CASE REPORT

Chemotherapy-induced acute psychosis in a patient with malignant germ cell tumour

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Accepted 10 March 2015

SUMMARY

A 25-year-old Thai woman with ovarian germ cell tumour presented with behavioural changes after receiving an intensive dose of neoadjuvant chemotherapy with bleomycin, etoposide and cisplatin, for a relapse. Her initial symptoms of mood fluctuation and insomnia were noticed while hospitalised for the third cycle, and became more severe. She was very irritable, highly distracted and forgetful. She exhibited flights of ideas and hyperactivity, including compulsive shopping. She also had paranoid ideations, auditory hallucinations, and thoughts of being wealthy and close to the prime minister. She was not depressed. She was diagnosed with axis I psychotic disorder not otherwise specified. The incremental dosage of olanzapine from 5 to 20 mg/day was given but failed to control her psychotic symptoms during the first week, and was therefore switched to risperidone. At 4 mg/day, her symptoms were dramatically controlled. This novel evidence suggests the rare possibility of an association between chemotherapy and the development of psychotic attacks.

BACKGROUND

Patients who have suffered from germ cell tumour usually receive a chemotherapy regimen that comprises of bleomycin, etoposide and cisplatin (BEP).^{1–3} While serious pulmonary toxicity from BEP⁴ and other side effects such as peripheral neuropathy and haematological toxicities have been commonly reported, psychological complication has been rarely noted.

Only one case of a psychotic attack after BEP chemotherapy has been previously reported. The report presented a case of a 16-year-old boy with testicular germ cell tumour who developed a psychotic attack after his first BEP chemotherapy cycle.⁵ The authors concluded that psychotic attack was most likely secondary to multiple factors. While that seemed to be the case, their analysis was unable to distinguish other major factors, especially history of traumatic brain injury, untreated depression and domestic violence.

Our report of a young Thai woman who developed a psychotic attack after chemotherapy for her ovarian germ cell tumour relapse, presented a different and more in-depth analysis of a condition similar to the earlier case. Unlike Campbell's report, this case has no major confounding factors, so our detailed analysis can give a better idea of the potential isolated effect of chemotherapy on the development of psychotic attack.

CASE PRESENTATION

A 25-year-old Thai woman presented with massive ascites about a year prior to consultation at our facility. Whole body positron emission tomography (PET) CT scan revealed multiple nodules and masses in the peritoneal cavity, which were considered to be extensive peritoneal carcinomatosis. The patient was provisionally diagnosed based mainly on cytopathology and some biomarkers in March 2013, because of her initially severe clinical condition. Malignant cells of adenocarcinoma type consistent with ovarian primary were identified from peritoneal fluid whereas α -fetoprotein (AFP) was 41 183 ng/mL, β -human chorionic gonadotropin (β -HCG) was 216.90 mIU/mL and lactate dehydrogenase was 533 u/L. The patient received four EP cycles and two more cycles later on. Her clinical condition improved and the weekly follow-up of all biomarker levels had decreased to normal range within 3–4 months.

In July 2013, exploratory laparotomy was performed to get the tissue. The final pathological diagnosis was germ cell tumour (teratoma). As the patient already received chemotherapy, identification of histological subtype and International Federation of Gynaecology and Obstetrics (FIGO) staging were limited. However, based on clinical and imaging evidence of metastasis, this patient was in stage 4.

During December 2013–February 2014, her AFP had increased to 69.6–108 ng/mL, along with positive PET CT scan in January 2014, suggesting a relapse. She therefore received BEP for three cycles during February–March 2014. Her clinical condition was fairly good when she developed the psychiatric illness. Ondansetron and low-dose dexamethasone (20 mg/day) were given as part of the chemotherapy protocol.

During the last cycle of BEP, the patient's family noticed some changes in her mood as well as sleep disturbances. A week after discharge from the hospital, the symptoms became more prominent. Her behaviour had been increasingly disorganised. She could not remember her mother and went to her neighbour's house thinking it was hers. She was irritable and hyperactive. She believed that the King had transferred 50 million baht into her bank account. She spent a lot of money buying things and she also had delusions of grandeur as well as some paranoia. However, she was clearly not in a depressed state.

She had no history of psychiatric disorder or recreational drug misuse. There was no family history of psychiatric illness. According to her mother, she understood about her cancer diagnosis and had

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To cite: Puangthong U, Pongpirul K. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-208982

been coping well over the last 1.5 years. She continued studying until she had finished her bachelor's degree. She had never expressed feelings of hopelessness or depression. There was no report of other psychological stressors at the time. Her physical examination revealed no abnormalities. Her mental status was mildly increased psychomotor activities and elevated mood. Auditory hallucinations were suspected. Urine and routine blood examinations were normal. MRI of the brain was performed and revealed no definite malignant intracranial abnormality. There was no suggestive evidence of brain metastasis. Therefore, the patient was diagnosed with axis I psychotic disorder not otherwise specified, according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR).

INVESTIGATIONS

Radiological investigations

Serial PET CT scan of the whole body had been performed over 1 year. The first scan demonstrated large amount of ascites, extensive peritoneal carcinomatosis and subcutaneous metastasis. Seeding tumour or direct invasion from intra-abdominal mass was noted. There was no radiological sign of gut obstruction. Three follow-up PET CT scans showed partial response of carcinoma and decreased fluorodeoxyglucose activity before the relapse, which was later revealed in the fifth PET CT scan in January 2014. The sixth PET CT scan performed in May 2014 suggested partial response to the treatment. In November 2014, the latest PET CT scan revealed complete response.

MRI of the brain during psychosis revealed no definite malignant intracranial abnormality or evidence of brain metastasis.

Cerebrospinal fluid examination was not carried out because of poor patient cooperation during her psychiatric episode.

The following laboratory investigation are presented based on the most recent results.

Haematology

White cell count 8400 cells/ μ L, neutrophil 85.2%, lymphocyte 12.1%, monocyte 2.4%, eosinophil 0%, basophil 0.3%, red blood cell count 3.26×10^6 cells/ μ L, haemoglobin 9.9 g/dL, haematocrit 29.8%, mean corpuscular volume 91.5 fL, mean corpuscular haemoglobin (MCH) 30.2 pg, MCH content (MCHC) 33 g/dL, red cell distribution width 16% and platelet count 298 000 cells/ μ L.

Biochemistry

Sodium 134 mmol/L, potassium 4.5 mmol/L, chloride 106 mmol/L, bicarbonate 21 mmol/L, calcium 8.7 mg/dL, magnesium 2.2 mg/dL, phosphate 3.6 mg/dL, blood urea nitrogen 12 mg/dL, creatinine 0.6 mg/dL, total protein 6.2 g/dL, albumin 3.8 g/dL, globulin 2.4 g/dL, direct bilirubin 0.1 mg/dL, total bilirubin 0.4 mg/dL, alkaline phosphatase 51 u/L, serum glutamic oxaloacetic transaminase/aspartate transaminase (SGOT/AST) 19 u/L, serum glutamate-pyruvate transaminase/alanine transaminase (SGPT/ALT) 13 u/L and γ -glutamyl transferase 10 u/L.

Hormones

AFP 9.6 ng/mL, β -HCG 0.3 mIU/mL, free triiodothyronine 3.02 pg/mL, free thyroxine 1.10 ng/dL, thyroid-stimulating hormone 1.418 μ U/mL, carcinoma antigen (CA-125) 10.6 U/mL, CA 19-9 3.8 U/mL and carcinoembryonic antigen 1.15 ng/mL.

DIFFERENTIAL DIAGNOSIS

A patient with cancer who develops a psychiatric condition should be assessed for potential organic aetiologies, especially

cancer metastasis. However, our exhaustive investigations revealed no medical conditions, metabolic disorders or metastases. Paraneoplastic syndrome previously reported in patients with ovarian teratoma⁶ can be excluded because of the good response of the cancer to chemotherapy. Common psychiatric disorders such as adjustment disorder, delirium and depression were also considered.^{7 8} However, the history and clinical symptoms were not compatible with functional psychiatric disorders.

TREATMENT

The incremental dosage of olanzapine from 5 to 20 mg/day failed to control the patient's psychotic symptoms during the first week and therefore was switched to risperidone. At 4 mg/day, her symptoms were dramatically controlled within the second day of risperidone.

The medical management of her germ cell tumour was according to international protocol and therefore is not discussed here.

OUTCOME AND FOLLOW-UP

The patient's clinical and psychological condition has dramatically improved over the past 6 months of follow-up and she has completely returned to normal. She finally discontinued risperidone. Her cancer treatment protocol was changed to modified BEP plus radiation, which led to near remission as of November 2014.

DISCUSSION

Psychiatric disorders in patients with existing medical problems are not uncommon but usually not regarded as medication side effects, mainly because of two reasons. Not only do they occur rarely but also the definite conclusion is difficult because of some confounders. In Campbell's report of a young male patient, the conclusion was confounded by patient's history of multiple psychiatric conditions (untreated depression, suicidal ideation, domestic violence) and traumatic brain injury.⁵

Our case also presented the medical dilemma of continuing the chemotherapy protocol with potential side effects versus changing the treatment regimen for a better quality of life for the patient. A decision such as this should be made after a multidisciplinary team discussion^{9 10} with the patient. The current literature also suggests more patient involvement in his or her own cancer care.¹¹ However, reduced cognitive ability from chemotherapy psychiatric side effects might limit a patient's ability to be involved in the decision-making process.

Our experience suggests that risperidone could be used for initial management of organic psychosis. The failure of olanzapine in our patient suggests that the blocking of muscarinic 1 receptor might play an important role in the patient's worsened condition. Atypical antipsychotics with less muscarinic 1 receptor antagonistic activity were therefore chosen and gave a much better outcome in this case.

Learning points

- ▶ Psychiatric disorders in patients with existing medical problems are not uncommon but usually not regarded as medication side effects, especially because they rarely occur.
- ▶ Proceeding with chemotherapy with potential side effects versus stopping the chemotherapy for a better quality of life for the patient remains a medical dilemma.
- ▶ Our experience suggests that risperidone could be used for initial management of organic psychosis.

Acknowledgements The authors would like to thank Dr Surasit Saleh Issarachai for his useful comments.

Contributors UP was the psychiatrist responsible for the patient. UP and KP drafted and finalised the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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