 DOI: 10.18231/2455-8478.2017.0040

Metastatic retinoblastoma presenting as abdominal mass

S Chandrasekhara Reddy[1,*], S. Banerjee[2], Y. Radhakrishnaiah[3], T. Srinivasa Rao[4]

[1]Dept. of Ophthalmology, [2]Dept. of Pathology, [3]Dept. of Radiotherapy, [4]Dept. of Surgery, Rangaraya Medical College & Govt. General Hospital, Kakinada, Andhra Pradesh

***Corresponding Author:**
Email: profscreddy@gmail.com

Abstract

A 5-year-old girl was diagnosed as a case of retinoblastoma in the left eye and enucleation was done. There was recurrence of the tumour in the orbit for which radiotherapy was given; and the tumour resolved completely. Fifteen months after the completion of radiotherapy, she presented with abdominal mass. The mass was removed from retro uterine space by laparotomy; and the biopsy report was consistent with retinoblastoma. After comparing with the histological findings of the enucleated eyeball slide, it was confirmed as metastatic retinoblastoma in the retro uterine space. She was given chemotherapy since there was slight widening of mediastinum and mild pleural effusion on the right side, which subsided after chemotherapy. This case is reported in view of rare occurrence of secondary in the abdomen in a child with retinoblastoma.

Keywords: Retinoblastoma, Enucleation, Radiotherapy, Chemotherapy, Distant metastasis.

Introduction

Retinoblastoma is the most common primary intraocular malignancy of childhood and accounts for about 3% of all childhood cancers. The average age of presentation is within the first year of life in bilateral cases and around 2 years of age in unilateral patients. Leukocoria (white pupillary reflex) is the most common presentation (60%), followed by strabismus (20%); the others being painful red eye with secondary glaucoma, poor vision, orbital inflammation mimicking orbital cellulitis, anterior uveitis with pseudohypopyon, and proptosis due to extension of tumour into orbital. Fundus examination shows an intra retinal tumour, a homogeneous, white lesion that becomes irregular or projects into the vitreous as white mass, with vascularization (endophytic tumour), or multilobular subretinal white masses causing retinal detachment (exophytic tumour).[(1)]

Investigations like ultrasonography B-scan, plane X-rays orbits, CT scan orbits and brain will show the extent of tumour mass within the eye, calcification and extension of tumour into the orbit and brain. Preauricular lymphadenopathy, submandibular and cervical lymphadenopathy; presence of malignant cells in cerebrospinal fluid after doing lumbar puncture, and in bone marrow aspirate will indicate distant spread (metastasis) of the tumour.[(1)]

It is not uncommon to see distant metastasis in advanced cases of retinoblastoma at the time of disgnosis. However, retinoblastoma occurring at a different site after few months/years of primary treatment is very rare, and only few such cases are reported in the literature.[(2-6)] Only two cases of metastatic retinoblastoma in the liver has been reported earlier by Cullen et al.[(2)] To the best of our knowledge, we report the first case of metastasis in the abdomen (retro uterine space) in a child with retinoblastoma who presented with abdominal mass after fifteen months of post enucleation radiotherapy to the left orbit.

Case Report

A 5-year-old girl came to the eye clinic with a complaint of swelling, redness and pain in the left eye of one week duration. There was no history of trauma to the eye. She was given some eye drops by a local general practitioner, which did not relieve the symptoms. On examination, right eye vision was 6/6; anterior segment, and fundus were normal. Left eye showed vision of hand movements. There was edema of both eyelids with chemosis of conjunctiva. Cornea, anterior chamber and iris were normal. Pupil was slightly dilated and sluggishly reacting to light. There was a white reflex in the pupillary area. Lens was normal. Ocular movements were normal. Intraocular pressure (IOP) with Tonopen was 28 mmHg in left eye and 18 mm Hg in right eye. The diagnosis of retinoblastoma with secondary glaucoma in the left eye was made and the parents were explained about the condition of left eye. The child was admitted in the hospital for further investigations and treatment. The child was treated with Timolol eye drops bid, Homatropine eye drops bid, Dorzolamide eye drops tid, and Dexamethasone eye drops tid in the left eye. The congestion and edema of conjunctiva became less after three days.

X-ray of orbits and X-ray of optic foramen were normal on both sides. X-ray chest was normal. CT scan orbits and brain was not done due to lack of facilities in the hospital. Examination under general anaesthesia showed normal corneal diameter, IOP 26 mmHg. Dilated pupils fundus examination showed a white tumour mass on the temporal side of the optic disc near the macula, protruding into the vitreous. Since the patient was under anaesthesia, bone marrow aspiration and lumbar puncture were also performed; and the specimens were sent for malignant cells. There were no malignant cells

in cerebrospinal fluid and bone marrow. The diagnosis of retinoblastoma was conformed without any distant metastasis.

Parents were explained that the child has cancer in the left eye and the treatment is removal of the eyeball. However, parents did not agree for operation and wanted to discuss at home with relatives. The child was discharged on the same treatment in left eye.

Parents brought the child to the hospital after two weeks for operation. Enucleation of left eye was done under general anaesthesia and the eyeball was sent for histopathology which showed poorly differentiated retinoblastoma with massive areas of necrosis. Cut end of optic nerve was free of malignant cells. The conjunctival wound healed well and the child was discharged after one week. However, during the follow up after three weeks, parents complained of fullness in the left eye for the past five days. Examination of left eye showed fullness of the left socket with an uneven surface (Fig. 1A). Under topical anaesthesia, a small, lobulated, hard mass was felt in the left orbit.

The child was referred to radiotherapy department for further treatment of the recurrence of tumour in the left orbit. The Cobalt- 60 external beam radiation therapy (200 cGy per day for 5 days in a week) was given over a period of four weeks (total 4000 cGy). The child was followed up once in three months. The mass in the orbit regressed completely and the socket was hollow in the left eye (Fig. 1B) and there was no recurrence of the tumour during the follow up visits.

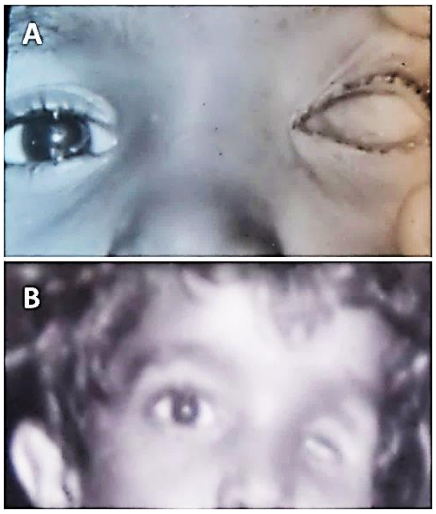

Fig. 1: Showing (A) post enucleation recurrence of tumour in the left orbit, and (B) empty socket in the left orbit (three months after radiotherapy)

Fifteen months after the completion of radiotherapy, the child presented with complaint of a mass in the lower abdomen and loss of appetite of two weeks duration. She was referred to surgery department. On examination, diffuse, mobile, intra-abdominal mass of 6 x 4 cm size was noted in the suprapubic region. Liver and spleen were not palpable. Surgeon has advised removal of the mass in the abdomen.

Full blood counts examination showed normal values. X-ray chest showed normal lungs on both sides, with minimal plural effusion on the right side. X-ray skull, and spine were normal. X-ray abdomen showed a mass in the lower abdomen. Since the CT scan facilities were not available in the hospital; and the parents could not afford financially to go to state headquarters for this investigation, CT scan orbits and brain was not done. The child was transferred to surgical ward. Explorative laparotomy was performed under general anaesthesia. A large, vascularized, well encapsulated tumour mass was removed from the retro uterine space (Fig. 2A), and sent for histopathology which showed poorly differentiated malignant cells with focal areas of necrosis (Fig. 2B), suggestive of retinoblastoma. These findings were compared with the histological features of the enucleated eyeball of this child; and the diagnosis was confirmed as secondary from retinoblastoma in the abdomen.

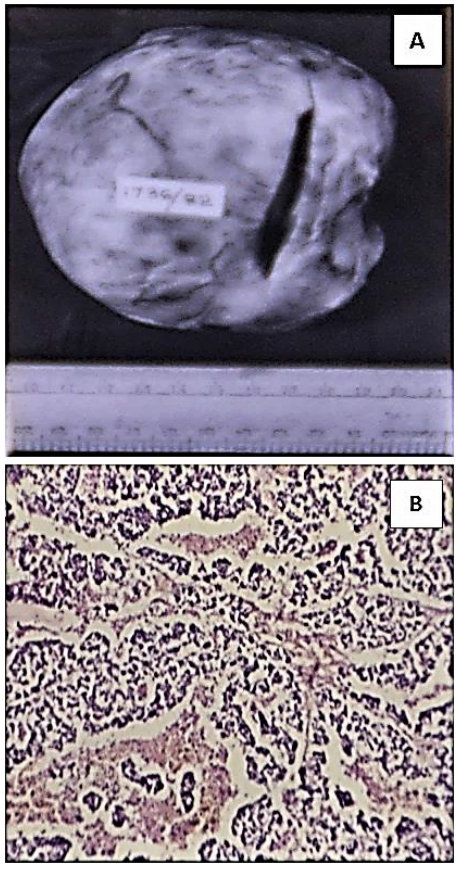

Fig. 2: Showing (A) large tumour mass removed from the abdomen (9 x 8 cm size) with a vertical incision area from where tissue was taken for histopathology, (B) nest/groups of poorly differentiated malignant cells and focal areas of necrosis, H & E stain, x 100

Post operative period was uneventful and the abdominal wound healed well. The patient was

transferred back to the eye ward. Since there was mild pleural effusion in the right lung, chemotherapy was given -- Tab. Cyclophosphamide (25 mg daily) and weekly intravenous injections of Mitomycin C (2 mg) for one month. X-ray chest showed complete resolution of plural effusion. The child was discharged from the hospital and oral cyclophosphamide was continued. There was no recurrence of the tumour in the orbit or in the abdomen during the follow up of next three months. Unfortunately, the child defaulted further follow up. On telephonic enquiry, father told that few days before the follow up date the child collapsed in the house suddenly and died.

Discussion

Distant metastasis occurs by (a) lymphatic spread to preauricular and cervical lymph nodes, (b) extension by continuity to optic nerve and brain, and (c) by haematogenous spread via choroid to the lungs, brain, cranial and other bones. Metastasis to other organs like liver is usually rare.[7]

The signs of inflammation (swelling of the eyelids, chemosis of the conjunctiva) at presentation in this child suggest the possibility of tumour necrosis in a patient of retinoblastoma; and it was confirmed by the presence of many areas of necrosis in the histopathology of the enucleated eyeball. The recurrence of tumour in the orbit (three weeks after enucleation) could probably be due to blood spread through choroid into the orbit because malignant cells were not seen at the cut end of the optic nerve histologically. The tumour regressed completely following radiotherapy to the left orbit without any recurrence. After a long period of orbital radiotherapy (fifteen months later), occurrence of mass in the abdomen and presence of minimal pleaural effusion in the right lung indicate the possibility of blood spread of retinoblastoma in this child. The histological findings of the abdominal mass removed were similar to that of the enucleated eyeball of this child, which confirmed the mass was secondary in the abdomen. Our patient was treated with the chemotherapy drugs available in the hospital. The complete resolution of pleaural effusion after chemotherapy supports the haematogenous route of spread of the tumour in this child.

Dunkel et al[2] from USA reported four cases of metastatic retinoblastoma (without any metastasis at the time of diagnosis) in four cases. The time from diagnosis to metastasis was 4 months in a 44-year-old male patient, 5 months in a 33-year-old female patrient, 3 months in a 28-year-old male patient, and 5 months in a 17-year-old female patient. The site of metastases was in bone marrow, base of skull in the first patient; bone marrow, bone, orbit, liver in the second patient; bone marrow, orbit, liver in the third patient; and bone marrow, bone, orbit in the fourth patient. The diagnosis was made after MRI and CT scan investigations.

Moshfeghi et al[3] from USA reported a 3-year-old girl with retinoblastoma in the right eye. Two years after enucleation she developed metastases in bone marrow, right humerus, and both supraorbital bones which was treated with chemotherapy, orbital irradiation and bone marrow transplantation. Seven months later presented with back pain and urinary retention. A right ovarian mass was removed by laparotomy which showed metastatic retinoblastoma. She was given chemotherapy and was a symptomatic for 9 months. She died due to brain stem metastasis.

Taguchi et al[4] from Japan reported a 4-year-old boy whose left eye was enucleated for retinoblastoma. Histopathology showed tumour cells invading the sclera but not the cut end of the optic nerve. Ten months later, the child was brought with painless swelling in the left side of face. A soft swelling in the left lower gingiva with ulceration was present. The diagnosis was confirmed with CT scan, MRI, biopsy histopathology and immunohistochemistry. New metastases were observed in the left elbow and bone marrow 12 months later. Patient died 19 months later with extensive tumour metastasis despite additional chemotherapy.

In a retrospective study of retinoblastoma cases diagnosed over 20 year period, Cozza et al[5] from Italy reported four cases of metastatic retinoblastoma in orbit, cerebrospinal fluid (CSF), meningeal (6 months from diagnosis); CSF, meningeal (12 months from diagnosis); pineal gland (15 months from diagnosis); and orbit, bone, bone marrow (6 months from diagnosis).

Castelino-Prabhu et al[6] from USA reported a case of metastatic retinoblastoma presenting as a left shoulder soft tissue mass in a 14-year-old female with a history of familial bilateral retinoblastomastatus post radiation therapy. Fine needle aspiration cytology showed some features of inconspicuous Flexner-Wintersteiner or homer-Right rosette formation. They have stated that metastasis to the soft tissue is very rare.

In a retrospective study of 80 cases of retinoblastoma with no evidence of metastasis at diagnosis and presence of high-risk characteristics for metastasis on histopathology reports (anterior chamber seeding, iris infiltration, ciliary body infiltration, massive choroidal infiltration, invasion of optic nerve lamina cribrosa, retrolaminar optic nerve invasion, invasion of optic nerve transection, scleral infiltration, and extrascleral extension) Honavar et al[8] reported that postenucleation adjunct therapy is effective in significantly reducing the occurrence of metastasis.

In general, prognosis is poor in patients with metastatic retinoblastoma when conventional treatment is given,[9] while a multidisciplinary treatment that includes high dosage chemotherapy may improve the outcome.[2,10] In addition to high dose chemotherapy with carboplatin, thiotepa, with epitoside Dunkel et al[2] have given autologous stem cell rescue therapy and radiation therapy in four patients with metastatic retinoblastoma and all of them survived for 46-80 months from the time of diagnosis of metastasis.

Conclusion

Retinoblastoma, the most common intraocular malignant tumour in children, can remain within the eye or can spread into the orbit, cranium, and other parts of the body (lymph glands, bones, lungs, liver). The spread can be detected by ultrasonography, CT scan, MRI, cerebrospinal fluid examination after lumbar puncture and bone marrow aspirate. A rare case of retinoblastoma metastasis in the abdomen, most probably due to haematogenous spread, is reported.

Conflicts of interest: There are no conflicts of interest for all authors.

References

1. Bowling B. Kanski's clinical ophthalmology. A systematic approach. 8th ed. Elsevier Ltd, 2016. p 499-502.
2. Dunkel IJ, Aledo A, Kernan NA, et al. Successful treatment of metastatic retinoblastoma. Cancer 2000;89:2117-21.
3. Moshfeghi DM, Wilson MW, Haik BG, et al. Retinoblastoma metastatic to the ovary in a patient with Waardenburg syndrome. Am J Ophthalmol 2002;133:716-8.
4. Taguchi A, Suei Y, Ogawa I, et al. Metastatic retinoblastoma of maxilla and mandible. Dentomaxillofacial Radiology 2005;34:126–31.
5. Cozza R, De Ioris MA, Ilari I, et al. Metastatic retinoblastoma: single institution experience over two decades. Br J Ophthalmol 2009;93:1163-6.
6. Castelino-Prabhu S, Stoll LM, Li QK. Metastatic retinoblastoma presenting as a left shoulder soft tissue mass: FNA findings and review of literature. Diagn Cytopathol 2010;38:440-6.
7. Khurana AK. Comprehensive ophthalmology, 4th ed, New Delhi: New age International (P) Ltd, 2007. p 282.
8. Honavar SG, Singh AD, Shields CL, et al. Postenucleation adjunt therapy in high-risk retinoblastoma. Arch Ophthalmol 2002;120:923-31.
9. Chantada G, Fandino A, Casak S, et al. Treatment of overt extraocular retinoblastoma. Med pediatr Oncol 2003;40:158-61.
10. Mastubara H, Makimoto A, Haga T, et al. A multidisciplinary treatment strategy that includes high dosage chemotherapy for metastatic retinoblastoma without CNS involvement. Bone Marrow Transplant 2005;35:763-6.