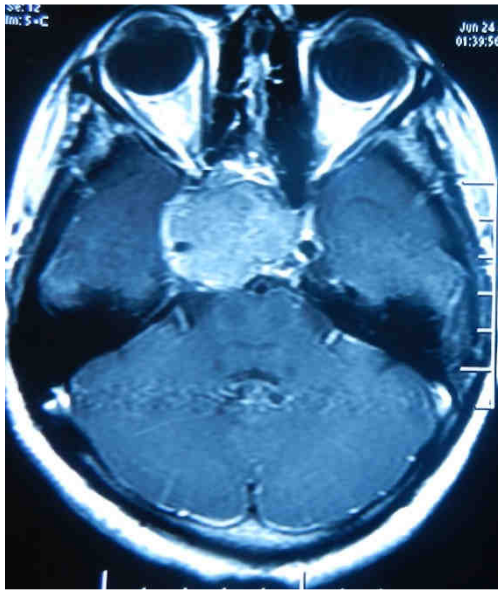

Figure 3 - MRI brain, contrast enhanced, image sowing homogeneous hyperintense mass in sell causing encasement of bilateral internal carotid artery (pre-op)

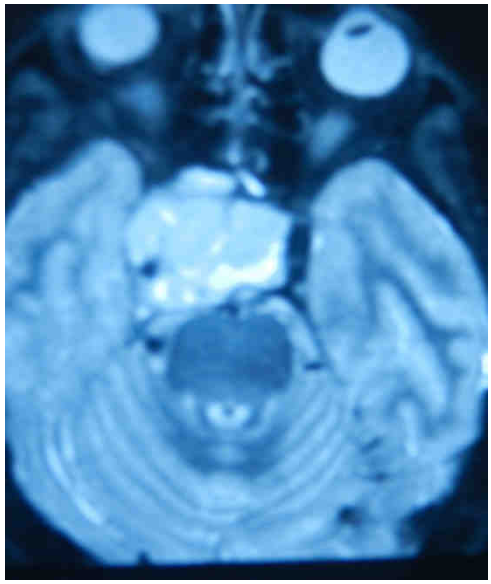

Figure 4 - MRI brain, T2WI , showing heterogeneous lesion in sella with areas of CSF like intensity suggestive of apoplexy in residual pituitary adenoma (Follow-up scan after 5 -year of surgery)

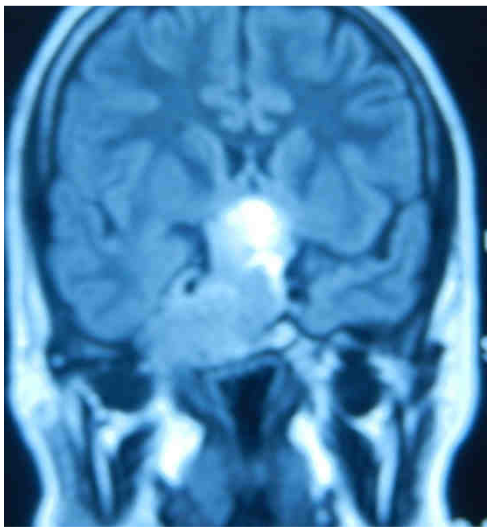

Figure 5 - MRI brain, T1W image, coronal section image, showing descent of suprasellar part with recurrent adenoma with apoplexy (Follow-up scan after 5 -year of surgery)

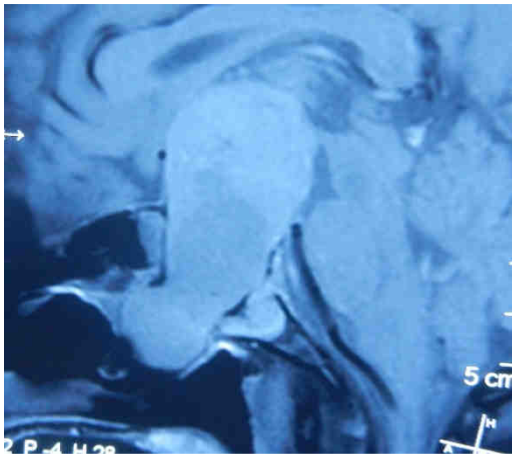

Figure 6 - MRI brain, sagittal section image, showing descent of suprasellar part with recurrent adenoma into sella due to deficient sellar floor due to past surgery, with apoplexy

Illustrated Case II

A 27 - year-old male presented with headache and sudden onset complete vision loss involving both eyes since three days prior to admission. He was operated pituitary macroadenoma by subfrontal route in 1997. He also received radiotherapy for residual pituitary adenoma. On admission his vitals were stable. Neurological examination revealed, visual acuity in the right eye was just positive for perception of light and the left was negative for perception of light. Fundi revealed bilateral primary optic atrophy. The routine haematological and biochemistry parameters were normal. Endocrinological evaluation showed serum cortisol - 14 µ g / dl (normal 5 - 18), serum prolactin 8 ng /ml (normal 1.3-24), TSH- 5 µ IU /dl (normal 0.4- 4.6), free T3-1.2 pg/ml (2.2- 5) and, free T4- 0.4 ng /dl (0.7-1.8). Growth hormone-4 (upto-5ng/ml). Contrast CT scan of cranium revealed sellar-suprasellar mass with fluid level. A transnasal transsphenoidal radical decompression of tumour was carried out as an emergency procedure. At surgery altered dark blood with grayish tumor which was evacuated. Morphological work-up on immune-histochemistry was negative growth and prolactin hormones. He showed remarkable improvement in the vision in postoperative period, 6/36 in the right eye and 6/18 in the left eye. He was continued on cortisol and thyroxin replacement therapy. Contrast enhanced MRI done at six months after second surgery revealed small residual in suprasellar region only which was not abutting the optic chiasma. Gamma knife therapy was given for residual adenoma. He was well at last follow-up one year after gamma knife therapy.

Discussion

Pituitary apoplexy is common clinical syndrome (1-4, 6-8, 15-19). Pituitary adenoma possesses comparatively bleeding frequency of 5.4 times higher than any primary intracranial neoplasm. (1) The incidence of pituitary adenoma with apoplectic presentation varies in literature between 1.5 - 27.7 %. (2, 3, 12) It is considered as complex clinical events, occurring following fulminate expansion of a pituitary tumor by haemorrhage, infarction, or combination of two, which involves adenoma and adjoining and surrounding pituitary gland. (4) Clinically it may have wide spectrum of presentation; which may vary from sub-clinical infarction which could only be noticed during the surgery or on preoperative imaging to full blown apoplexy that mimics

subarachnoid haemorrhage. (3) Although most cases are reported to occur spontaneously. Although, some predisposing factors are reported ie. head trauma, (6) cerebral angiography, (7) endocrine manipulation, (8) bromocriptine therapy, (5) coughing and sneezing, (9) radiotherapy of pituitary tumours (10, 11) lumbar puncture, (13) pneumoencephalography (13), and raised intracranial pressure, (13) Weisberg et al (11) reported a series of 14 cases of pituitary apoplexy, out of which eight cases were associated with radiation therapy. These patients were treated with radiotherapy as primary mode of treatment without any prior surgery for pituitary adenoma. Pituitary apoplexy occurred in five cases, which were receiving radiation therapy. It occurred in three cases during the first week of initiation of radiotherapy, one in third weeks and another one towards completion stage of radiotherapy treatment. In rest of cases, the onset of pituitary apoplexy were noted three to four years after completion of radiation therapy. However, surgery was required in these cases after pituitary apoplexy during the course of radiation therapy. In the present study, our both cases were subjected to transcranial decompression of pituitary adenoma along with radiotherapy for the residual tumour and after a varying period of follow-up developed apoplectic manifestation.

Various hypothesis put forward for pituitary apoplexy occurrence in post radiated pituitary adenoma, his rapid enlargement of cyst, which can cause compression over solid portion, resulting in ischemia and hypoxic necrosis. This leads to less radio-responsiveness and more likely to undergo hemorrhagic necrosis with initiation of radiotherapy. Even radiotherapy can cause vascular damage to endothelium of fine blood vessel and damage neovascularity of tumour leading to hemorrhagic necrosis. Goel et al (14) reported pituitary apoplexy in the residual tumour after partial decompression following transcranial surgical approach in two cases. However, re-exploration was required within 45 minutes in one case, while 12 hours after in the second case. Rovit et al (4) reported higher incidence of apoplexy in patients in acromegalic or ACTH producing adenoma. Weisberg et al (11) also noticed higher incidence in acromegalic after radiotherapy. However, our cases were with chromophobe pituitary adenoma.

Goel et al (14) reported sudden release of feeding tumour vessel from internal carotid artery, compromise of venous drainage, tumour manipulation, swelling and compression of hypophyseal artery at diaphragma sella resulting in ischemia and secondary tumour necrosis after partial decompression of pituitary adenoma. They further observed that attempt should be made to excise these tumours as radically as possible. Similarly both of our patients underwent transsphenoidal decompression of pituitary adenoma and had uneventful postoperative period. A group of patients with residual pituitary adenoma following radiotherapy show re-growth, continuing vascular damage to blood vessel endothelium, and adenoma growth may outstrip the vascular requirement for adenoma leading to apoplexy, years after of surgery and radiotherapy. Damage to

neovascularity of tumour can lead to hemorrhagic necrosis. The mechanism of pituitary apoplexy is not clear. Ischemic necrosis of adenomatous tissue, compression of superior hypophyseal arteries against diaphgrama sellae and intrinsic vasculopathy of pituitary tumour has been suggested.

Further effect of apoplexy on pituitary function was assessed by Marouf et al, who analyzed a total of 19 cases of pituitary apoplexy, who underwent surgery for pituitary apoplexy. (21) Authors assessed the function of residual pituitary gland function in the postoperative phase, only five cases retained normal pituitary function, while eight cases developed pan-hypopituitarism, and the rest six with partial hypopituitarism. The MRI study in the post-operative follow-up period demonstrated residual pituitary gland in 13 patients, out of which four had normal functional pituitary gland. (21)

Conclusion

Every case of pituitary adenoma with past history of surgical intervention or radiotherapy, showing clinical feature of apoplexy, should be investigated with imaging and if needed urgent surgical opportunity may be given to preserve good neurological outcome. The tumour decompression should be carried out as emergency procedure. During the first surgery itself, the aim should be radical decompression of adenoma to avoid residual adenoma, which carries a potential risk for apoplexy.

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