8747 POSTER

Single Agent Bevacizumab for Recurrent Malignant Glioma

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Background: Malignant gliomas are aggressive primary brain tumours, which include anaplastic gliomas & glioblastoma (GBM). The majority of patients relapse following initial therapy & treatment options are limited. We reviewed patients with recurrent glioma treated with single agent bevacizumab at our centre from May 2009 to Dec 2010.
Materials and Methods: Patients were identified from the pharmacy database & their records reviewed.
Results: 15 patients were identified; data was available for 12. There were 9 men and 3 women with mean age at diagnosis of 47 (16–62). Histology at original presentation was GBM in 7 patients, anaplastic astrocytoma in 4 and oligoastrocytoma in 1. All had at least subtotal debulking, with subsequent radiation. In 9 (75%), radiation was concurrent with temozolomide − 8 proceeded to temozolomide alone, 1 patient had progressive disease. 2 (17%) patients had radiation followed by procarbazine, lomustine, vincristine (P.C.V.) − chemotherapy was stopped early in both, due to toxicity in one and progressive disease in the other, this patient then received temozolomide. The 1 patient who originally had an oligoastrocytoma subsequently transformed to GBM, he had radiation followed by temozolomide at that point. Upon progression of disease, 5 patients had further debulking, with insertion of carmustine wafers in 2. Patients started on bevacizumab a median of 16 months from initial diagnosis (5−92), 9 had 10 mg/kg 2 weekly, 3 received 7.5 mg/kg secondary to performance status concerns. There was a median of 11 cycles administered (1−22). 4 patients are alive, 1 continues on bevacizumab at 4 months, 3 are off treatment due to decreased performance status, at a median 6 months (6−10) from commencing therapy. The other 8 patients died a median of 6 months from starting bevacizumab (1−12). 1 bled into their tumour, 1 had a saddle pulmonary embolism, the remainder died of progressive disease. All patients were on steroid therapy, 7 (58%) had a reduction in steroid dose on bevacizumab. 3 (25%) patients had an improved scan on treatment. The median overall survival was 6 months from commencement of bevacizumab.
Conclusion: The management of patients with recurrent malignant glioma is challenging. Despite a median overall survival of 6 months in an unselected cohort, in addition to the ability to reduce steroid dose − which compares reasonably to historical controls -outcome for this group is still disappointing overall. We continue to seek novel therapeutic options for this aggressive disease.

8748 POSTER

Medulloblastoma in Young Adults and Pancytopenia − Treatment Complication or Recurrence?

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Background: Medulloblastoma is a rare cental nervous system (CNS) tumour accounting less than 0.5−1% of all intracranial tumours. Pancytopenia is not an infrequent sign but secondary MDS shortly after treatment of medulloblastoma in adulthood or isolated bone marrow involvement is very rare.
Case 1: A 25-year-old man was admitted to emergency unit with a complaint of headache. Magnetic Resonance Imaging (MRI) revealed multiple masses located in the right parietal lobe and cerebelum. Craniotomy revealed medulloblastoma. After 30 Gray whole brain radiotherapy (WBRT). 6 cycles of VCE (vincristine 1.4 mg/m^2 in day 1, carboplatin 375 mg/m^2 in day 1, and etoposide 50 mg/m^2 in day 1) were given without any complication. Complete response wasreported on MRI. Prophylactic external spinal radiotherapy was given afterwards. Fifteen months after diagnosis of medulloblastoma pancytopenia was detected. There were no signs of recurrence on MRI or Positron Emission Tomography (PET) scanning. Pathological findings of repeated bone marrow biopsy was consistent with MDS.
Case 2: A 24-year-old man was admitted to emergency unit with the complaints of headache and vertigo. Left cerebellar mass on MRI was detected. After curative operation, medulloblastoma was diagnosed. Ten months after the completion of propylactic craniospinal radiotherapy, patient was re-admitted with severe generalized pain. Since deep anemia and thrombocytopenia were detected, bone marrow biopsy was done, consistent with medulloblastoma recurrence. Staging was done by PET scanning that was confirming diffuse bone marrow involvement. Chemoterapy consisted of cyclophospamide 1900 mg/m^2 day 1, cisplatin 140 mg/m^2 day 1, vincristine 1.4 mg/m^2 day 1 (SCV) was and 6 cycles was completed. Two months after a 2nd line PCV chemotherapy was initiated upon systemic progression. After 2 cycles of chemotherapy progression of lymph nodes and persistent pancytopenia was detected and carboplatin and etoposide was started. After 2 cycles of chemotherapy pancytopenia deepened and severe hyperbilirubinemia developed and he died because of disease progression.
Conclusion: Although medulloblastoma is very rare in adults, bone marrow metastasis and/or treatment related MDS were even rarer. In case of pancytopenia intensive evaluation for the differential diagnosis should be done.

8749 POSTER

Carboplatin Chemotherapy in Patients With Recurrent High-grade Glioma

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Background: To investigate the efficacy of carboplatin chemotherapy in patients with recurrent high-grade glioma (HGG) who had received a first alkylating line of chemotherapy.
Material and Methods: Case notes of patients who had received chemotherapy with carboplatin for recurrent HGG between June 2006 and July 2010 were reviewed. Baseline characteristics and outcomes after treatment were recorded.
Results: Forty-eight patients received carboplatin as second line chemotherapy for recurrent HGG (grade III n = 6; grade IV n = 42). The median number of cycles completed was 4. Fifteen patients (28%) had at least minor response, 22 (49%) had stable disease and 11 (23%) had progressive disease. Six month progression-free survival was 30% (52% in patients with grade III glioma and 18% in patients with grade IV glioma). The median time to disease progression from the first treatment with carboplatin was 3.2 months. The median survival was 8 months (10 months for patients with grade III glioma and 7 months for patients with grade IV glioma). Among patients with either stable disease or a partial response, the median survival was 12 months compared with 3 months in patients with progressive disease. No survival or response rate differences were noted regarding the type of previous chemotherapy, nitrosoureas or temozolomide.
Conclusions: Single-agent carboplatin has modest activity in patients with recurrent HGG previously treated with one line of chemotherapy, nitrosoureas or temozolomide. Despite the improvement of median survival of patients achieving stable disease or a partial response to treatment, more effective regimens are required for this patient population.

8750 POSTER

Bevacizumab Alone at 5 mg/kg in an Every-3-week Schedule for Patients With Recurrent Glioblastomas − a Single Center Experience

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Background: To investigate the efficacy of a 3-week schedule of bevacizumab in patients with recurrent glioblastomas (GBMs) who had received at least one previous alkylating line of chemotherapy.
Material and Methods: Case notes of patients who had received bevacizumab 10 mg/kg every 3 weeks for recurrent GBMs between June 2008 and July 2010 were reviewed. Baseline characteristics and outcomes after treatment were recorded.
Results: Of 13 patients selected (7 men and 6 women with median age of 48 years), 6 patients had received >1 previous alkylating chemotherapies (temozolomide and lomustine). The median number of bevacizumab doses was 3 (range 2−8) and 4 patients received >5 cycles. No toxicities or intracerebral bleeding were observed. Four patients (30%) had partial response, six of them (46%) had stable disease and 3 patients (24%) had progressive disease. Interestingly, when noted, clinical improvement followed the second week of first cycle. In two patients with radiological response, a second surgery was performed. Six month progression-free survival was 27%. The median time to disease progression from was 3.2 months. The median survival was 6 months. Among patients with either stable disease or a partial response, the median survival was 8.8 months compared with 3 months in patients with progressive disease. Both patients who had second surgery are still alive.
Conclusions: An every 3-week schedule of single-agent bevacizumab showed modest activity and a safe profile in patients with recurrent GBM previously treated with at least one line of chemotherapy, nitrosoureas or temozolomide. When feasible, a second surgery seems to improve the survival of these patients. However, the impact of this interesting approach needs a validation in a larger patient cohort.