The role of giant macroadenoma resection in psychotic vs. prolactin disorder: two year follow-up

Uloga resekcije gigantskog makroadenoma u psihotičnom naspram prolaktinskog poremećaja: dvogodišnje praćenje - prikaz slučaja

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ABSTRACT

Introduction: psychosis is defined by presence of hallucinations, delusions or both. Sometimes, the only presentation of brain tumours in general may be psychosis. However, pituitary tumours are also found in association with psychosis. Aim: to present the patient outcome with psychosis associated macroadenoma two years after resection. Case report: 36-year-old male psychiatric patient was managed for acute polymorphic psychotic disorder with symptoms of schizophrenia. After stabilization of disease the therapy was excluded in 2009. In 2016, the patient had been examined by neurosurgeon due to recurrence of psychotic episodes. One month prior to admission to our department disconnected speech, restlessness and aggression with sleep disturbance were found. A giant skull base tumour in the sphenoidal sinus, sellar, parasellar and clival region was found with hyperprolactinemia of 255,000 μIU/ml (reference values for males 78-380 μIU/ml). The patient underwent a transfacial skull base approach with subtotal tumour resection. Postoperatively, the prolactin level decreased to 96,280 μIU/ml initially and 10230 μIU/ml in last control examination. In 2017 the patient was re-hospitalized due to anxiety and stereotyped behaviour. Conscious and disorientation were major complaints while it was difficult to establish contact due to distant thought flow followed by agitation and aggression. Regression of symptoms was achieved through antipsychotic therapy. After two years, final magnetic resonance imaging (MRI) scan showed a satisfactory postoperative finding with tumour regression and a residual component in both cavernous sinuses with no signs of compressive effect to the basal forebrain. Conclusion: Pituitary tumours and psychiatric disorders are quite rare in association. While the presence of endocrinological disturbances is a good indication for the possible need of surgery, diagnosis of psychiatric disorders is not. According to extreme hyperprolactinemia and tumour location surgery provides good results and a fast decline in prolactin level. Even though symptoms were found in regression, the exact relation between giant adenomas resection and psychotic disorder regression could not be well established for two years follow up. Cases like this require a multidisciplinary approach due to possible adverse effects of drugs and potential substitute therapy requirements.

Key words: pituitary adenoma, hyperprolactinemia, psychotic disorder

SAŽETAK

Uvod: Psihoza je definisana prisutnošću halucinacija, deluzija ili oboje. Nekada se, kao jedina manifestacija tumora mozga može javiti psihoza. Također, pituitarni tumori se mogu javiti u korelaciji sa psihozom. Cilj: Prikazati ishod pacijenta sa makroroadenomom povezanim sa psihozom dvije godine nakon resekcije. Prezentacija slučaja: Pacijent starosne dobi 36 godina je tretiran od 2004. godine kao akutni polimorfni psihotični poremećaj sa simptomima šizofrenije. Nakon stabilizacije bolesti terapija je isključena 2009. Godine 2016., pacijenta je pregledao neurohirurg zbog recidiva psihotičnih epizoda. Mjesec dana prije prijema na naš odjel pojavili su se nepovezan govor, nemir i agresija sa poremećajem spavanja. Pronađen je giganstski tumor baze lobanje u sfenoidalnom sinusu, selarnoj, paraselarnoj regiji i klivusu, je evidentiran uz hiperprolaktinemiju od 255, 000 μIU/ml (ref vrijednosti za muškarce 78-380 μIU /ml). Pacijent je tretiran transfacijalnim skull base pristupom sa subtotalnom resekcijom tumora. Postoperativno, nivo prolaktina smanjio se na 96,280 μIU/ml u početku i 10230 μIU/ml na posljednjem kontrolnom pregledu. U 2017 godini pacijent je ponovno hospitaliziran zbog anksioznosti i stereotipnog ponašanja. Svijest i dezorijentacija bile su dominantne tegobe dok je bilo teško uspostaviti kontakt zbog distanciranog toka misli praćenog uznemirenošću i agresivnošću. Regresija simptoma postignuta je antipsihotičkom terapijom. Nakon dvije godine, kontrolno snimanje magnetskom rezonancom (MRI) pokazalo je zadovoljavajući postoperativni nalaz s regresijom tumora i manjom rezidualnom komponentom u oba kavernozna sinusa bez znakova kompresijskog učinka na bazalni mozak.

Zaključak: Pituitarni tumori i psihotični poremećaj su veoma rijetki u korelaciji. Dok su endokrinološki poremećaji dobro definirani kao indikacija za hirurgiju, psihijatrijski poremećaji su veoma upitni. Posmatrajući ekstremne vrijednosti prolaktina i lokaciju tumora, hirurgija pruža dobre rezultate i brzu deklinaciju prolaktinskih vrijednosti. Iako su psihotični simptomi u regresiji, tačan odnos resekcije giganstkog adenoma i psihotičnog poremećaja se ne može uspostaviti, nakon dvije godine praćenja. Slični slučajevi zahtjevaju multidisciplinarni pristup shodno mogućim sporednim efektima lijekova i potrebe za supstitucionom terapijom.

Ključne riječi: adenomi hipofize, hiperprolaktinemija, psihotični poremećaj

INTRODUCTION

According to DSM-5, disordes is classified as psychotic or on the schizophrenia spectrum if presented symptoms include hallucinations, delusions, disorganized thinking, grossly disorganized motor behavior, or negative symptoms (1). Rarely, the only presentation of brain associated tumours may be psychosis and this is most common for tumours found in the pituitary gland region (2). As stated in the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), F06.2 is classified as Organic delusional (schizophrenia-like) disorder, which primarily occurs due to cerebral disease. Additionally, diagnosis F23.1 is classified as an acute polymorphic psychotic disorder with symptoms of schizophrenia, for which there is no indication of organic causation (3). Pituitary adenomas are the most common form of tumour occurring in the sellar region and are also the most common cause for pituitary disease in adults (5). In pituitary disease, some of the presented symptoms include acromegaly, severe depression, strong headaches, drug-seeking behaviour and other psychological disturbances (6). Therefore, the aim of this case report is to observe the correlation between sellar tumours and psychosis and other cognitive processes.

AIM

To present the patient outcome with psychosis associated macroadenoma two years after resection.

CASE REPORT

We present a 36 years old psychiatric patient managed since 2004 as acute polymorphic psychotic disorder with symptoms of schizophrenia. After stabilization of disease the therapy was excluded in 2009. The patient was evaluated by a neurosurgeon in 2016 after psychotic episodes. One month prior to admission to our department disconnected speech, restlessness and aggression with sleep disturbance were found. The patient was admitted and treated at the Psychiatric Clinic. However, Computed Tomography (CT) followed by brain Magnetic Resonance Imaging (MRI) was performed. A giant skull base tumour in the sphenoidal sinus, sellar, parasellar and clival region was found with hyperprolactinemia of 255,000 μIU/ml (reference values for males 78-380 μIU/ml). The patient underwent a transfacial skull base approach with subtotal tumour resection. A residual part of the tumour in both cavernous sinuses was left intentionally as a part of surgical strategy. The pathohistological finding confirmed pituitary adenoma. The early postoperative course was uneventful with regular control examinations by a psychiatrist. Postoperatively, the prolactin level decreased to 96,280 μIU/ml. The patient was transferred to the Department for Endocrinology for further treatment. The early postoperative brain MRI showed tumour subtotal resection. Still, disorientation with impaired cognitive function and dementia were presented and antipsychotic therapy was administered.

The patient was re-hospitalized at the Psychiatric Department in 2017, due to appearance of anxiety and symptoms of schizophrenia. Patient's major complaints were conscious disorder and disorientation. Also, it was difficult to establish contact due to patients agitation and aggression. If endocrinological therapy (cabergoline - a dopamine receptor agonist) influenced psychotic decompensation, the same therapy was excluded by a psychiatrist until the end of hospital treatment. Regression of symptoms was achieved through antipsychotic therapy. At the last annual check by an endocrinologist (in 2019), prior to planned monthly therapy prolactin levels of 10230 μIU/ml and low testosterone values of 1.2 nmol/L (reference values 4.6-23.2 nmol/L) were noticed. Regular hormonal substitution therapy with thyroxine and testosterone was ordinated. After two years final MRI showed a satisfactory postoperative finding with tumour regression and a residual component in both cavernous sinuses with no signs of compressive effect to the basal forebrain. The patient's current therapy includes Clozapine to be taken three times a day and a control examination every two months. In the final neurosurgical control exam, the patient was fully conscious without neurological disturbances.

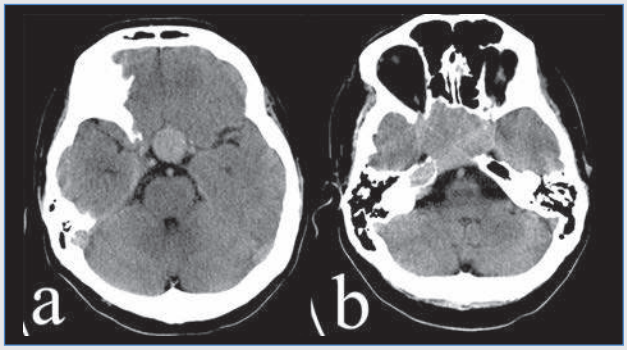

Figure 1 Image A and B: Preoperative CT scans. Hyperdense zone in the sellar region marks the tumour.

Note the tumour extension in the parasellar region. The tumour involves both cavernous sinuses.

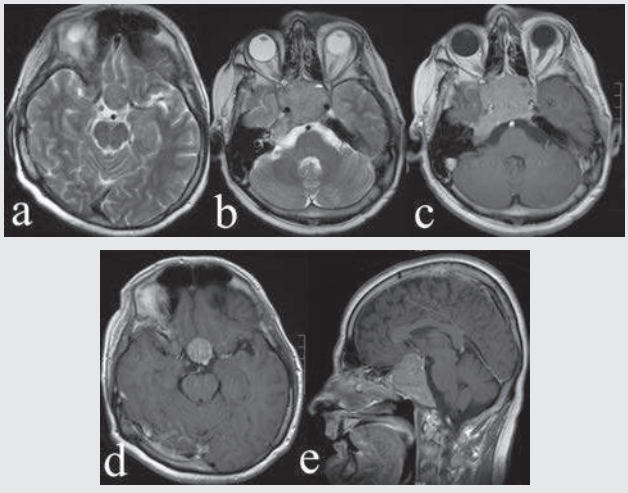

Figure 2 Image A and B: Preoperative MRI scans.

Note the tumour in the sellar region with lateral extensions in both cavernous sinuses. Both Internal Carotid Arteries are seen in their cavernous part. Image C, D and E. Gadolinium contrast MRI sequence in axial and sagital planes. Please note the contact between the tumour and the basal frontal lobe in the sagital scan. The tumour is extended distally in the clival region. The whole sphenoidal sinus area was involved in the tumour.

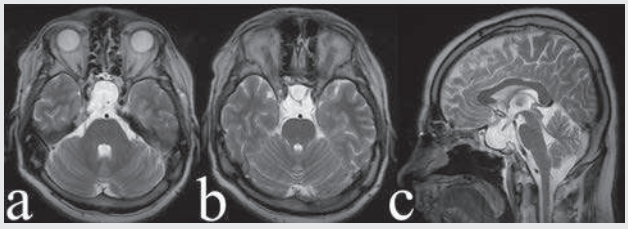

Figure 3 Images A, B and C: Postoperative T2 MRI images axial and sagital scans.

Postoperative residual cavum in sellar region after tumour resection. Note the optic chiasm in image B. There is no more compressive effect by tumour to the basal frontal lobe.

DISCUSSION

Brain tumours are a relatively frequent with the incidence of 10.82 per 100,000 persons per year (7). Presence of brain tumours may be followed by psychiatric symptoms (8), particularly in frontal or temporal regions. According to a meta-study analyzed by Madhusoodanan et al, in 22% of cases psychotic symptoms have been found in brain tumour patients (4). Nowadays, sellar tumours are rarely associated with psychotic syndrome.

In this illustrated case, the patient suffered from tumour in sellar region with psychiatric diagnosis as well (F 23.1). As one of the main symptoms was hyperprolactinemia, the patient underwent endocrinological treatment. Whether his endocrinologist treatment or macroadenoma caused any symptoms is uncertain. There are multiple case reports showing possible correlation between cabergoline and psychosis (9, 10, 11). However, our patient was presented with a giant skull base tumour with suprasellar extension which produced loss of visual aquity. We noticed in preoperative MRI scans that there was a direct contact between the basal frontal lobe and the tumour with possible compressive effect. (Figure 2C) It has been previously reported that tumor located in frontobasal region, due compressive effect on the frontobasal brain, could lead to psychiatric symptoms (12).

The patient underwent subtotal tumour resection by transfacial approach with usual postoperative outcome.

Some reports found most likely localized tumour in the pituitary gland if a patient experiences psychotic symptoms (8). In the period after the surgery, significant improvement in psychotic symptoms was not noticed in our case, an assumption that a correlation between psychosis and presence of pituitary tumour with suprasellar extension could not be proposed. We have noticed tumour reduction in early MRI scans but without expected descensus of the suprasellar component. However, visual improvement was noted. In a recent review done by Pertichetti et al, it is claimed that in patients with pituitary adenoma, after the operation, short-term memory, psychomotor speed and general quality of life had improved (13). Since our surgical strategy to prevent cerebrospinal fluid (CSF) leak is packing of the sphenoidal sinus with adipose tissue it could be the reason for still presented partial compressive effect to the basal part of frontal lobe followed by symptoms (Figure 3).

The other possible mechanism of symptoms presence was that we surgically blocked the pathway for the prolactin-inhibiting factor from the hypothalamus to the prolactin-secreting cells in anterior pituitary lobe.

Patient's initial prolactin levels were 255,000 μIU/ml. These extremely elevated levels could be explained by the presence of functional macroadenoma. After surgery, the patient's prolactin levels have decreased to 96, 280 μIU/ml, and are now 10230 μIU/ml. Although they are still above the normal value, they have overall decreased by 96%. Furthermore, there is a suggestion that tumour formation could be promoted with usage of first generation of antipsychotic drugs (14) which acts as dopamine antagonists (15,16). However, our patient was treated only with second generation antipsychotic drug clozapin what seems to increase pituitary hormone levels in general but without prolactin influence (14,17). Since the patient's last MRI scan shows that there is no residual tumour except in cavernous sinuses, it could be proposed that the absence of "functional" tumour leads to a decrease in prolactin levels. The value of 10230 μIU/ml was possibly related to existing adenoma in cavernous sinuses or decreased hypothalamic inhibition. However, we have not discussed additional surgery or stereotactic radiosurgery due to increased risk of cranial nerves deficit and satisfactory results with substitutional therapy.

Seven months after surgery, the patient was administered back to Psychiatry Department with similar symptoms but now organic delusional (schizophrenia-like) disorder. We could not find a correlation between tumour removal and diagnosis code shift. An earlier study by Mamta Sood et al. presented a patient who, even after surgery, still suffered from psychiatric disorder and consequently had to be treated with psychiatric approach but with the same IDC code (6). There are studies suggesting that tumours could be the underlying etiology of psychiatric disorders with an emphasis being on high values of prolactin (18,19,20). This study shows that more research should be done on the correlation between psychosis and pituitary adenomas and leads us to the conclusion that macroadenoma could have affected hyperprolactinemia, but psychotic symptoms could not be excluded to hyperprolactinemia only.

CONCLUSION

Pituitary tumours and psychiatric disorders are quite rare in association. While endocrinological disturbances are well defined as an indication for surgery, psychiatric disorders are quite doubtable. According to extreme hyperprolactinemia and tumour location surgery provides good results and a fast decline in prolactin level. Even though the symptoms were found to be in regression during the two years follow-up control exam, the exact relation between giant adenomas resection and psychotic disorder regression could not be established. Similar cases demand a multidisciplinary approach due to possible drug side effects and substitute therapy requirements.

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