# Relapsing intracranial Rosai–Dorfman disease

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**Abstract**

We report on two patients presenting with recurrent visual impairment due to relapsing intracranial Rosai-Dorfman disease. In both patients a pre-operative diagnosis of meningioma was made. Histological examination revealed the characteristic picture of S100$\beta$ and CD68 positive histiocytosis with prominent emperipolesis. In both cases complete tumor 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 us to suggest that postoperative radiotherapy may be advisable in all cases.

**Key words:** Rosai-Dorfman, sinus histiocytosis, multiple meningioma, intracranial neoplasms.

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**Introduction:** Rosai-Dorfman disease or sinus histiocytosis is a histiocytic proliferative disorder [24]. Generally patients present in their mid twenties with cervical lymphadenopathy (87%), frequently preceded by a short non-specific infection [7]. Extranodal involvement occurs in 25 to 43% [7, 14, 25] and affects 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 [7]. Intracranial lesions are extremely rare. To our knowledge 32 patients with intracranial masses have been described previously [1–5, 8–23, 25–31], including 3 with suprasellar lesions [2, 20, 31]. Eight patients experienced visual impairment [2, 8, 14, 16, 23, 26, 30, 31], which was the presenting sign in 6 of them [2, 8, 16, 26, 30, 31]. This report follows up the case of Bhattacharjee et al. [2] which was reported in this journal not having relapsed following surgery. A relapse however occurred after publication and we report the 11-year follow up together with a second case in which recurrence also occurred.

**Case #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 tumor resection. His condition remained stable until January 1990 [2]. The patient presented however with further impaired vision in February 1990 and the MRI revealed 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, following 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 following 10 years. He suffered from 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 unknown cause at the age of 89.

**Case #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 two 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 reveals a lumbar disc prolapse two years ago.

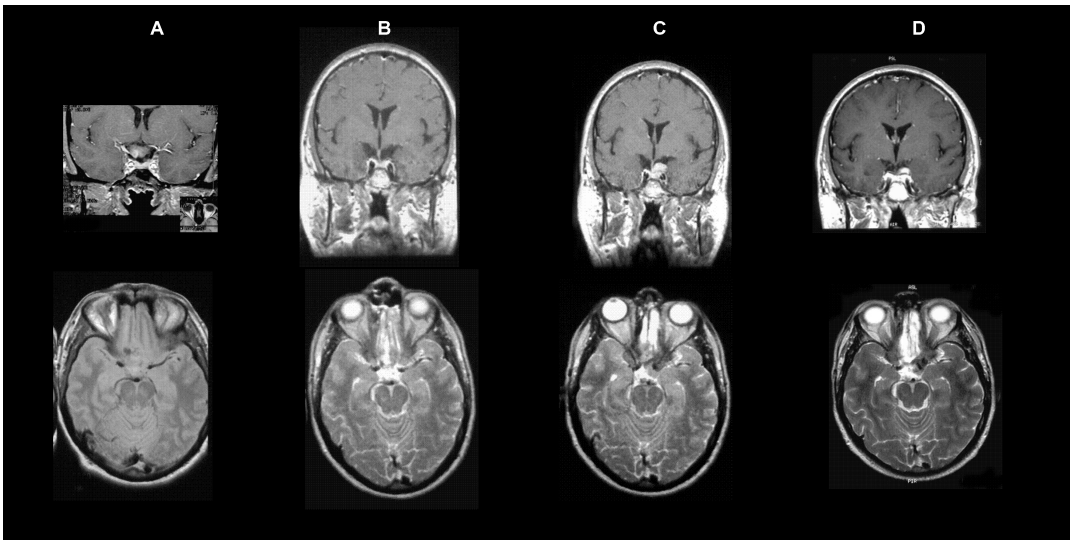


Figure 1: Coronal and axial MRI scans (post gadolinium) of case #2. Image (A) shows the sellar lesion pre-operative (17.7.1998). Image (B) displays the post-operative situation with some residual tissue in the region of the optic chiasm (18.8.1998). Image (C) demonstrates tumor regrowth 14 months post OP (09.09.1999). Image (D) is taken 6 months after local low dose radiation and shows decrease of the sellar mass with some residual tissue.

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 prolaps could be revealed. General examination was normal and there was no lymphadenopathy.

The CT scan at admission showed multiple mass lesions around the foramen magnum, in the chiasmatic cistern arising from the planum sphenoidale, above the cribriform plate, the right parafalcine region and the cerebello-pontine angle. These lesions were gadolinium-enhancing on the MRI T1 images and suggestive of multiple intracranial neoplasms, such as meningioma (figure 1 a). Chest X ray 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 revealed a decreased level 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 G/L with 12.8 G/L neutrophils, 1.2 G/L lymphocytes, 0.4 G/L monocytes, 0.1 G/L eosinophils. The erythrocyte sedimentation rate was normal (9 mm/h).

He underwent subtotal trans-glabellar resection of the suprasellar mass. The postoperative visual fields showed a small "island of vision" on the right and a superiorly-depressed field on the left. His visual acuity corrected to 6/5 on the left and to finger count on the right. The MRI one month after the operation revealed some residual gadolinium-enhancing tissue around the optic chiasm (figure 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 (figure 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 one year follow up the MRI showed decrease of the sellar mass (figure 1 d). We note that some residual tissue can still be seen on the axial images.

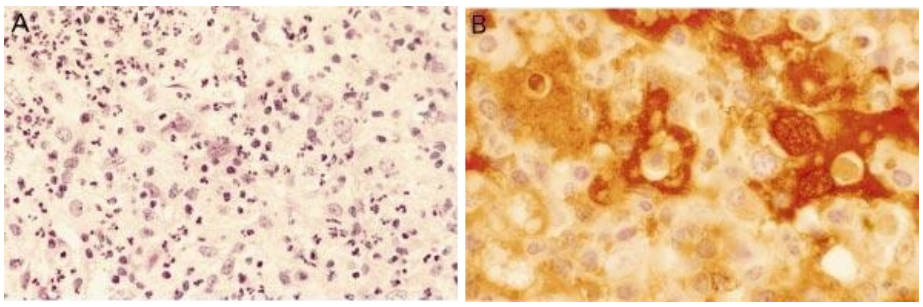


Figure 2: Histology from case #2: (A) Sheets of histiocytic cells with large vesicular nuclei, some with nuclear indentations are seen. There is an associated infiltrate of polymorphs and lymphocytes. Clearly lymphophagocytosis (emperiopolesis) by the histiocytic cells is seen. (H&E Mag x375)
(B) The histiocytic cells show strong nuclear and cytoplasmatic staining with S100 protein and lymphophagocytosis is also seen (S100 immunohistochemistry Mag x625).

**Histology:** The histology of case #1 has been discussed in detail by Bhattacharjee et al. and has been reviewed by one co-author (MT) and is identical to case #2.

Case #2: histology of the suprasellar dural mass (30x20x8 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 emperipolesis and phagocytosis of neutrophils and red blood cells by these cells was noted. Immunohistochemistry with positive labeling for S100b and CD68 (PKM1) and negative staining for CD1a confirmed the histiocytic cell lineage (figure 2).

**Discussion:** Rosai-Dorfman disease or "sinus histiocytosis with massive lymphadenopathy" was initially described in the French literature as a lipid storage disorder (adtes avec surcharge lipidique) possibly developing after inflammation. To our knowledge the first published case was a 24 year old male from Guadeloupe, biopsied in 1959 [6]. In 1969 Rosai and Dorfman summarized the triad of massive cervical lymphadenopathy, expanded lymph node sinuses and characteristic histiocytes showing emperipolesis as a new and distinct entity among the histiocytosis [24]. Emperiopolesis (lymphocytophagocytosis) 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 [7].

An over-representation of patients with extranodal disease is likely as publication of rare cases dominates the literature. CNS involvement remains however rare with 32 reported cases [1–5, 8–23, 25–31]. There is a male predominance of 65.6% (21 males, 11 females). The mean age is with 37 years (range 2-78 years, SD 19) slightly higher than the 20.6 years (SD 20.5) reported by Rosai and Dorfman for the entire entity [8]. 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 benign with spontaneous remission. If however the location of the tumor involves the brain or spinal cord relapsing disease becomes a serious problem.

Intracranial tumor regrowth or recurrence of symptoms has been reported in 14% (4[3, 21, 30] out of 29[1, 3–5, 8–23, 25–31]) patients excluding our case #1 [2] and two patients who died[8, 28]. The mean follow up for these patients was 10.1 years (median 5, range 0.5-30 years). Relapsing patients tend to be slightly older (mean 42 years) without remarkable gender preference (2 male, 2 female). In further 25% of patients with CNS involvement no follow up information could be obtained from the literature [8, 9, 17, 20, 22, 26]. We note that the mean follow up in patients reported as "stable" was 1.5 years (median 1 year, range 1 month - 2 years) [1, 4, 5, 11, 12, 14–16, 18, 19, 23, 25, 27–29]. But only in 52% of these patients brain imaging has been performed at follow up [5, 14, 18, 19, 23, 25, 27, 29].

From the surviving 30 patients (17 stable, 4 relapsing, 8 no follow up information available) 18 had no follow up brain imaging at all, 5 had CT [2,

3, 5, 18] and 7 had MRI [14, 19, 23, 25, 27, 29, 31]. Seventy percent of "stable" patients were male (11 male, 5 female). Two patients died. One directly related to disease (55 years, female) [8] and the other one (54 years, female) due to intracerebral hemorrhage following craniotomy [30].

Surgery was performed in 93% with the preoperative diagnosis being meningioma. One patient underwent laminectomy for a spinal mass lesion extending from C1-C6 [8]. In one patient transphenoidal biopsy established the diagnosis of intracerebral Rosai-Dorfman disease and radiation (1000 cGy in 200 cGy daily) lead to tumor resolution at 2 months follow up [27]. Three patients with spinal involvement (Foucar's case #1, #4 and #8) received radiation. Case #1 and #8 also had laminectomy and case #8 steroids. Case #1 and #8 improved with treatment. Patient #4 died 10 years later due to intracranial involvement [8]. Another case of subtotal surgery with additional radiation (1500 rads) and no relapse at 14 months follow up is reported by Trudel et al. [28].

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 pre-operative diagnosis remains meningioma, but histology should establish the diagnosis. In cases with subtotal tumor resection or recurrence of neurological symptoms we would treat with local low dose radiation rather early than late.

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