Cranial Plasmacytoma: A Case Series and Review of the Literature

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Abstract Plasmacytomas are malignant proliferations of plasma cells which can occur with different plasma cell dyscrasias. Solitary plasmacytomas of bone or extraosseous plasmacytomas, depending on the tissue of origin, develop in isolation without systemic manifestations of multiple myeloma. Three cases of cranial plasmacytomas are described, two in patients with multiple myeloma and one extraosseous plasmacytoma. Management options are discussed.

Keywords Cranial · Plasmacytoma · Multiple myeloma · Treatment

Introduction

The clinical course of three patients with cranial plasmacytomas is discussed. These cases illustrate the heterogeneity of plasmacytomas in their clinical presentation. Of special interest was a patient with visual loss whose vision improved on therapy. The management options for plasmacytomas are reviewed. Approval to report the cases was obtained from the Ethics Committee of the Faculty of Health Sciences, University of the Free State in Bloemfontein, South Africa, as well as the relevant heads of

department and the head of clinical services of the Universitas Academic Hospital complex.

Case 1

A 25-year-old male patient was referred to the haematology clinic with a four-week history of persistent headaches and pain on the right side of his face. He also complained of progressive diplopia and decreased visual acuity. His right eye was blind. A computer tomography of the brain was done, which revealed a mass situated in his right maxilla and pressing onto his orbit and optic chiasma. A biopsy revealed a plasmacytoma. According to the International Myeloma Working Group guidelines [1], he fulfilled the criteria for a solitary, extramedullary plasmacytoma, namely no monoclonal protein (M-protein) on serum or urine protein electrophoresis, normal bone marrow biopsy, normal skeletal survey and no related organ or tissue impairment, as well as normal serum calcium, creatinine and haemoglobin. He also had a normal free light chain ratio (Freelite[®], The Binding Site Group Ltd., Birmingham, UK).

A diagnosis of a solitary extramedullary plasmacytoma (SEP) of the maxilla compressing the optic chiasma was made. He was referred to the Department of Ophthalmology for an opinion. The patient had a relative afferent papillary defect (RAPD) and decreased light sensitivity in the right eye with only slight residual light perception. He also had a sensory exotropia. The rest of the anterior segment examination was normal. The right optic nerve was pink with a cup:disc ratio of 0.4×0.4 . The left eye was essentially normal on examination, visual acuity 20/20, with a cup:disc ratio of 0.4×0.4 . Findings of Humphrey's visual fields (30-2) performed in August 2009 are shown in Fig. 1a and b.

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Fig. 1 Case 1: **a** Humphrey's visual field (right eye) before treatment; **b** Humphrey's visual field (left eye) before treatment; **c** Humphrey's visual field (right eye) after treatment with six cycles of VAD; **d** Humphrey's visual field (left eye) after treatment with six cycles of VAD

Irradiation of the mass was not performed due to its close proximity to the optic chiasma. The patient was treated with six cycles of vincristine, daunorubicin and dexamethasone (VAD), which he tolerated well. Vincristine was omitted in the third cycle due to sensory/motor peripheral neuropathy in the hands and feet, which resolved completely after introduction of pyridoxine and discontinuation of vincristine. Vincristine was then reintroduced in the fourth cycle without any recurrence of the peripheral neuropathy. The patient reported an improvement in visual acuity after the first cycle of VAD, and this progressively improved.

He was followed up at the ophthalmology clinic a year later. At that time, visual acuity in the right eye had improved to counting fingers at 3 m. The visual acuity in his left eye was still 20/20. A grade 1 RAPD was found in the right eye. He was orthotropic and the rest of the anterior segment examination was normal. The left eye had remained the same as before, except for the optic nerve. On posterior pole examination, his cup:disc ratio was 0.9×0.9 (right) and 0.7×0.7 (left). Humphrey's visual fields (30-2) had improved significantly as shown in Fig. 1c and d.

Case 2

A 54-year-old female from a rural part of South Africa was referred to us with a history of multiple slow growing

cranial masses. The masses were palpable subcutaneously in her frontal, parietal and occipital regions. The masses were hard, non-tender and fixed. These were confirmed on computed tomography (CT) scan, as shown in Figs. 2 and 3. Neurological examination was surprisingly intact except for a left sided hemianopia. A biopsy of the frontal mass showed an infiltrate of plasma cells.

Fig. 2 Case 2: cranial plasmacytomas visible on CT scan before treatment

Fig. 3 Case 2: cranial plasmacytomas visible on CT scan before treatment

Multiple myeloma was diagnosed based on multiple plasmacytomas, a monoclonal protein of 41 g/l, corrected calcium of 2.7 mmol/l, haemoglobin of 7.8 g/dl as well as multiple lytic lesions on skeletal overview. Renal function was normal.

Bone marrow cytogenetics showed an inversion 9 (p13;q22.3) which was not considered to be clinically significant. Prior to initiation of therapy she was stage III according to the International Staging System [1]. She was treated with a combination of radiotherapy (3000 Gy) and chemotherapy consisting of melphalan and dexamethasone, as she was not considered eligible for stem cell transplantation. Despite her very late presentation, she has responded well to therapy. Her monoclonal protein has decreased to 6 g/l and her plasmacytomas have clinically and radiographically decreased in size, as seen in Fig. 4.

Case 3

A 76-year-old female from a neighboring country was referred to the Department of Neurosurgery with a slow growing cranial mass in her left frontal-parietal area. This mass was visible on plain X-ray (Fig. 5). Clinically the patient had lower motor neuron signs in her lower limbs, without any signs of cranial nerve involvement or signs of an upper motor neuron lesion. A biopsy of the mass revealed a plasmacytoma and the patient was subsequently referred to clinical haematology for further investigations.

Magnetic resonance imaging (MRI) of the spine was done pre-treatment, and revealed spinal stenosis in the L3–L5 vertebral region. However, after evaluation by the Department of Orthopedics, it was decided to treat the

Fig. 4 Case 2: CT scan after treatment with a combination of radio- and chemotherapy

stenosis conservatively. The diagnosis of multiple myeloma was made based on the documented plasmacytoma, lytic lesion on left humerus, and an M-protein of 3.3 g/l, which was of IgA subtype. The patient was hypercalcaemic with a bone marrow plasmacytosis (40%). Her kappa free light chains measured 21.6 mg/l, with a kappa/lambda ratio of 3.72. The patient was stage I using the International Staging System [1]. She was initially treated with melphalan and prednisone, to which she responded well. Her leg weakness resolved, the plasmacytoma has clinically disappeared and her M-protein has decreased to 1.97 g/l.

Fig. 5 Case 3: left frontal-parietal mass observed on plain X-ray

Discussion

Plasmacytomas are usually easy to diagnose morphologically, unless there is poor differentiation of the plasma cells (for example, plasmablastic or anaplastic cells) [2]. The management of plasmacytoma depends on the underlying diagnosis of the patient. An important aspect to consider is whether the patient has a solitary plasmacytoma of bone (SPB), a SEP, or multiple myeloma (MM). The distinction between the first two and the latter may be challenging. The addition of MRI and positron emission tomography combined with computer tomography (PET-CT), where available, appear to be of benefit [3, 4]. The diagnoses of plasma cell dyscrasia are based on the International Myeloma Working Group criteria [1, 5], which are summarised in Table 1.

Typically, the management of a SPB is based on localised radiotherapy due to the exquisitely sensitive nature of the tumour. The dose is usually in the order of 40–50 Gy given in 20–25 fractions over a four-week period, depending on tumour size [6]. Response rates to radiotherapy are typically in excess of 80% [7–9].

Whether or not additional chemotherapy is necessary after radiotherapy remains a difficult question. Due to the rarity of the disease only one prospective, randomised trial on the subject has been published [10]. This trial randomised participants to receive either no therapy or melphalan and prednisone (MP) after radiotherapy in patients with SPB. Fifty-three patients were randomised, 25 patients to the active treatment arm. Patients receiving MP showed an improved overall survival and disease-free survival after a median of more than 8 years of follow-up. However, due to the small nature of the trial, definitive conclusions could not be made [10].

Although initial local responses are excellent, the majority of patients will develop multiple myeloma [9, 11]. For this reason, regular follow-up of all patients treated for SPB needs to be emphasised.

The first case presented here was complicated by the proximity of the tumour to the optic chiasma. The attending physicians felt that the location of the tumour precluded therapy with radiotherapy or surgical intervention. Systemic therapy for multiple myeloma (VAD) was used and the patient showed a good response to therapy.

Solitary extramedullary plasmacytoma is a plasma cell dyscrasia associated with a tumour mass localised in soft tissue. SEP is less frequently encountered than SPB, and is most commonly localised to the head and neck region [12]. Treatment of these tumours is usually with radiotherapy. Doses of 40–50 Gy, similar to those in SPB, are used [13]. Local control is usually excellent with response rates described above 90% [14, 15]. The use of novel agents appears promising although experience is currently limited [16–18]. As with SPB, follow-up of these patients is important as a chance to develop multiple myeloma exists, although at a far lower rate than SPB [8, 19].

When a plasmacytoma is found in the setting of MM, as in the last two cases described here, the patient should be treated for MM. This subject has been reviewed extensively in the literature, with a number of potent novel agents available [20–23]. In addition, the plasmacytoma may be managed with additional radiotherapy typically given for pain relief if systemic therapy could not control it, or when neurological fall-out or impingement on vital structures occurs, as was done in the second case.

When no indication for radiotherapy can be identified after a careful history and full neurological examination, as occurred in the last case, therapy for multiple myeloma without the addition of radiotherapy is appropriate.

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Table 1 Diagnostic criteria for selected plasma cell dyscrasia (adapted from reference 5)

Solitary plasmacytoma of bone	Extramedullary plasmacytoma	Symptomatic multiple myeloma
No M-protein in serum and/or urine ^a	No M-protein in serum and/or urine ^a	M-protein in serum and/or urine
Single area of bone destruction due to clonal plasma cells	Extramedullary tumour of clonal plasma cells	Bone marrow (clonal) plasma cells or plasmacytoma
Bone marrow not consistent with multiple myeloma	Normal bone marrow	Related organ or tissue impairment (end organ damage, including bone lesions)
Normal skeletal survey (and MRI of spine and pelvis if done)	Normal skeletal survey	
No related organ or tissue impairment (no end organ damage other than solitary bone lesion)	No related organ or tissue impairment (end organ damage including bone lesions)	

^a A small M-component may occasionally be present

References

1. International Myeloma Working Group (2003) Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. *Br J Haematol* 121:749–757
2. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H et al (2008) WHO classification of tumours of haematopoietic and lymphoid tissues, 4th edn. IARC Press, Lyon
3. Mouloupoulos LA, Dimopoulos MA, Weber D, Fuller L, Libshitz HI, Alexanian R (1993) Magnetic resonance imaging in the staging of solitary plasmacytoma of bone. *J Clin Oncol* 11:1311–1315
4. Kim PJ, Hicks RJ, Wirth A, Ryan G, Seymour JF, Prince HM et al (2009) Impact of 18F-fluorodeoxyglucose positron emission tomography before and after definitive radiation therapy in patients with apparently solitary plasmacytoma. *Int J Radiat Oncol Biol Phys* 74:740–746
5. Greipp PR, San Miguel J, Durie BG, Crowley JJ, Barlogie B, Bladé J et al (2005) International staging system for multiple myeloma. *J Clin Oncol* 23:3412–3420
6. Soutar R, Lucraft H, Jackson G, Reece A, Bird J, Low E et al (2004) Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. *Br J Haematol* 124:717–726
7. Mayr NA, Wen BC, Hussey DH, Burns CP, Staples JJ, Doornbos JF et al (1990) The role of radiation therapy in the treatment of solitary plasmacytomas. *Radiother Oncol* 17:293–303
8. Tsang RW, Gospodarowicz MK, Pintilie M, Bezjak A, Wells W, Hodgson DC et al (2001) Solitary plasmacytoma treated with radiotherapy: impact of tumor size on outcome. *Int J Radiat Oncol Biol Phys* 50:113–120
9. Knobel D, Zouhair A, Tsang RW, Poortmans P, Belkacémi Y, Bolla M et al (2006) Prognostic factors in solitary plasmacytoma of the bone: a multicenter rare cancer network study. *BMC Cancer* 6:118
10. Avilés A, Huerta-Guzmán J, Delgado S, Fernández A, Díaz-Maqueo JC (1996) Improved outcome in solitary bone plasmacytoma with combined therapy. *Hematol Oncol* 14:111–117
11. Holland J, Trenkner DA, Wasserman TH, Fineberg B (1992) Plasmacytoma. Treatment results and conversion to myeloma. *Cancer* 69:1513–1517
12. Wax MK, Yun KJ, Omar RA (1993) Extramedullary plasmacytomas of the head and neck. *Otolaryngol Head Neck Surg* 109:877–885
13. Creach KM, Foote RL, Neben-Wittich MA, Kyle RA (2009) Radiotherapy for extramedullary plasmacytoma of the head and neck. *Int J Radiat Oncol Biol Phys* 73:789–794
14. Tournier-Rangear L, Lapeyre M, Graff-Caillaud P, Mege A, Dolivet G, Toussaint B et al (2006) Radiotherapy for solitary extramedullary plasmacytoma in the head-and-neck region: a dose greater than 45 Gy to the target volume improves the local control. *Int J Radiat Oncol Biol Phys* 64:1013–1017
15. Michalaki VJ, Hall J, Henk JM, Nutting CM, Harrington KJ (2003) Definitive radiotherapy for extramedullary plasmacytomas of the head and neck. *Br J Radiol* 76:738–741
16. Katodritou E, Speletas M, Pouli A, Tsitouridis J, Zervas K, Terpos E (2007) Successful treatment of extramedullary plasmacytoma of the cavernous sinus using a combination of intermediate dose of thalidomide and dexamethasone. *Acta Haematol* 117:20–23
17. Nakazato T, Suzuki K, Mihara A, Sanada Y, Kakimoto T (2009) Refractory plasmablastic type myeloma with multiple extramedullary plasmacytomas and massive myelomatous effusion: remarkable response with a combination of thalidomide and dexamethasone. *Intern Med* 48:1827–1832
18. Wei JY, Tong HY, Zhu WF, Liu H, Zhang FJ, Yu WJ et al (2009) Bortezomib in treatment of extramedullary plasmacytoma of the pancreas. *Hepatobiliary Pancreat Dis Int* 8:329–331
19. Susnerwala SS, Shanks JH, Banerjee SS, Scarffe JH, Farrington WT, Slevin NJ (1997) Extramedullary plasmacytoma of the head and neck region: clinicopathological correlation in 25 cases. *Br J Cancer* 75:921–927
20. Stewart AK, Richardson PG, San-Miguel JF (2009) How I treat multiple myeloma in younger patients. *Blood* 114:5436–5443
21. Bladé J, Rosiñol L, Cibeira MT, Rovira M, Carreras E (2010) Hematopoietic stem cell transplantation for multiple myeloma beyond 2010. *Blood* 115:3655–3663
22. Morabito F, Gentile M, Mazzone C, Bringhen S, Vigna E, Lucia E et al (2010) Therapeutic approaches for newly diagnosed multiple myeloma patients in the era of novel drugs. *Eur J Haematol* 85:181–191
23. Harousseau JL (2009) Integrating novel therapies in the transplant paradigm. *Cancer J* 15:479–484