La radiologia medica (2021) 126:89–98
https://doi.org/10.1007/s11547-020-01226-7

MAGNETIC RESONANCE IMAGING

MR imaging of cerebral involvement of Rosai–Dorfman disease: a single-centre experience with review of the literature

Marco Varrassi[1] · Antonella Corridore[2] · Emanuele Tommasino[2] · Giorgia Saltelli[3] · Federico Bruno[2] · Alessandra Di Sibio[1] · Alessandra Splendiani[2] · Ernesto Di Cesare[2] · Carlo Masciocchi[2]

Received: 3 November 2019 / Accepted: 12 May 2020 / Published online: 26 May 2020

Abstract

Rosai–Dorfman disease (RDD) is a rare, benign, non-Langerhans cells histiocytosis with massive lymphadenopathy of uncertain aetiology. It is commonly characterized by massive, painless, non-tender, bilateral cervical lymphadenopathy. Extra-nodal involvement is usually seen in 50% of patients, with the brain being affected in only 5% of cases, usually as dural-based lesions. Clinical presentation is heterogeneous and strongly dependent on the localization of the lesions. Although the histopathological findings are essential for the final diagnosis, brain magnetic resonance imaging (MRI) currently represents the first-line strategy for the detection of the lesions across the central nervous system (CNS); moreover, it may provide additional elements for the differential diagnosis versus other more common lesions. We performed a case-based literature review to highlight possible aetiologic and pathogenetic theories of this disease, along with imaging features of RDD, with a particular focus on the MRI characteristics of the CNS involvement (CNS–RDD). Finally, we provided a novel insight on the current therapeutic approaches, either surgical or medical.

Keywords Rosai–Dorfman disease · RDD · MRI · Spectroscopy

Abbreviations

CT	Computed
MRI	Magnetic resonance imaging
RDD	Rosai–Dorfman disease
T1WI	T1-weighted image
T2WI	T2-weighted image
TE	Echo time
TR	Repetition time
MRS	Magnetic resonance spectroscopy
PWI	Perfusion weighted imaging
rCBV	Relative cerebral blood volume

Introduction

Rosai–Dorfman disease (RDD) is a rare, benign, non-Langerhans cells histiocytosis with massive lymphadenopathy of uncertain aetiology, firstly described in 1965

✉ Emanuele Tommasino
emanuele.tommasino@gmail.com

Marco Varrassi
mvarrassi27@yahoo.it

Antonella Corridore
antonella.corridore@gmail.com

Giorgia Saltelli
saltelli.giorgia@hotmail.it

Federico Bruno
federico.bruno.1988@gmail.com

Alessandra Di Sibio
adisibi@hotmail.com

Alessandra Splendiani
alessandra.splendiani@cc.univaq.it

Ernesto Di Cesare
ernesto.dicesare@cc.univaq.it

Carlo Masciocchi
carlo.masciocchi@cc.univaq.it

[1] Radiology Department, Ospedale "San Salvatore", Via L. Natali 1, 67100 L'Aquila, Italy

[2] Department of Biotechnological and Applied Clinical Science, University of L'Aquila AQ, Via Vetoio 1 AQ, 67100 L'Aquila, Italy

[3] Anesthesiology and Intensive Care, Department of Surgical and Medical Science and Translational Medicine, University "La Sapienza", Rome, Italy

by Destombes and recognized 4 years later, in 1969, as a unique histio-lymphoproliferative disease of lymph nodes by Rosai and Dorfman [1, 2].

It is usually characterized by massive, painless, non-tender, bilateral cervical lymphadenopathy, and it can be associated with systemic symptoms such as fever, weight loss, malaise, leucocytosis and anaemia [3].

RDD is usually diagnosed in children, adolescents and young adults, but it can potentially occur at any age; this condition has a male preponderance with a male/female ratio of 3:1 and more frequently affects males of African descent [4].

Although RDD is more frequently localized in single or regional lymph nodes, extra-nodal involvement is often recognized.

Due to its different locations, it has been classified into 3 types: nodal (classic RDD), extra-nodal and mixed involvement type [2].

Extra-nodal RDD has been documented in up to 43% of cases, with skin, soft tissues, upper respiratory tract, bone, orbit, nasopharynx, salivary glands, central nervous system (CNS), testes and endocrine glands being the most affected sites. Extensive disease with involvement of visceral organs and vital structures is mostly seen in black patients [5].

The clinical course is unpredictable with episodes of exacerbations and remissions; however, it is a self-limiting disease, even if death can rarely occur.

Herein, we perform a literature review of MR imaging of cerebral involvement of RDD with some illustrative clinical cases from our institution.

Patient selection and literature review

We retrospectively reviewed in our database 4 RDD cases with CNS involvement, in the period between January 2014 and March 2019, all with a final immunohistochemical diagnosis. Three of them presented systemic involvement, with general lymphadenopathy, weight loss, leucocytosis and anaemia. None showed spinal localization.

One out of the four cases had an history of oncologic disease, and we have to admit that this could have represented a confusing factor when analysing radiological findings.

For the literature review, we searched the English literature using the 3 major databases PubMed, Scopus and Cochrane in the period between January 1999 until May 2019, typing the keywords "Rosai–Dorfman disease; cerebral Rosai–Dorfman disease; Rosai–Dorfman disease spine; MR imaging cerebral Rosai–Dorfman disease; cerebral Rosai–Dorfman disease therapy".

MRI data acquisition and processing

All images were acquired using a 3T scanner (Discovery™ MR750w GEM—70 cm, 3T, GE healthcare, Chicago, USA) or a 1.5T scanner (Signa GEM, 1.5T, GE healthcare, Chicago, USA). For the 3T and 1.5T, with a 32-channels and 24-channels head coil, respectively, the standardised MRI acquisition protocol included a three-dimensional T1-weighted BRAVO sequence, DWI b1000 sequence, T2 TSE-weighted sequences, a T2* GRE sequence, a T2 FS FLAIR sequence and, in some cases, DSC perfusion sequence, MRA sequences 3D TOF Multislab and Sag 3D Vel and multiple and Single-Voxel MR Spectroscopy.

CT and scintigraphy

CT axial unenhanced and contrast-enhanced CT was performed using a 640-slice CT (Toshiba Aquilion ONE 320-row detectors, Toshiba Medical Systems, Outerwear, Japan) with section thickness, 3.0 mm; field of view [FOV] 1818 cm; 140 kV; 200 mA/slice). For contrast-enhanced CT, 90 mL iomeprol (Iomeron 400) was injected at 3–4 mL/s. A CT99MDP—740 MBq Musculoskeletal scintigraphy was also performed in one patient.

Illustrative cases

Patient 1

A 78-year-old Caucasian male patient, with a history of colon carcinoma and Non-Hodgkin lymphoma, was addressed to our Department after two episodes of acute weakness of the right side with gait impairment and falls, 2 months earlier. No other neurological symptoms were described. Specifically, patient underwent surgical resection of the left testicle for diffuse large B cell lymphoma CD20+, followed by radio- and chemotherapy, 5 years prior to the first episode of weakness.

Head CT showed a slightly hyperdense lesion (1 cm) in the right frontal lobe (precentral gyrus), with associated peripheral oedema (Fig. 1a). This lesion showed homogenous enhancement after contrast administration (Fig. 1b).

MRI showed a nodular lesion (8 mm) in the right semi-oval centre, iso-hypointense in the T2-weighted images and slightly hyperintense in the T1-weighted images, with restricted diffusivity (Fig. 1c, d) and homogeneous, avid enhancement after contrast agent administration. Another similar small lesion was identified at the ipsilateral post-central gyrus. These lesions were accompanied by an extensive vasogenic oedema.

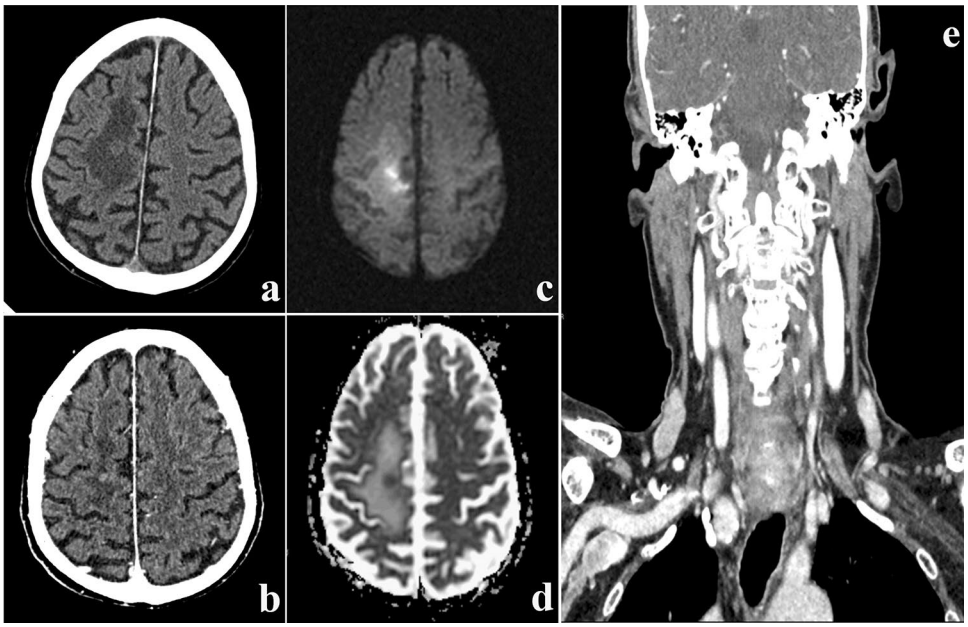

Fig. 1 **a** CT head scan showing a slightly hyperdense/isointense lesion in the right precentral gyrus. **b** Contrast-enhanced CT (CECT) head scan showing the same lesion mildly enhancing. **c**, **d** DWI and ADC map displaying in the same region an area of restricted diffusivity. **e** CECT neck scan does not reveal any significant lymphadenopathy

According to the radiological aspects, these lesions were reported as suspicious metastatic localizations of the patient's neoplastic conditions. Therefore, patient was referred to the local neurosurgeons and oncologists after a defined corticosteroid treatment for the vasogenic oedema was prescribed.

Lumbar puncture with cytological liquor examination was normal.

Total-Body CT examination also revealed a pulmonary involvement, interestingly without any cervical lymphadenopathy, typical of the disease (Fig. 1e).

One month later, follow-up MRI examination revealed reduction in the perilesional oedema and focal enhancement in the known lesion in the right semioval centre (Fig. 2a–d); on the contrary, a new lesion (1 cm), with

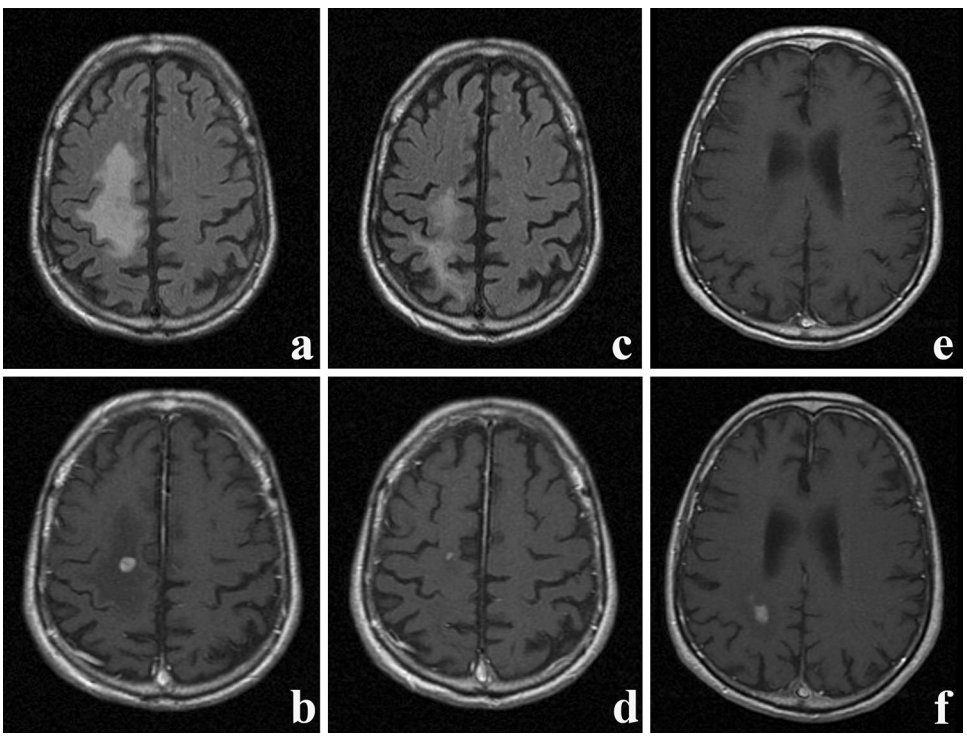

Fig. 2 **a**, **b** FLAIR and contrast-enhanced T1-w images at first MRI control show an iso-hypointense lesion surrounded by oedema, enhancing uniformly after contrast administration. **c**, **d** 1-Month follow-up, after corticosteroid therapy, showing partly reduction in the oedema and focal enhancement. **e**, **f** A new lesion appears in the parietal right lobe, with the same imaging features, associated with a smaller contrast nodule

similar imaging features, localized in the deep white matter of the right parietal lobe (Fig. 2e, f) appeared.

Hence, patient underwent a neurosurgical frameless image-guided stereotactic brain biopsy procedure, followed by histological analysis, that revealed a CNS involvement of the Rosai–Dorfman disease (RDD).

Patient 2

A 57-year-old Caucasian man was addressed to our department with a 6-year history of progressive right visual and hearing loss with tinnitus.

A brain CT scan was performed in our department. It revealed slightly hyperdense, multiple, bilateral, extra-axial and homogenously enhancing lesions. Particularly, these lesions were found in the cerebral falx, in the right perirolandic region, in the right temporal pole region and insula, adhered to the atrium of the right ventricle and to the homolateral petroclival region. The latter, with a diameter of 7 cm, exhibited a considerable mass effect on the surrounding structures, specifically on fourth ventricle and brainstem.

Head MRI examination revealed multiple, bilateral, extra-axial and homogenously enhancing lesions. In particular, these lesions showed iso-hypointense signal in the T1- and T2-weighted images, with dural attachment and homogeneous enhancement after contrast administration.

Imaging findings firstly supported the neuroradiological diagnosis of multiple meningiomas.

The patient underwent surgical treatment of the major temporal mass with subsequent histopathological examination. The final report confirmed the diagnosis of intracranial RDD.

Subsequently, a post-operative total-body CT examination showed other localizations of the disease: a paravertebral mass (Fig. 3a), mediastinum swollen lymph nodes and splenomegaly (Fig. 3b).

Patient 3

A 69-year-old Caucasian male patient comes to our observation for sudden onset of dysarthria associated with disturbances of thinking.

Brain MRI with spectroscopy and perfusion study showed a large area with altered intensity, slightly hyperintense in the T2 weighted sequences and isointense in the T1-weighted images, involving the parietal, temporal and occipital lobe, with restricted diffusivity and avid contrast enhancement in two smaller nodular lesions. Perfusion MRI showed a slightly increased rCBV in the enhancing lesions (Fig. 4a, b); single- and multi-Voxel Spectroscopy MRI documented a NAA reduction with evidence of a lactate peak (Fig. 5a–d).

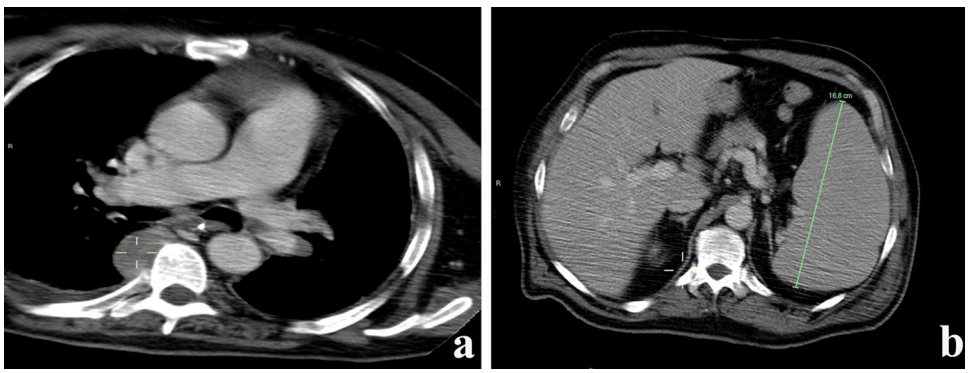

Fig. 3 **a**, **b** The systemic involvement of RDD. **a** CT scan at the level of the superior segment of the right inferior lobe. **b** significant splenomegaly is detected during a total-body CT scan

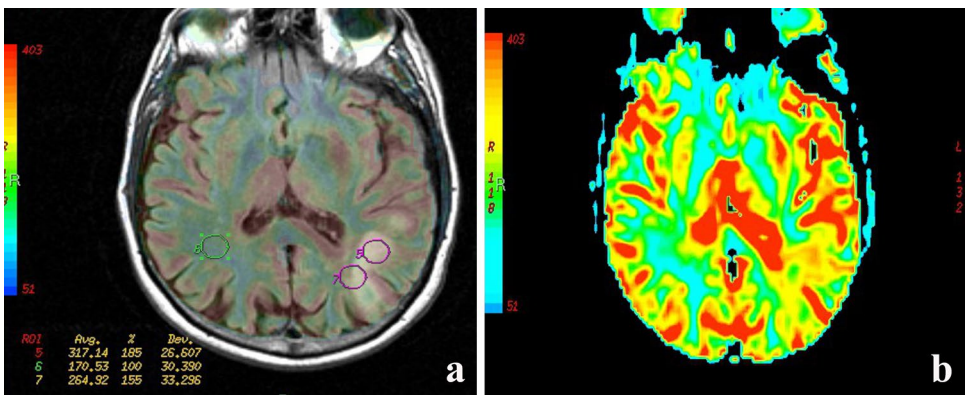

Fig. 4 **a** FLAIR sequence matched with the perfusion map (**b**), showing a slight increase in rCBV in the affected area, compared to normal-appearing temporo-occipital right white matter

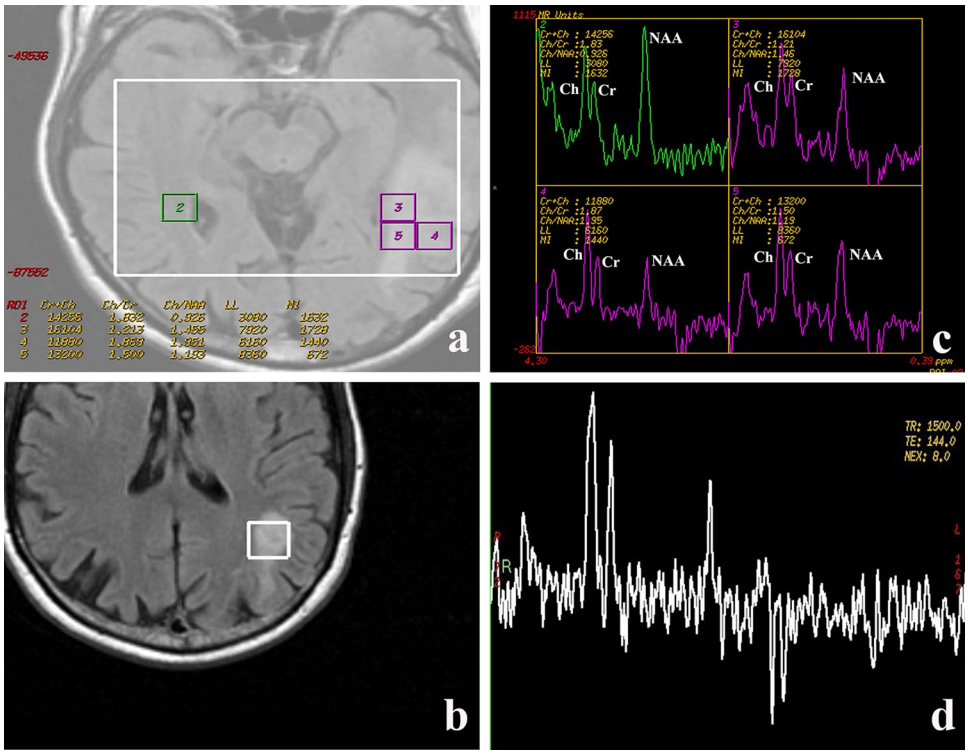

Fig. 5 **a** Multi- and **b** single-voxel MRS with **c** and **d** respective maps, showing an evident reduction in NAA peak with evidence of Lac peak in the cerebral lesion

Table 1 Anagraphic and radiological data of our single-centre CNS-RDD cases

Patient	Sex	Age	Onset symptoms	Localization	CT	MRI	Systemic involvement
Nr. 1	M	78	Falling for acute weakness of the right side with gait impairment	right hemisphere (semioval centre and post-central gyrus)	Weakly hyperdense	T1: Slightly hyperintense T2: Iso-hypointense DWI: Restricted diffusivity Enhancement: Intense and homogeneous	Lung
Nr. 2	M	57	Progressive right visual and hearing loss with tinnitus	multiple, bilateral and extra-axial	Slightly hyperdense	T1: Isointense T2: Isointense Enhancement: Intense and homogeneous DWI: No restricted diffusivity	Paravertebral dorsal mass, mediastinum swollen lymph nodes and splenomegaly
Nr. 3	M	69	Dysarthria and thinking alterations	parietal, temporal and occipital lobe	–	T1: isointense; T2: Hyperintense; Enhancement: Intense and homogeneous	Lungs and pericardium
Nr. 4	M	33	Acute postural instability with dizziness, nausea, vomiting and headache	Right cerebellar paravermian region	Slightly hypodense	T1: slightly hypointense T2: slightly hyperintense DWI: no restricted diffusivity Enhancement: Intense and homogeneous	None

Imaging findings were compatible with possible low-intermediate glial heteroplasia (Grade II or III); therefore, decision was taken to perform a cerebral biopsy. Histological analysis diagnosed RDD (Table 1).

Finally, the total-body CT examination depicted also pulmonary and pericardial involvements, but bone scintigraphy with Tc99mMDP—740 MBq showed only hyperfixation in the D11 vertebral body.

Patient 4

A 33-year-old man arrived in our Department to perform a brain magnetic resonance (MR) examination after a head CT scan in the emergency Department 3 days before showed a slightly hypodense area in the right cerebellar paravermian region. Patient referred an episode of acute postural instability with dizziness, nausea, vomiting and headache; symptoms were still present, although attenuated. Neurological examination showed tendency to left lateropulsion at Romberg's test.

MRI examination confirmed an altered signal intensity area in the right cerebellar tonsil measuring about $11 \times 8 \times 16$ mm, (AP × LL × CC). This lesion was slightly hypointense in T1-weighted sequences, slightly hyperintense in T2-weighted sequences and hyperintense in FLAIR sequence; water diffusivity was not restricted, and supratentorial findings were normal. MR angiography sequences did not show any significant alterations nor a pathological vascularisation pattern around the lesion (Fig. 6a, b). After intravenous administration of contrast medium, the lesion showed avid and homogeneous enhancement and it was suspected to be a possible ependymoma.

The patient was then referred to the Department of Neurosurgery for surgical removal.

Histological examinations performed on the specimen showed histiocytes presenting positivity to CD68 and CD31; these findings allowed to diagnose an infratentorial localization of RDD.

MR follow-up examination, performed 7 months after surgery, confirmed complete removal of the lesion, with normal post-surgical findings (Fig. 7a–c).

The total-body CT examination did not show other localizations.

Patient reported resolution of symptoms.

Discussion

CNS involvement of Rosai–Dorfman disease

CNS involvement in Rosai–Dorfman disease (RDD) is exceptional: indeed, less than 300 cases have been reported in the literature, being the first case of multiple intracranial RDD lesions reported in 1989 by Song et al. [2, 6].

Particularly, primary and isolated intracranial involvement in RDD accounts for approximately 5% of all cases

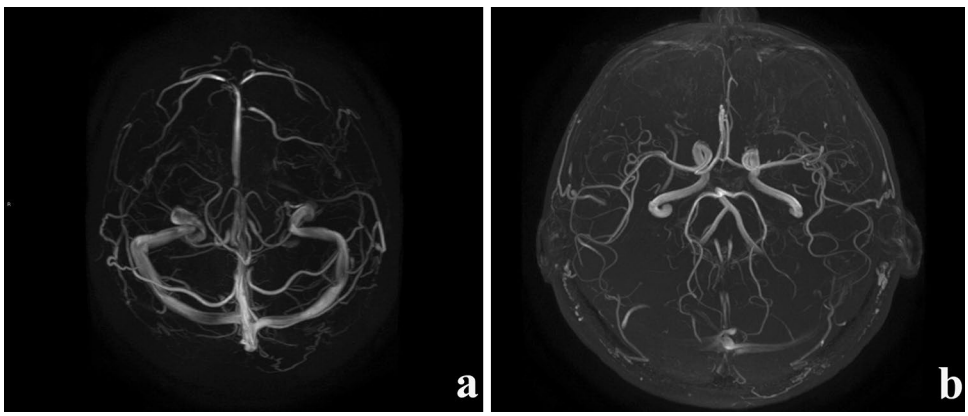

Fig. 6 **a**, **b** Venous and arterial-phase MRA did not show any abnormal vascularization pattern

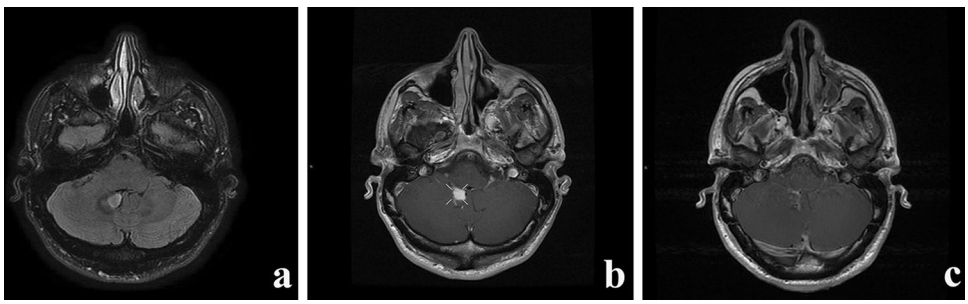

Fig. 7 **a** FLAIR and **b** post-contrast T1-w sequences showing a well-circumscribed lesion in the right cerebellar tonsil with homogeneous enhancement. **c** MRI follow-up after surgical excision

of extra-nodal RDD. In addition, in only 20% of CNS-RDD manifestations, there is also a spinal involvement and in lower cases, spine could be the only affected site [7].

Usually, cases with CNS-related RDD are described both in adult and paediatric population; nevertheless, the subjects described in our case series tend to be older than RDD patients without systemic involvement (third–fourth decade of life), with a mean age of 39 years.

Cerebral involvement usually manifests as dural-based lesions, often clinically and radiologically mistaken with meningiomas, before surgical treatment and histological diagnosis [8].

Intraparenchymal involvement is far less common, with lesions primarily mimicking lymphomas or intraparenchymal tuberculous granuloma. Furthermore, intraventricular lesions have been reported in some cases, whereas symptomatic intramedullary spinal cord involvement is extremely rare [9, 10].

The common sites of primary CNS-RDD are the brain convexity, skull base, parasagittal region, suprasellar region, cavernous sinus and petroclival region [11].

Nevertheless, two cases of CNS-RDD involving lateral ventricles have also been described so far in the literature, in a 2-year-old child and in a 40-year-old woman, respectively [12, 13].

No neurodegenerative pattern has been described in patients with RDD, unlike different histiocytosis such as neurological Langerhans cell histiocytosis and neurological Erdheim–Chester disease [14].

Aetiology and pathogenesis

Aetiology of RDD is still widely unknown, even if some hypotheses have been proposed.

A possible role for Epstein–Barr virus (EBV), cytomegalovirus, Brucella and human herpes virus-6 (HHV-6) was suspected, although a cause–effect relationship is still lacking [15].

Theories dealing with immunological modulation seem to be promising since RDD belongs to the wide spectrum of granulomatous lesions and is frequently associated with autoimmune conditions and haematological malignancies. According to these theories, immunodeficiency, perhaps caused by cross-reactive infections, or cytokine-mediated migration of monocytes, could lead to histiocytic reactions and accumulation [4].

A possible relationship has been recently hypothesized between RDD and IgG4-related disease [16]. These pathological conditions, indeed, can both involve CNS in similar sites (e.g. cavernous sinus), causing lesions that present similar imaging characteristics. Moreover, some cases analysis reported herein showed that some patients with RDD presented increased numbers of IgG4-positive plasma cells. In most of these RDD cases, however, an IgG4/IgG ratio greater than 0.4 was lacking, as well as the typical storiform fibrosis with obliterative phlebitis, today considered as the histological hallmark of IgG4-related disease [17]; moreover, most of RDD patients usually do not respond to corticosteroid treatment, which is considered nowadays as the mainstay in the treatment of IgG4-related disease. For all these reasons, RDD should not be included in the IgG4-related disease spectrum.

Lastly, genetic studies showed correlations between RDD and mutations disabling SLC29A3 gene; this gene, mapped in chromosome 10q22.1, encodes an intracellular nucleotide transporter (hENT3), which seems to be involved in the apoptotic pathways [18].

Clinical manifestations

Rosai–Dorfman disease is a systemic heterogeneous entity. Although RDD is commonly identified as a benign disease, the clinical course is unpredictable, in most cases with a slow evolution and sometimes with spontaneous regression. It is usually considered a self-limiting disease, but in some cases, recurrences and progression are possible, and in rarer occasions, it could also be fatal due to massive organ involvement.

The typical manifestation is a massive, painless, bilateral lymphadenopathy, in the cervical and submandibular regions. Less frequently other peripheral nodes regions, such as the axillary, inguinal and mediastinal, can also be involved [1, 3].

Patients often present constitutional symptoms such as fever, weight loss, night sweat, malaise and asthenia.

Laboratory analyses show raised serum erythrocyte sedimentation rate, hyperglobulinemia, normocytic/microcytic anaemia.

Rosai–Dorfman disease has been described in association with Hodgkin's and non-Hodgkin lymphoma, other histiocytoses or autoimmune diseases [14].

In CNS-RDD, systemic signs are usually absent and clinical manifestations depend on the localization, size and number of the lesions. Usually symptoms may include seizures, headaches, endocrine abnormalities or focal neurological deficits due to mass effects and oedema. Visual changes, weakness, loss of sensation, gait impairment, pituitary dysfunction have been also described or, if spine is involved, spinal cord dysfunction with paraparesis and paraplegia.

The spine is involved in about 20–25% of cases of CNS-RDD; about 70–75% of cases involving the spine are isolated, while the remaining show intracranial and spinal lesions simultaneously [19].

Spinal lesions have been described in some reports as dural-based lesions, both in the epidural and in the subdural

space, more commonly in the thoracic and cervical spine [19, 20].

These lesions are often clinically responsible for numbness, hypaesthesia, weakness, hyporeflexia and pain to upper or lower limbs, according to the location.

Anatomopathological findings

The diagnosis of RDD can only be confirmed by the histopathological/immunohistochemical examinations.

Generally, the RDD typical pattern is characterized by a massive expansion of large histiocytes with large vesicular nuclei and pale eosinophilic cytoplasm. They contain intact lymphocyte or erythrocytes in their cytoplasm, and this manifestation is known as emperipolesis, which is considered the cytological hallmark of RDD, even if it is not specific of this disease [2]. A lymphoplasmacytic inflammatory cell infiltrate and necrotic areas are also present.

Histiocytes are thought to be activated by the macrophages derived from circulating monocytes. As a consequence of the process of emperipolesis, lymphocytes enter in the cytoplasm of histiocytes. These histiocytes with abundant pale cytoplasm typically express S-100 antigen and are strongly positive for CD68, CD163, α1-antitrypsin, whereas they are negative for CD1a, CD15 and CD30 [19]. Haematoxylin–eosin-stained sections are usually performed to obtain correct diagnosis.

Radiological features

Primary Rosai–Dorfman disease involving the CNS (CNS-RDD) is ubiquitous and affects either intracranial or spinal structures. In this regard, approximately 77% of all cases concern intracranial involvement, whereas intraspinal disease accounts for 14% and both cranial and spinal involvement accounts for 9% of all cases [5].

Most CNS-RDD cases present with dural-based, well-circumscribed lesions; instead, the rare intraparenchymal disease can occur in all areas of the brain or the spinal cord, either supratentorial or infratentorial, superficially or deeply at the white or grey matter [21, 22].

Its rarity and occurrence throughout the CNS and ability to mimic meningiomas and primary brain tumours may often delay the diagnosis.

On CT scan, the lesion usually appears hyperdense with high-contrast enhancement, surrounded by perilesional oedema with mass effect on the contiguous structures and, in some cases, midline shift.

At MRI examination, on T1-weighted sequences, the lesion generally appears homogeneously isointense with strong and homogeneous enhancement after contrast administration. On T2-weighted sequences, lesion is usually hypo-isointense, with perilesional oedema. There may be sulcal effacement or mild cortical thickening in RDD, implicating a certain degree of pachymeningitis [23, 24].

Often RDD is misdiagnosed with meningiomas; therefore, it is important to summarize the differences between them.

Meningiomas can be hypo-iso-hyperintense on T2-weighted sequences, while RDD lesions are generally hypointense. Meningiomas present demarcated margins, while in RDD, they may be irregular with parenchymal/subarachnoid involvement and sulcal effacement. At subtraction angiography, meningiomas are generally hypervascular, while RDD lesions are hypovascular. Moreover, meningiomas often present bony changes, such as hyperostosis, bone destruction and calcifications; these findings are generally absent in RDD [25, 26].

Advanced MRI techniques such as perfusion weighted imaging and spectroscopy can be helpful to provide a correct diagnosis [27].

For example, in meningiomas, Alanine is typically elevated in proton spectroscopy studies. In RDD lesions, on the other hand, spectroscopy generally shows elevated lipid and N-acetyl aspartate peaks, suggestive of granulomatous inflammatory pathology, and a raised choline peak.

Data about the applicability of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in CNS-RDD are limited. The potential use of 18F-FDG PET/CT to diagnose relapsed intracranial RDD was recently studied but needs further exploration [28].

Moreover, a variety of different pathological conditions with radiological appearance of dural-based lesions should be considered as possible differential diagnoses.

Among them lymphoproliferative disorders, plasma cell granuloma and dural metastases are the most common.

Dural metastases typically present as multiple lesions, iso-hypointense in T1-weighted sequences and iso-hyperintense in T2-weighted sequences to adjacent cortex.

In MRS studies, dural metastases show increased choline–creatine ratio, prominent lipid peak and absence of NAA peak.

Regarding to the neuroimaging, the best diagnostic clues for diagnosing CNS-RDD appear to be represented by the hypo-isointensity in the T2-weighted sequences and the relatively low rCBV perfusion values, likely due to the abundant fibrous tissue.

These findings, however, are not specific and not always present, and the final diagnosis is often still histological.

In exceptional cases of CNS-RDD involving lateral ventricles, different ventricular neoplasms such as ependymoma, choroid plexus papilloma and carcinoma should be ruled out.

These neoplasms, however, are usually either more structurally inhomogeneous (ependymoma) or highly vascularized (papilloma and carcinoma) than CNS-RDD.

Radiologically, spinal lesions show similar imaging characteristics with the cerebral lesions, usually appearing as isointense in T1-weighted sequences and iso-hypointense in T2-weighted sequences; homogeneous enhancement is usually present.

In the majority of cases, however, these lesions are misdiagnosed with meningiomas and final diagnosis is performed on specimens after surgical resection [29].

Even if relatively rare, a spinal involvement should always be suspected in patients presenting cerebral RDD, especially if clinical signs of myelopathy are present.

Therefore, an ideal MR imaging protocol should, whenever available, include MRS and perfusion imaging of the brain, which may be helpful in differentiating different dural-based lesions, and a complete study of the spine, performing pre- and post-contrastographic sequences.

Treatment and prognosis

Rosai–Dorfman has usually a good outcome and is considered a benign self-limiting disease with a clinical course characterized by exacerbations and remissions; however, in 5–11% of patients, death occurs.

Patients with systemic and extra-nodal involvement tend to have a protracted clinical course and poorer prognosis. The severity correlates with the number and localization of extra-nodal lesions. Commonly, patients with aggressive and extensive disease do require treatment, although no standard treatment exists.

Therapeutic approach is determined case by case.

Currently, the first therapeutic option in cerebral RDD is represented by surgery that provides relief of symptoms caused by mass effect and tissue for histological examinations. In case of lesions affecting sites less amenable to radical surgical excision, biopsy is considered a valid option.

Other viable treatment approaches consist of:

- "wait and see" strategy
- systemic steroids for decreasing nodal size and alleviating symptoms; nevertheless, recurrences are common after cessation.

Patients with extra-nodal RDD involving vital organs (liver, CNS) or presenting life-threatening complications (upper way obstruction) may require urgent therapeutic intervention, usually consisting in surgery approach.

Radiation therapy is considered a valid therapeutic option in case of post-surgical recurrences, since cerebral RDD is considered moderately radiosensitive.

Lastly, chemotherapeutic agents, such as Mercaptopurine [30–32], CD20-specific monoclonal antibody, immunosuppressants and other therapies, have been described in particular cases of RDD.

Conclusions

MRI represents nowadays the main diagnostic technique in the evaluation of patients with suspected intracranial RDD, enabling to accurately detect number and localization of cerebral lesions.

Advanced MRI techniques, such as MRS and PWI, can be very helpful in the differential diagnosis between RDD and different lesions and in the follow-up of these patients after conservative or surgical treatment.

However, an imaging-based diagnosis is often difficult and histopathological examinations still represent the gold standard to establish a final diagnosis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent from all the patients was obtained, before undergoing MRI examination.

References

1. Rosai J, Dorfman RF (1969) Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol 87:63–70
2. Song SK, Schwartz IS, Strauchen JA et al (1989) Meningeal nodules with features of extranodal sinus histiocytosis. Am J Surg Pathol 13(5):406–412
3. Adeleye AO, Amir G, Fraifeld S et al (2010) Diagnosis and management of Rosai–Dorfman disease involving the central nervous system. Neurol Res 32(6):572–578
4. Emile JF, Abla O, Fraitag S et al (2016) Revised classification of histiocytosis and neoplasms of the macrophage-dendritic cell lineages. Blood 127(22):2672–2681
5. Qin G, Ye J, Lan S et al (2019) Rosai–Dorfman disease with spinal and multiple intracranial involvement: a case report and literature review. Br J Neurosurg 18:1–5
6. Luo Z, Zhang Y, Zhao P et al (2017) Characteristics of Rosai–Dorfman disease primarily involved in the central nervous system: 3 case reports and review of Literature. World Neurosurg 97:58–63
7. Xu H, Zhang F, Lu F et al (2017) Spinal Rosai–Dorfman disease: case report and literature review. Eur Spine J 26(Suppl 1):117–127
8. Catalucci A, Lanni G, Ventura L et al (2012) A rare case of intracranial Rosai–dorfman disease mimicking multiple meningiomas. A case report and review of the literature. Neuroradiol J 25(5):569–574

9. Zhai X, Zhou M, Chen H et al (2019) Differentiation between intraspinal schwannoma and meningioma by MR characteristics and clinical features. Radiol Med 124(6):510–521
10. Maiti TK, Gangadharan J, Mahadevan A et al (2011) Rosai–Dorfman disease presenting as cervical extradural lesion: a case report with review of literature. Neurol India 59:438–442
11. Tian Y, Wang J, Li M et al (2015) Rosai–Dorfman disease involving the central nervous system: seven cases from one institute. Acta Neurochir (Wien) 157(9):1565–1571
12. Ludermann W, Banan R, Samii A et al (2015) Cerebral Rosai–Dorfman disease. Childs Nerv Syst 31(4):529–532
13. Patwardhan PP, Goel NA (2018) Isolated intraventricular Rosai–Dorman disease. Asian J Neurosurg 13(4):1285–1287
14. Zaveri J, La Q, Yarmish G et al (2014) More than just Langerhans cell histiocytosis: a radiologic review of histiocytic disorders. Radiographics 34(7):2008–2024
15. Joshi SS, Joshi S, Muzumdar G et al (2019) Cranio-spinal Rosai Dorfman disease: case series and literature review. Br J Neurosurg 33(2):176–183
16. Liu L, Perry AM, Cao W et al (2013) Relationship between Rosai–Dorfman disease and IgG4-related disease: study of 32 cases. Am J Clin Pathol 140(3):395–402
17. Varrassi M, Gianneramo C, Arrigoni F et al (2018) Neurological involvement of IgG4-related disease: description of a case and review of the literature. Neuroradiol J 31(2):196–202
18. Morgan NV, Morris MR, Cangul H et al (2010) Mutations in SLC29A3, encoding an equilibrative nucleoside transporter ENT3, cause a familiar histiocytosis syndrome (*Faisalabad histiocytosis*) and familiar Rosai–Dorfman disease. PLoS Genet 6(2):e1000833
19. Huang BY, Zhang H, Zong WJ et al (2016) Rosai–Dorfman disease of rare isolated spinal involvement: report of 4 cases and literature review. World Neurosurg 85:367.e11
20. Tu J, Li WT, Yang C (2017) Rosai–Dorfman disease of the subdural spine with a long segment lesion: a case report and literature review. J Int Med Res 45(2):875–881
21. Dalia S, Sagatys E, Sokol L et al (2014) Rosai–Dorfman disease: tumor biology, clinical features, pathology, and treatment. Cancer Control 21(4):322–327
22. Konishi E, Ibayashi N, Yamamoto S, Scheithauer BW (2003) Isolated intracranial Rosai–Dorfman disease (sinus histiocytosis with massive lymphadenopathy). Am J Neuroradiol 24:515–518
23. Sundaram C, Uppin SG, Prasad BC et al (2005) Isolated Rosai Dorfman disease of the central nervous system presenting as dural-based and intraparenchymal lesions. Clin Neuropathol 24:112–117
24. Kinoshita Y, Yasukouchi H, Tsuru E et al (2004) Case report of Rosai–Dorfman disease mimicking pachymeningitis. Neurol Surg 32:1051–1056
25. Hong CS, Starke RM, Hays MA et al (2016) Redefining the prevalence of dural involvement in Rosai–Dorfman disease of the central nervous system. World Neurosurg 90:702.e13–702.e20
26. Wen JH, Wang C, Jin YY et al (2019) Radiological and clinical findings of isolated meningeal Rosai–Dorfman disease of the central nervous system. Medicine (Baltimore) 98(19):e15365
27. Zhang S, Huang J, Chen Y (2018) Primary isolated intracranial Rosai–Dorfman disease: report of a case and review of the literature. Neurol Neurochir Pol 52(3):390–393
28. Idir I, Cuvinciuc V, Uro-Coste E et al (2011) MR perfusion of intracranial Rosai–Dorfman disease mimicking meningioma. J Neuoradiol 38(2):133–134
29. Mariniello G, Bruganti F, De Caro ML et al (2012) Cervical extradural "en-plaque" meningioma. J Neurol Surg A Cent Eur Neurosurg 73(5):330–333
30. Le Guenno G, Galicier L, Uro-Coste E et al (2012) Successful treatment with azathioprine of relapsing Rosai–Dorfman disease of the central nervous system. J Neurosurg 117(3):486–489
31. Cooper SL, Jenrette JM (2012) Rosai–Dorfman disease: management of CNS and systemic involvement. Clin Adv Hematol Oncol 10(3):199–202
32. Arnao V, Riolo M, Savettieri G et al (2016) Mercaptopurine treatment in an adult man with orbital and intracranial Rosai–Dorfman disease. Case Rep Neurol Med 2016:1030478