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CASE REPORT

Pregnancy in a Rare Case of Intracranial Rosai Dorfman Disease (RDD)

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Introduction

Rosai–Dorfman disease (RDD) is an uncommon benign idiopathic lymphoproliferative disorder. While RDD most commonly affects lymph nodes, extra nodal involvement of multiple organs has been reported including the CNS. Pregnancy following chemotherapy for RDD is rather remote. Exacerbation of RDD during pregnancy and the need to resort to radiotherapy using cyber knife due to aggravation of symptoms and remarkable recovery thereafter are highlighted in this case report.

Case Report

A 38 year-old-gravida 1 married for 12 years, nonconsanguineous marriage with history of two failed cycles of invitro fertilization (IVF) 2 years ago, gave history of being diagnosed with extra nodal Rosai–Dorfman disease (RDD) and having undergone six cycles of chemotherapy with cyclophosphamide 1300 mg, Vinblastine 10 mg and prednisolone 2 months prior to diagnosis of pregnancy. Patient gave history of polycystic ovarian syndrome with irregular cycles previously. She underwent a diagnostic hysterolaparoscopy during workup for infertility prior to the IVF cycles. Patient had menstrual cycle one month following the last chemotherapy after which she had amenorrhea. She was not on any contraception and had given up hopes of having a baby. Ultrasound revealed a single live intrauterine pregnancy of 7 weeks gestation. Patient continued the pregnancy despite the risk of teratogenicity.

History of RDD

Patient first presented to the neurosurgeon with complaints of feeling unsteady while walking which worsened with movement of head for a duration of 2–3 months. She had headache and nasal block since one month, Neurological examination revealed horizontal gaze dependent nystagmus bilaterally, decreased hearing in the left ear and tandem ataxia. MRI of head and neck showed left petroclival meningioma with compression of brain stem. Large mass lesion in right maxilla, ethmoid, sphenoid sinuses with extension to right orbit and enlarged upper cervical lymph nodes. A differential diagnosis of meningioma/lymphoma/Wegeners Granulomatosis/fungal infection was made. Biopsy of paranasal sinus lesion was advised. Patient underwent Septoplasty with right inferior turbinectomy with FESS (functional endoscopic sinus surgery) and biopsy under GA. Histopathology from the lesional tissue revealed dense inflammatory infiltrates with histiocytes showing features of Emperipolesis (the presence of an intact cell within the cytoplasm of another cell) and on immunohistochemistry the histiocytes were positive for S100 and CD 68. Morphology and immunohistochemistry features confirmed the diagnosis of RDD (Fig. 1).

PET CT scan showed metabolically active lesions in the paranasal sinuses, nasal cavity, spleen, manubrium sternum and cervical lymph nodes. Metabolically active lesions in the brain -extra axial, infratentorial lesion was noted on the right side, extending to the cerebellopontine angle measuring

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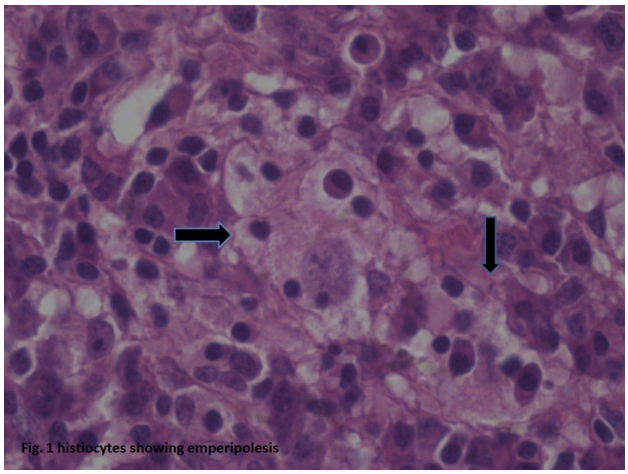

Fig. 1 Histiocytes showing emperipolesis

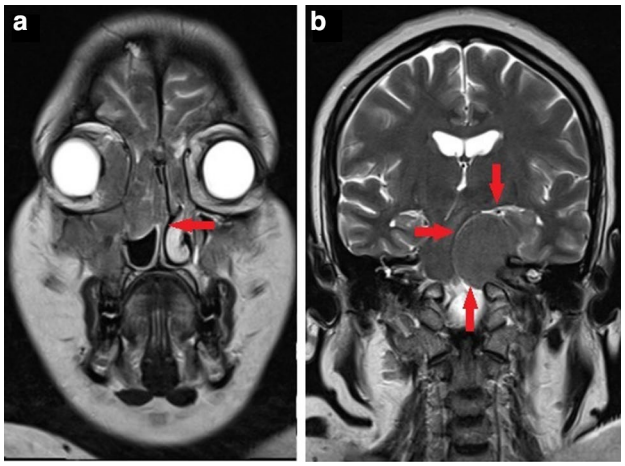

Fig. 2 **a** Cornal T2W image showing right sinonasal and orbital mass lesion. **b** Cornal T2W image showing extradural hypointense mass lesion in left CP angle

45 × 34 mm compressing the cerebellum and pons, 4th ventricle was effaced with no midline shift.

Chemotherapy was started on patient (CVblP regime along with premedication and adequate hydration). Repeat PET CT after four cycles of chemotherapy showed partial decrease in the size of lesions. In view of partial response to the therapy, patient was advised two more cycles of chemotherapy three weeks apart.

At the time of booking visit patient had a BMI of 34.5, hemoglobin of 9.8 gm%. Patient was started on folic acid, 1st trimester screening showed low risk for trisomy 21, 13 and 18. However the uterine artery Doppler showed a mean PI of 1.7 which is considered to be screen positive for PIH as a result of which patient was started on Tab. Ecosprin 150 mg at night. Anomaly scan done at 19 weeks and a late anomaly scan done at 26 weeks, both revealed mild left hydronephrosis. Patient had developed GDM by 24 weeks and was started on Insulin. Patient had difficulty in balancing herself in the upright position and found it difficult to walk without support. Hence MRI was done at 23 weeks gestation which showed a marginal increase in the size of the intracranial lesion as compared to the PET CT done after the 4th cycle of chemotherapy (Fig. 2). Patient was administered prophylactic steroids for fetal lung maturity at 32 weeks on an inpatient basis as she required blood sugar monitoring. Serial interval growth scans done showed adequate growth of the baby and elevated PI of umbilical artery (PI 1.2). The patient's total weight gain was 8 kgs (BMI was 40.3 @ 37 weeks). As her symptoms worsened, decision for elective LSCS under GA was taken at 37 weeks. Spinal anesthesia was contraindicated due to increased intracranial pressure and risk of herniation of brainstem.

Elective LSCS was done at 37 + 1 week gestation under GA, a live male baby weighing 2.69 kg was delivered. Baby had imperforated anus, atrial septal defect (ASD) and PUJ obstruction on the left side. Pediatric surgeon was involved and baby underwent colostomy on the 1st neonatal day. Patient had delay in the initiation of lactation but by day 4 of the postnatal period lactation was initiated. Two and half months after delivery patient was admitted for supportive care with antiedema measures as she developed diplopia, right sided peri-orbital edema and imbalance while walking. She was advised stereotactic body radiation therapy by the medical oncologist. Patient received radical radiation with cyber knife stereotactic radiation therapy at dose of 20 Gy in five fractions to the residual disease in the right orbital cavity and left CP angle lesion with supportive antiedema medication over five days. Patient was advised repeat MRI and PET CT after 3 months to evaluate response to treatment. Post radiation therapy, patient is symptomatically better, there is reduction in cerebellar signs, proptosis and diplopia.

Discussion

RDD is a rare histiocytic disorder and was first described by Rosai and Dorfman in 1969. It was termed as Sinus histiocytosis with massive lymphadenopathy (SHML). It usually presents with bilateral painless cervical lymphadenopathy, fever, night sweats and weight loss. 43% of cases have extra nodal involvement with lesions occurring in the skin, soft tissue, upper respiratory tract, bone, eyes and retro orbital tissue. In 22% of cases there is head and neck involvement with nasal cavity being affected more frequently followed by parotid gland [1], Intracranial RDD is rare and is not well characterized [2].

Characteristic histopathology features are histiocytes showing emperipolesis and immunohistochemistry showed

histiocytes positive for S100 and CD 68 and negative for CD1a [3].

Clinical course of RDD is unpredictable with episodes of exacerbation and remission that could last many years. The causes of RDD are not fully understood and treatment strategies can differ according to severity or vital organ involvement [1].

Impact of the Disease on Pregnancy

Though the disease has no direct impact on pregnancy, the chemotherapy received immediately preceding the pregnancy had left its marks on the baby in the form of imperforate anus, ASD (atrial septal defect), left PUJ obstruction (pelviuretero junction). Cyclophosphamide also causes follicular and oocyte depletion leading to high rates of ovarian failure. In studies on mice, cyclophosphamide has shown to be mutagenic to preovulatory oocytes.

Mice oocytes exposed to vinblastine before the first meiotic division lead to aneuploidy.. The mechanism of action of alkylating agents like cyclophosphamide is by cross-linking DNA strands, interruption of RNA and protein synthesis and affecting the cell cycle non-specifically. Vinca alkaloids (Vinblastine) bind tubulin and cause dissociation of the microtubule apparatus. They act on G1 and S phase of cell cycle only [4].

Impact of Pregnancy on RDD

There was worsening of patient's symptoms with severe imbalance and diplopia as pregnancy progressed. A repeat MRI during the pregnancy showed increase in the size of CNS lesions as compared to the imaging done after four cycles of chemotherapy. Patient could not do simple exercises like walking to help control her blood sugar as she had ataxia. She had proptosis on the right side and had to undergo an elective LSCS under GA at 37 weeks as spinal anesthesia was contraindicated in her case. Meenu Gill et al. reported a case of RDD with bilateral massive cervical swelling in a 22-year-old pregnant woman. The swelling of the cervical lymph nodes progressively increased in size after the onset of pregnancy. FNAC diagnosed RDD [5].

Raychaudhuri et al. reported a case of intracranial RDD in pregnancy where the patient complained of headache and was diagnosed to have a large parafalcine mass following her second delivery. Patient underwent neurosurgery and excision of the lesion. Histopathology clinched the diagnosis of RDD [6].

Conclusion

There is worsening of the condition during pregnancy as seen in our case and also that reported by Meenu Gill et al. Managing pregnancy in this case was challenging as counselling about teratogenicity and decision to either terminate/continue pregnancy was crucial. Symptomatic treatment, managing blood sugars and timing of delivery with right choice of anesthesia and multidisciplinary approach all lead to a successful outcome.

Compliance with Ethical Standards

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this paper and they have not received any grant.

Informed Consent Informed consent was obtained from the patient for presentation of the case report.

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