SHORT REPORT

Relapsing intracranial Rosai-Dorfman disease

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Abstract

Two patients presenting with recurrent visual impairment due to relapsing intracranial Rosai-Dorfman disease are described. In both patients a preoperative diagnosis of meningioma was made. Histological examination disclosed the characteristic picture of S100 and CD68 positive histiocytosis with prominent lymphophagocytosis. In both patients complete tumour removal by surgery was impossible with residual tissue being the origin of relapsing disease. Low dose radiation led to partial recovery of vision and resolution of the intracranial mass. Review of the literature on intracranial Rosai-Dorfman disease leads to the suggestion that postoperative radiotherapy may be advisable in all cases.

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Rosai-Dorfman disease or sinus histiocytosis is a histiocytic proliferative disorder.¹ Generally patients present in their mid-20s with cervical lymphadenopathy (87%), often preceded by a short non-specific infection.² Extranodal involvement occurs in 25% to 43%²⁻⁴ and affects the skin (12%), paranasal sinuses (11%), soft tissue (9%), bone (9%), salivary gland (5%), oral cavity (3%), kidney (2%), lower respiratory tract (2%), larynx (1%), and, rarely, other locations.² Intracranial lesions are extremely rare. To our knowledge 32 patients with intracranial masses have been described previously,³⁻³⁰ including three with suprasellar lesions.^{9 10 16} Eight patients experienced visual impairment,^{3 5-11} which was the presenting sign in six of them.⁵⁻¹⁰ This report follows up the patient of Bhattacharjee *et al*⁶ which was reported in this *Journal* not having relapsed after surgery. A relapse, however, occurred after publication and we report the 11 year follow up, together with a second patient, in which recurrence also occurred.

Patient 1

A 78 year old retired Welsh farmer presented at Moorfields Eye Hospital in June 1989 with progressive bilateral visual impairment. He underwent bifrontal craniotomy with subtotal tumour resection. His condition remained

stable until January 1990.⁹ The patient presented, however, with further impaired vision in February 1990 and the MRI disclosed evidence of local recurrence of the mass around both optic nerves, which enhanced with gadolinium on T1 axial brain scans. His visual acuity had declined to 6/24, N24 and 2/13 Ishihara plates on the right; counting fingers at 1 m and only the Ishihara control plate on the left. In addition to the previous bitemporal hemianopia the left nasal field had decreased to a small "island of vision". Both fundi showed loss of nerve fibre layer.

The patient underwent low dose radiotherapy, after which he showed improvement of his visual acuity to 6/18, 11/17 Ishihara plates on the right; 6/18, 16/17 Ishihara plates on the left. He remained clinically stable for the next 10 years. He had diabetes mellitus and a transient ischaemic attack in 1998. In 1999 he complained of some confusion and blurred vision. No further investigation was undertaken. He died of an unknown cause at the age of 89.

Patient 2

A 47 year old service engineer with rapidly developing right sided visual loss presented at the National Hospital for Neurology and Neurosurgery in July 1998. Six weeks previously he had complained of visual impairment and was found to have visual acuity of 6/24 on the right. Vision had decreased to light perception only 2 weeks later. On reflection the patient thought the loss of vision had begun 2 years previously. On presentation he had left shoulder pain, weakness in his right leg, fatigue, and frequent headaches starting in the neck and radiating to the occiput. The medical history showed a lumbar disc prolapse 2 years previously.

On examination his visual acuity corrected to 6/6, N12 and 13/13 Ishihara charts correctly identified on the left. No light could be perceived on the right and there was a right afferent pupillary defect. Loss of nerve fibre layer was apparent on the right. Apart from a lateralised Weber test to the right with normal Rinne all other cranial nerves were normal. Sense of smell was not tested at the time. Sensory examination, tone, power and reflexes in the lower limbs were normal. No residual deficit from the previous disc prolapse could be shown. General examination was normal and there was no lymphadenopathy.

Brain CT at admission showed multiple mass lesions around the foramen magnum, in the chiasmatic cistern arising from the planum sphenoidale, above the cribriform plate, the

Figure 1 Coronal and axial MRI (post gadolinium) of patient 2. Image (A) shows the sellar lesion preoperatively (17 July 1998). Image (B) displays the postoperative situation with some residual tissue in the region of the optic chiasm (18 August 1998). Image (C) demonstrates tumour regrowth 14 months postoperatively (9 September 1999). Image (D) was taken 6 months after local low dose radiation and shows a decrease of the sellar mass, with some residual tissue.

right parafalcine region, and the cerebellopontine angle. These lesions were gadolinium enhancing on the MRI T1 images and suggestive of multiple intracranial neoplasms such as meningioma (fig 1 A). Chest radiography was normal for heart and lungs, but the left acromion showed a cystic lesion. No additional skeletal lesions were detected in whole body scintigraphy.

The laboratory investigation showed a decreased concentration of thyroid stimulating hormone (0.2 mU/l, normal range 0.25–5.0 mU/l) but normal T3 and T4; increased blood glucose (9.8 mmol/l, normal range 3.3–9.0 mmol/l), and increased white cell count of $14.5 \times 10^6/l$ with $12.8 \times 10^6/l$ neutrophils, $1.2 \times 10^6/l$ lymphocytes, $0.4 \times 10^6/l$ monocytes, and $0.1 \times 10^6/l$ eosinophils. The erythrocyte sedimentation rate was normal (9 mm/h).

He underwent subtotal translabellar resection of the suprasellar mass. The postoperative visual fields showed a small “island of vision” on the right and a superior depressed field on the left. His visual acuity corrected to 6/5 on the left and to finger count on the right. The MRI 1 month after the operation showed some residual gadolinium enhancing tissue around the optic chiasm (fig 1 B).

One year later the patient complained of recurrence of the visual symptoms. His visual acuity worsened to 6/9 on the left and to light perception on the right. His sense of smell was now impaired. On MRI the sellar mass had increased in size and extended superiorly, causing bowing of the infundibulum and tilting the optic chiasm (fig 1 C). The patient underwent radiotherapy (20 Gy over 10 fractions). Three months later visual acuity had improved to counting fingers on the right and 6/5 on the left. His visual fields and colour vision were full on the left. On the right he could perceive hand movements in all quadrants apart from the lower temporal. At 1 year follow up the MRI showed decrease of the sellar mass (fig 1 D). Some residual tissue could still be seen on the axial images.

HISTOLOGY

The histology of patient 1 has been discussed in detail by Bhattacharjee *et al* and has been reviewed by one coauthor (MT); it is identical to that of patient 2.

For patient 2 histology of the suprasellar dural mass (30×20×8 mm) showed collagenous tissue with mixed chronic inflammatory cells and numerous polymorphs with very occasional eosinophils. Interspersed within this infiltrate were large cells with vesicular nuclei, some with indented nuclear membranes and abundant cytoplasm. Prominent lymphophagocytosis (fig 2 A) and phagocytosis of neutrophils and red blood cells by these cells was noted. Immunohistochemistry with positive labelling for S100 (fig 2 B) and CD68 (PKM1) and negative staining for CD1a confirmed the histiocytic cell lineage.

Discussion

Rosai-Dorfman disease or “sinus histiocytosis with massive lymphadenopathy” was initially

Figure 2 Histology from patient 2. (A) Sheets of histiocytic cells with large vesicular nuclei, some with nuclear indentations, are seen. There is an associated infiltrate of polymorphs and lymphocytes. Lymphophagocytosis (emperipolesis) by the histiocytic cells is clearly seen (haematoxylin and eosin, original magnification $\times 375$). (B) The histiocytic cells show strong nuclear and cytoplasmic staining with S100 protein and lymphophagocytosis is also seen (S100 immunohistochemistry, original magnification $\times 625$).

described in the French literature as a lipid storage disorder (*adénites avec surcharge lipidique*) possibly developing after inflammation. To our knowledge the first published patient was a 24 year old man from Guadeloupe, biopsied in 1959.³¹ In 1969 Rosai and Dorfman summarised the triad of massive cervical lymphadenopathy, expanded lymph node sinuses, and characteristic histiocytes showing emperipolesis as a new and distinct entity among the histiocytosis.¹ Lymphocytophagocytosis (emperipolesis) describes the presence of lymphocytes within the histiocytes. Because of the occurrence of extranodal disease in about 43% of patients the term “Rosai-Dorfman disease” is widely used in the literature for this subgroup.²

An overrepresentation of patients with extranodal disease is likely as publication of rare cases dominates the literature. Involvement of the CNS remains, however, rare with 32 reported cases.^{3–30} There is a male predominance of 65.6% (21 males, 11 females). The mean age is 37 (SD 19) years (range 2–78 years), slightly higher than the 20.6 years (SD

20.5) reported by Rosai and Dorfman for the entire entity.⁶ Neurological symptoms preceded the diagnosis by a mean of 3 years. Focal neurological signs, seizures, or headache are the most frequent presenting symptoms.

In general, the natural history of nodular sinus histiocytosis has been reported to be benign, with spontaneous remission. If, however, the location of the tumour involves the brain or spinal cord relapsing disease becomes a serious problem.

Intracranial tumor regrowth or recurrence of symptoms has been reported in 14% (four^{8 12 22} out of 29^{3–30}) of patients, excluding our patient 1⁹ and two patients who died.^{6 26} The mean follow up for these patients was 10.1 years (median 5, range 0.5–30 years). Relapsing patients tended to be slightly older (mean 42 years) without remarkable sex preference (two men, two women). In a further 25% of patients with CNS involvement no follow up information could be obtained from the literature.^{6 7 13 16 18 24} The mean follow up in patients reported as “stable” was 1.5 years (median 1 year, range 1 month–2 years)^{3–5 11 14 17 19–21 25–30}, but only in 52% of these patients was brain imaging performed at follow up.^{3 4 11 14 19 20 25 30}

From the surviving 29 patients (17 stable, four relapsing, eight no follow up information available) 18 had no follow up brain imaging at all, five had CT,^{9 19 22 25} and seven had MRI.^{3 4 10 11 14 20 30} Seventy per cent of “stable” patients were male (11 male, 5 female). Two patients died, one directly related to disease (55 years, female)⁶ and the other one (54 years, female) due to intracerebral haemorrhage after craniotomy.⁸

Surgery was performed in 93% with the preoperative diagnosis being meningioma. One patient underwent laminectomy for a spinal mass lesion extending from C1–C6.⁶ In one patient transphenoidal biopsy established the diagnosis of intracerebral Rosai-Dorfman disease and radiation (1000 cGy in 200 cGy daily) led to tumour resolution at 2 month follow up.³⁰ Three patients with spinal involvement (patients 1, 4, and 8 of Foucar *et al*⁶) received radiation. Patients 1 and 8 also had laminectomy and patient 8, steroids. Patients 1 and 8 improved with treatment. Patient 4 died 10 years later due to intracranial involvement.⁶ Another case of subtotal surgery with additional radiation (1500 rads) and no relapse at 14 month follow up was reported by Trudel *et al*²⁴

In summary it seems advisable to ensure a 5 year follow up period (median relapse time) including brain imaging in patients with intracranial Rosai-Dorfman disease. The main preoperative diagnosis remains meningioma, but histology should establish the diagnosis. In cases with subtotal tumour resection or recurrence of neurological symptoms we would treat with local low dose radiation early rather than late.

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