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Orbital Rhabdomyosarcoma – Clinical Profile and Outcome Following Multimodal Management

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INTRODUCTION

- Rhabdomyosarcoma is the most common soft tissue sarcoma in pediatric population.

- Orbital variant comprises of 25-30% of rhabdomyosarcoma of head and neck region.

Intergroup Rhabdomyosarcoma Study Committee (IRSG)

- Four major trials- I to IV (1972-1991)
- Staging and classification of rhabdomyosarcoma
- Dramatic advances have been made by IRS in the understanding of the behaviour and management of rhabdomyosarcoma.

IRSG Staging

Stage	Description
I	Completely resected localized disease implying both gross resection and microscopic confirmation of complete resection and absence of regional lymph node involvement
II	Residual disease, regional lymph node involvement, or both
III	Incomplete resection with biopsy or gross residual disease at site of origin or in regional lymph nodes
IV	Distant metastasis present at onset

IRSG: IV- Current recommendations for treatment of orbital rhabdomyosarcoma

Stage	Radiation Therapy	Chemotherapy
1	None	VA for 32 weeks (regimen 44, VA)
2	4140 cGy CFI	VA
3	5040 cGy CFI or 5940 cGy HFI	VA +C for 52 weeks (regimen 41 VAC) or VA + I for 52 weeks (regimen 42 VAI) or VI +E for 52 weeks (regimen 43 VIE)

Orbital Rhabdomyosarcoma

	Before IRSG Trials	After IRSG Trials
Modalities of treatment	Orbital exenteration, Chemotherapy	Chemotherapy + Adjuvant Radiotherapy (Avoiding Orbital exenteration)
3 Years survival	**30%**	**93%**

PURPOSE

To study the clinical presentation, histopathological features, and outcome following multimodal management in primary orbital rhabdomyosarcoma.

MATERIALS AND METHODS

- Study design:
  - Retrospective, non-comparative, interventional case series

- Study population:
  - 35 consecutive patients presenting with orbital rhabdomyosarcoma.

- Data was reviewed with respect to:
  - Demographics:
    - Age, gender, laterality
  - Clinical features:
    - Symptoms, duration of symptoms, initial diagnosis
    - Examination: Affected eye, visual acuity, ocular motility, proptosis
    - Data regarding tumor: Referral diagnosis, prior management, tumor location, size, appearance on imaging

- Management:
  - Modalities of tumor management:
    - Surgery, Chemotherapy, Radiotherapy
  - Histopathological analysis
  - Clinical response to treatment
- Outcome measures:
  - Final visual outcome
  - Local tumor control
  - Regional lymph node outcome
  - Systemic outcome

RESULTS

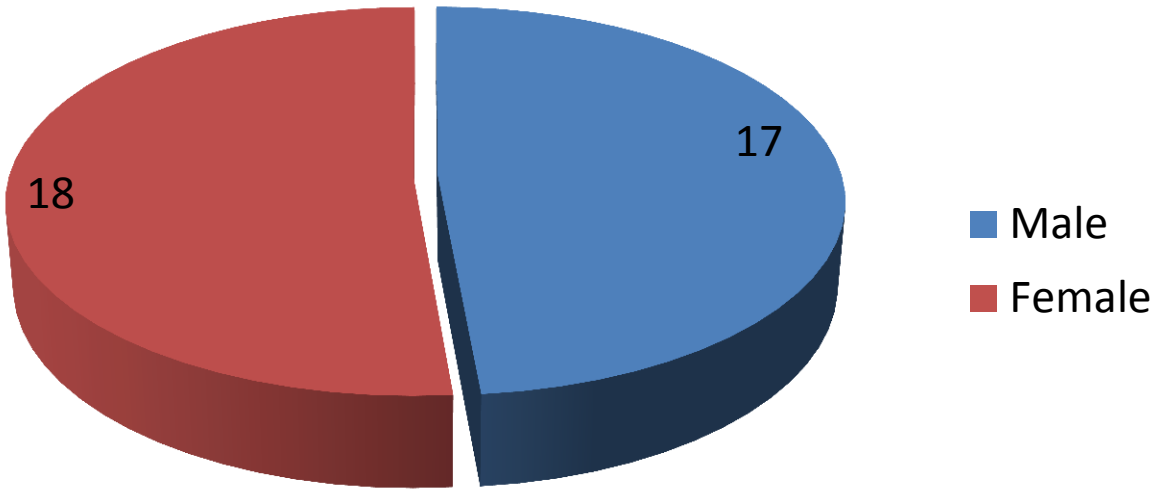
Age distribution (n=35)

Age Group (Years)	Number	Percentage
0-5	12	34%
6-10	9	26%
10-15	11	31%
15-20	2	6%
>20	1	3%

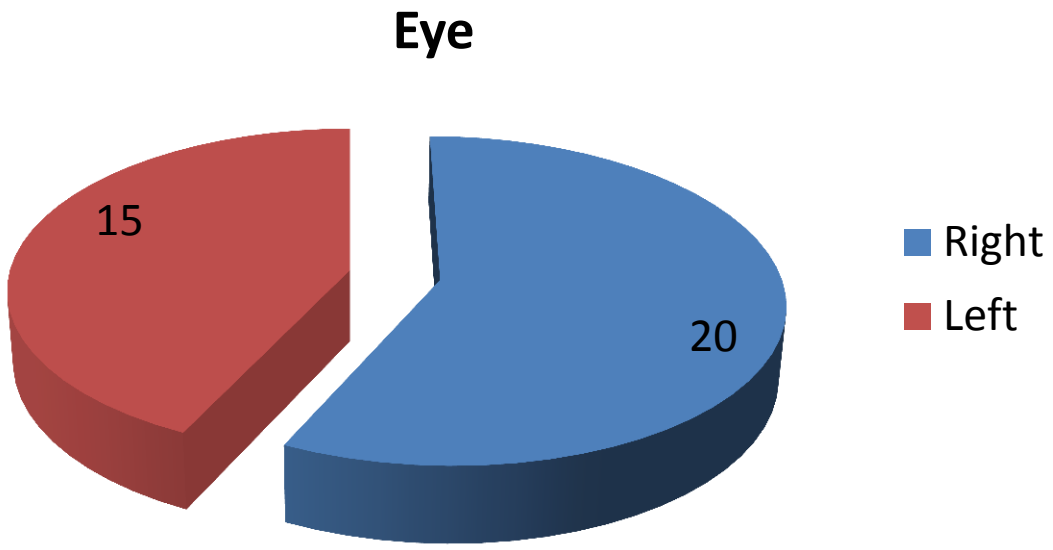
Mean : 9 years

Range: 1 month -40 years

Sex distribution



Laterality: 100% Unilateral



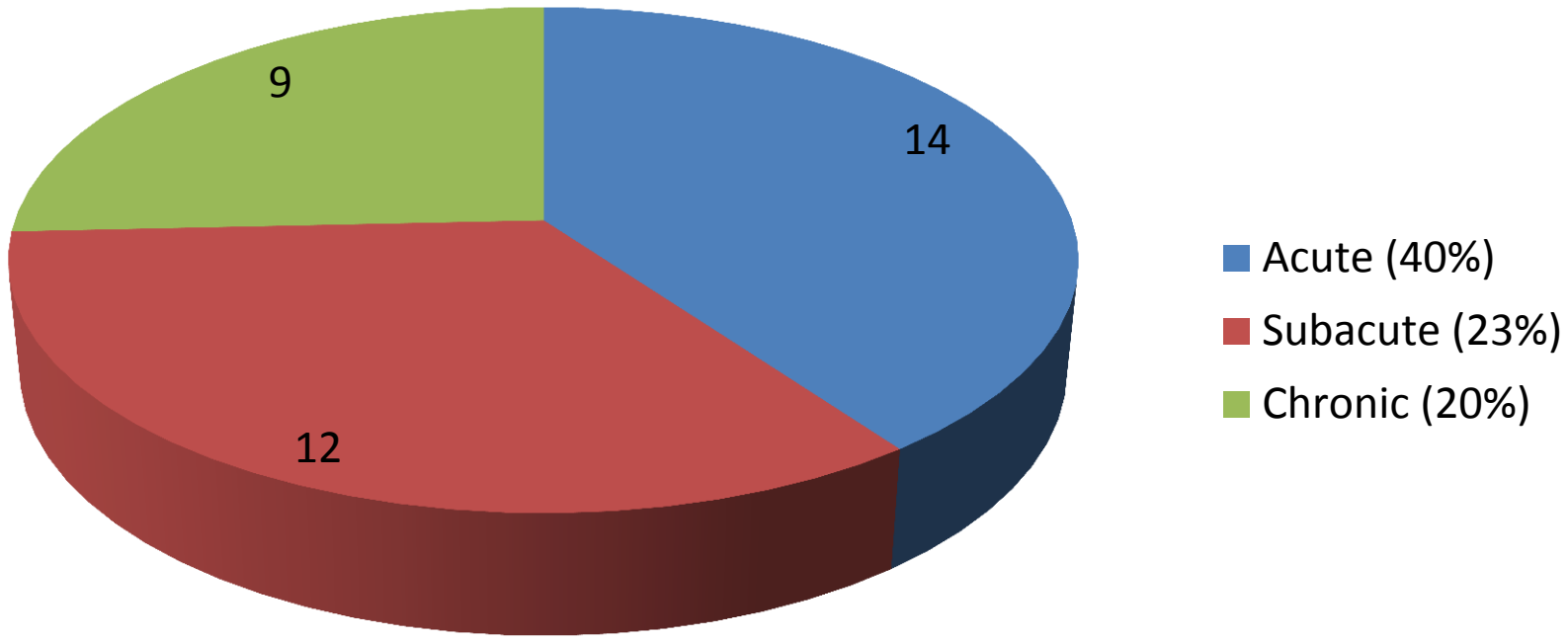
Clinical features at presentation

Symptom	Number	Percentage
Proptosis	18	51%
Palpable orbital mass	13	37%
Pain	6	17%
Diminution of vision	5	14%
Ptosis	2	6%
Diplopia	1	3%

Systemic associations

Associated Illness	Number	Percentage
Other Malignancies 1) Olfactory Neuroblastoma (s/p Maxillectomy) 1) Small cell neuroendocrine carcinoma of nose	1 1	3% 3%
Neurofibromatosis 1	1	3%
Hepatomegaly	1	3%

Onset of symptoms



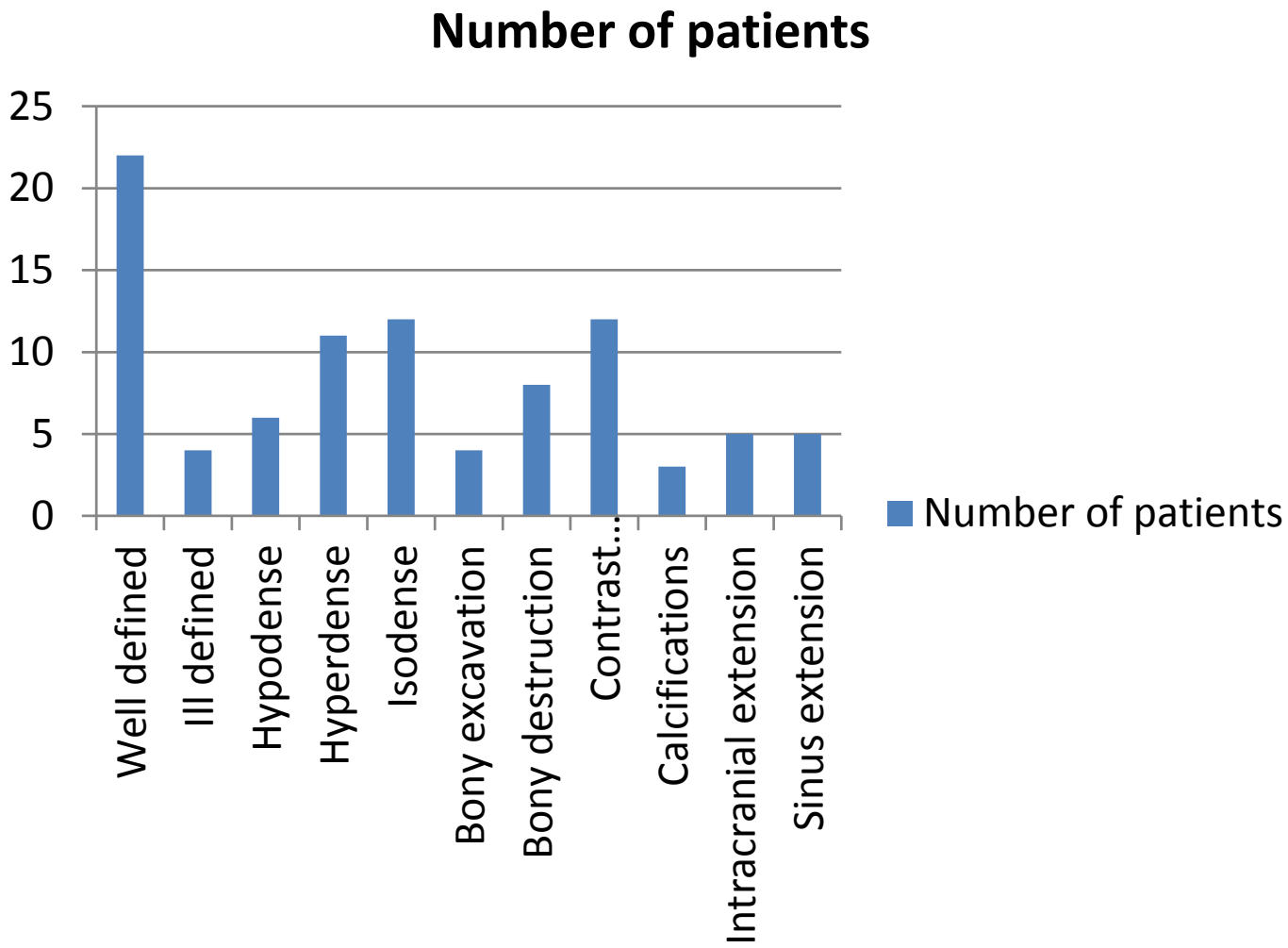
Visual acuity at presentation

Visual acuity	Number	Percentage
20/20 – 20/40	14	40%
20/40 – 20/200	12	34%
<20/200	8	23%
No PL	1	3%

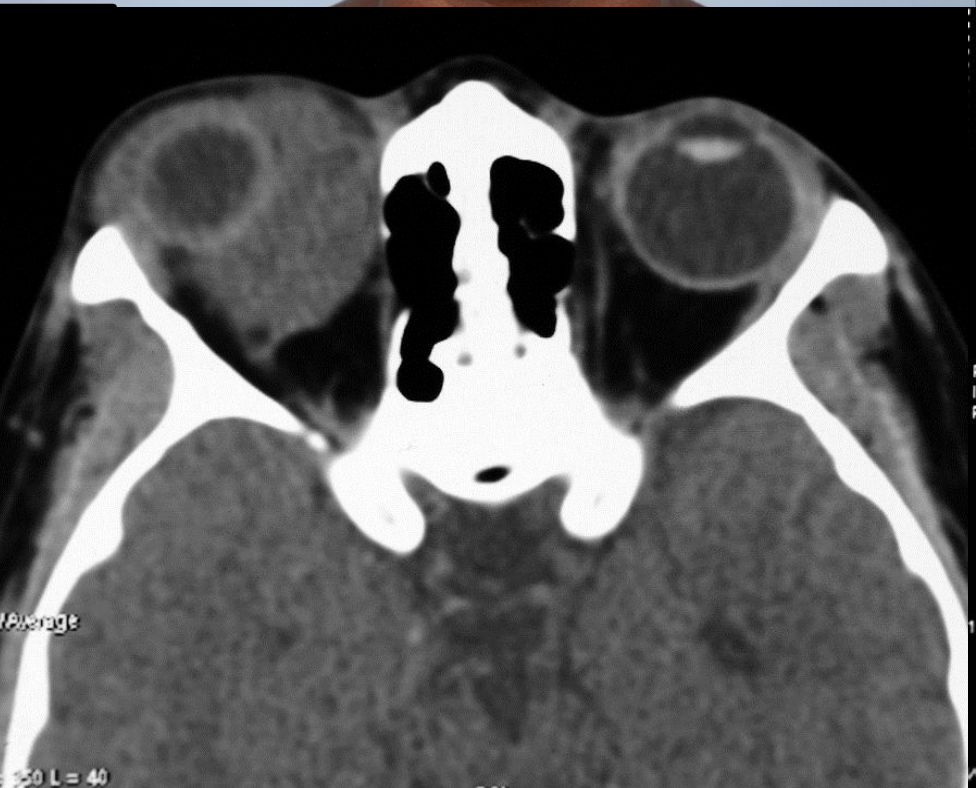
Clinical Signs

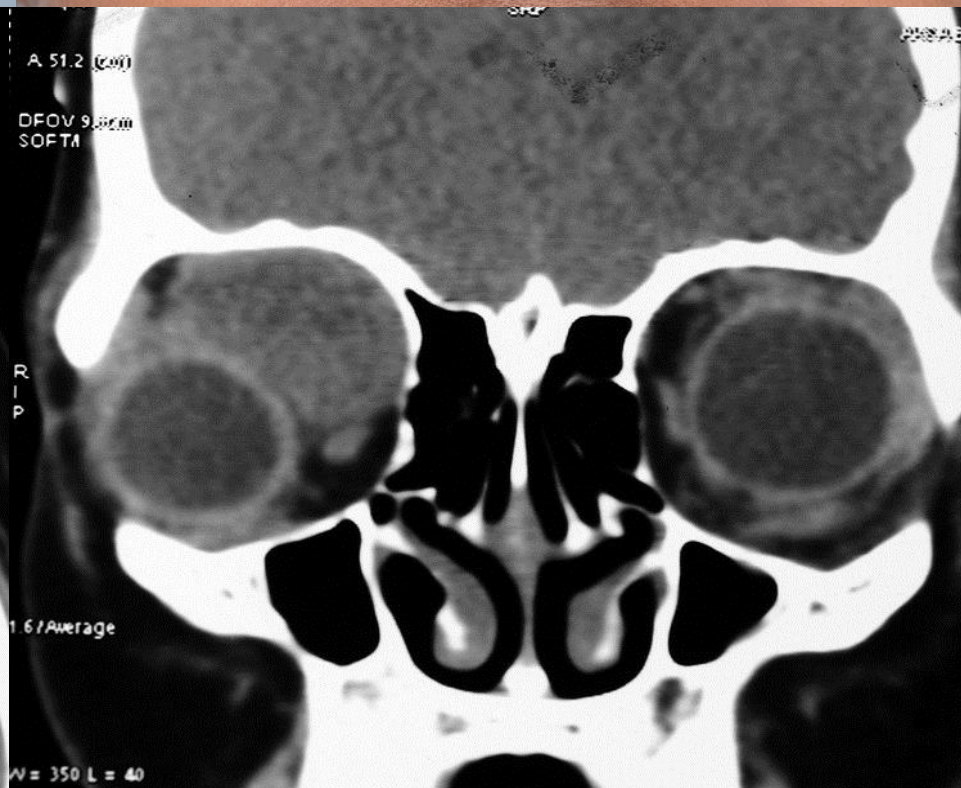
Clinical signs	Number	Percentage
Ocular motility restriction	19	54%
Proptosis	18	51%
Conjunctival congestion	8	23%
RAPD	8	23%
Ptosis	5	14%
Papilledema	5	14%
Corneal exposure	4	11%
Choroidal folds	4	11%
Strabismus	2	6%
Optic atrophy	1	3%

CT scan characteristics



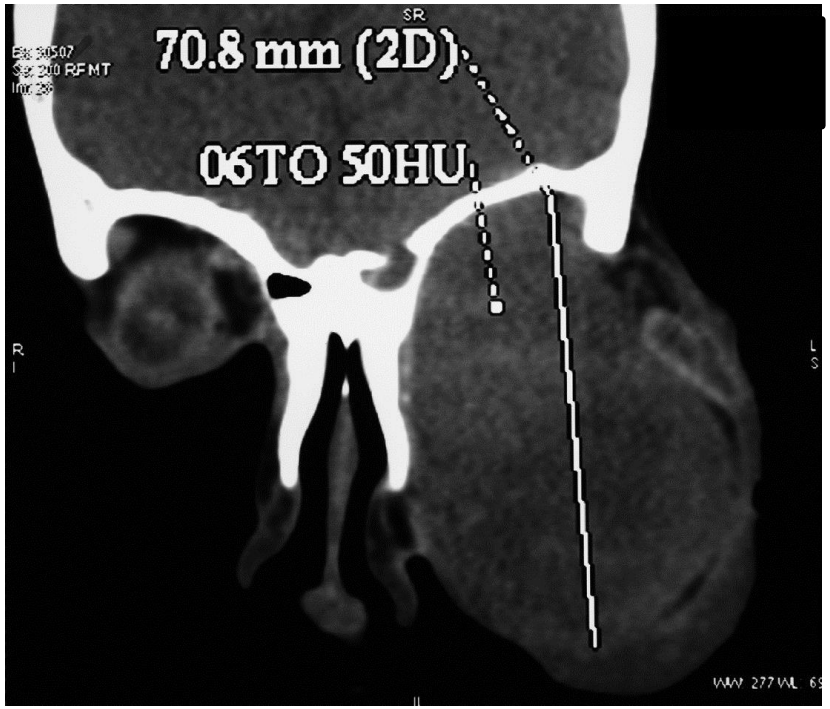
Case 1





Case 2

Case 3



Management

Surgery

- Incisional biopsy
- Debulking
- Excision biopsy

Histological confirmation of diagnosis

Chemotherapy

- 6 Cycles of VAC (A) + IE (B) at 3 weekly interval

Radiotherapy

- Stereotactic radiotherapy sandwiched between 2 sets of 3 cycles of chemotherapy

Chemotherapy

Drug	Dose	Duration
Vincristin	1.5mg/m2	Day 1
Actinomycin D	500µg/m2	Day 1 to day 5
Cyclophosphamide	1250mg/m2	Day 1
Ifosphamide	1500- 2000mg/m2	Day1 to day 5
Etoposide	100mg/m2	Day 1 to day 5

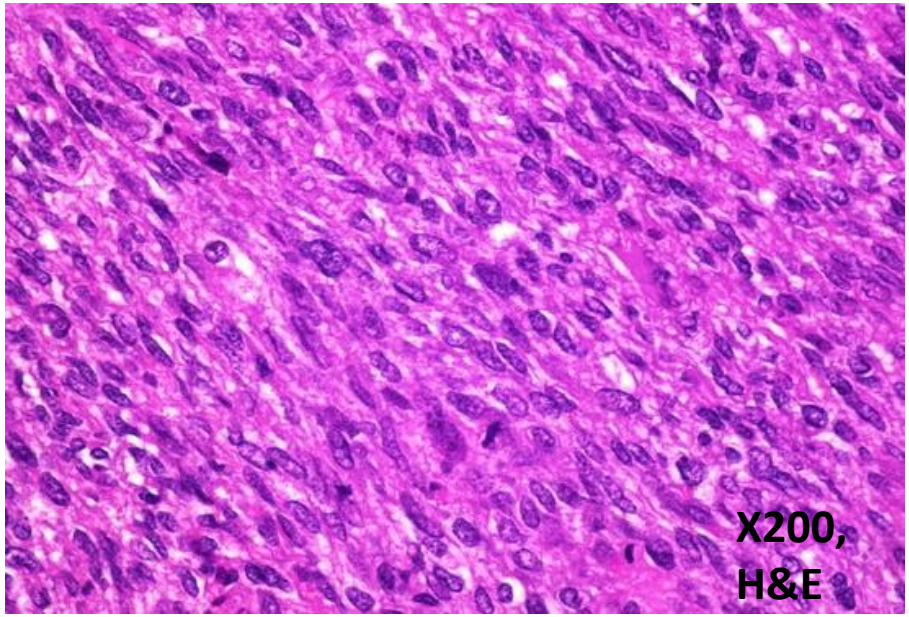
Radiotherapy

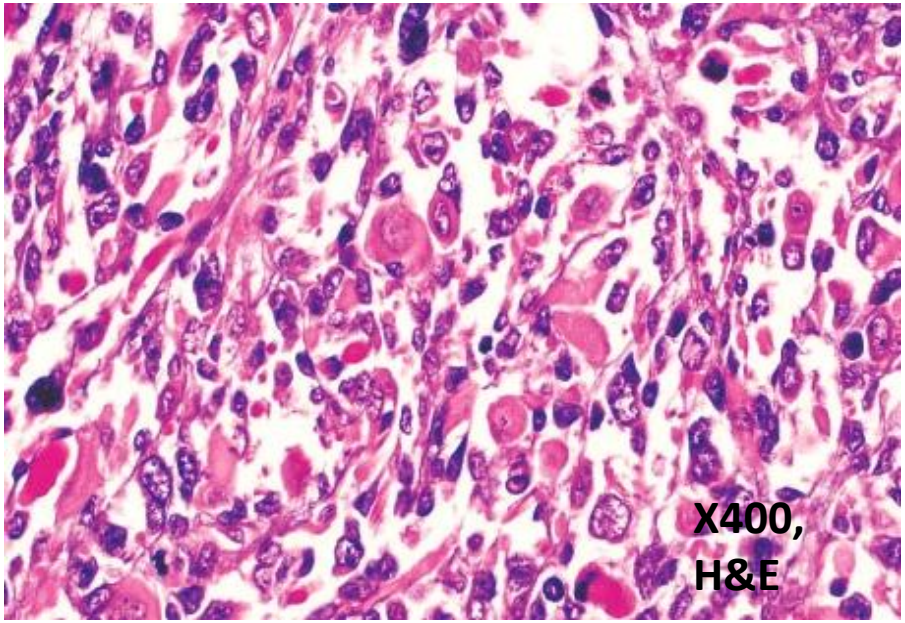
- No residual disease: 4500 cGy to 5000 cGy
- Residual disease: 5000 cGy to 5500 cGy
- Dose rate: @ 180-200 cGy/ fr

Histopathology

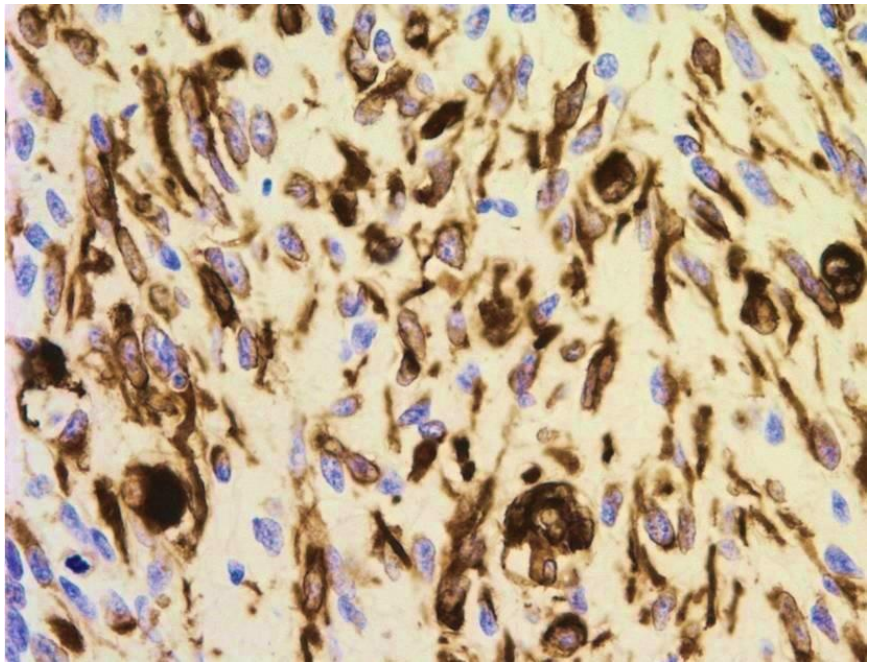
Type	Number	Percentage
Embryonal	20	57%
Alveolar	12	34%
Anaplastic	2	6%
Botryoid	3	3%

Histopathology





Immunohistochemistry



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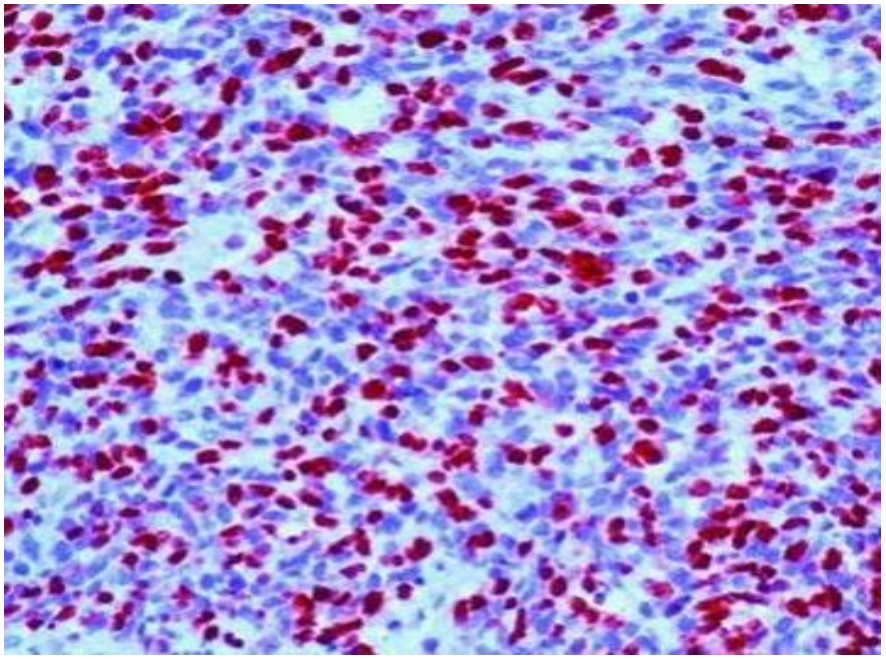


Myogenin

Final visual outcome

Outcome	Number	Percentage
20/20-20/40	12	34%
20/40- 20/200	9	26%
<20/200	14	40%

Local and systemic tumor outcomes

Outcome	Number	Percentage
Local tumor outcome		
Regression	30	86%
Recurrence	5	14%
Regional Lymph node outcome		
No lymph node Metastasis	32	91%
Lymph node metastasis	3	9%
Systemic outcome		
No distant metastasis	34	97%
Distant metastasis	1	3%
Final status		
Alive	34	97%
Dead	1	3%

Complications

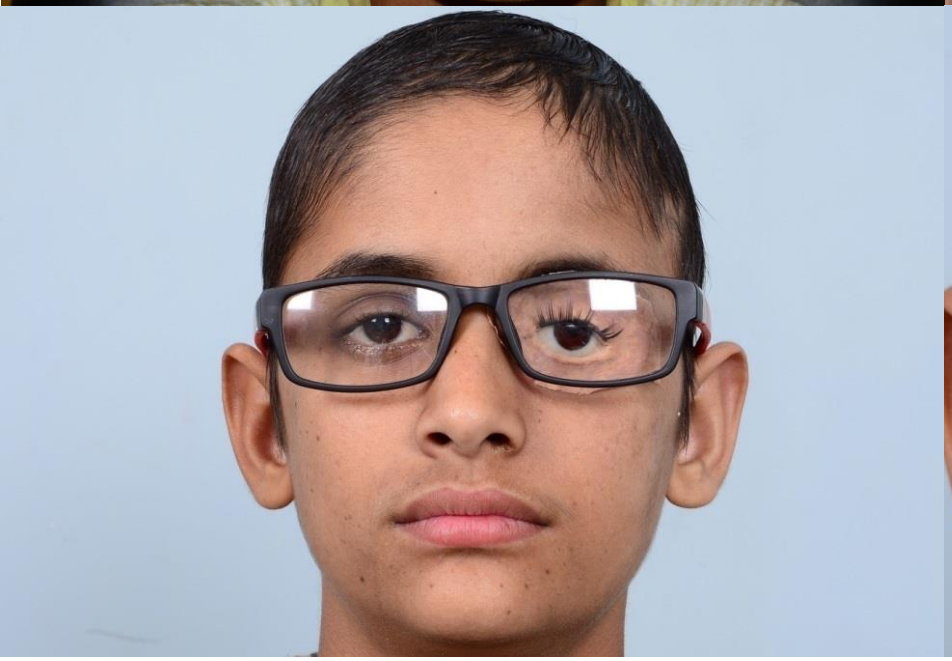
Complication	Number	Percentage
Orbit		
Strabismus	1	3%
Restriction ocular motility	1	3%
Diplopia	1	3%
Eyelid		
Ptosis	1	3%
Ocular surface		
Dry eye	1	3%
Exposure keratopathy	2	3%
Intraocular		
Cataract	1	3%
Optic neuropathy	2	6%
Radiation retinopathy	1	3%


Pre
Post


Pre
Post


Pre


Post



DISCUSSION

- Rhabdomyosarcoma displays a strong tendency for local invasion, local recurrence, and hematogenous and lymphatic metastases
- Treatment protocols involving both chemotherapy and radiotherapy have shown good outcomes.
- Recurrent tumors in the orbit are usually treated with orbital exenteration, supplemented with chemotherapy and radiotherapy as needed.

	IRSG data (n=264)	Shields et al (n=33)	Our study (n=35)
Stages I II III IV	 3% 20% 74% 3%	 12% 36% 48% 3%	 0 0 97% 3%
Rhabdomyosarcoma subtype Embryonal Alveolar Anaplastic Botryoid	 80% 9% 4% 4%	 90% 10% 0 0	 57% 34% 6% 3%
Average follow up	7.5 years	8.3 years	3.3 years
Survival rate	Alveolar: 74% Embryonal 94%	>90%	97%

	Shields et al	Our study
Local tumor outcome		
Regression	85%	86%
Recurrence	18%	14%
Regional Lymph node outcome		
No lymph node Metastasis	94%	91%
Lymph node metastasis	6%	9%
Systemic outcome		
No distant metastasis	94%	97%
Distant metastasis	6%	3%
Final status		
Alive	97%	97%
Dead	3%	3%

- Our study describes the outcomes in cases of advanced rhabdomyosarcoma (IRSG stage III &IV).
- Embryonal being the most common subtype (57%) alveolar subtype was also found in 34%.
- Eye salvage was possible in 33 (94%) of cases.
- Life salvage at the end of mean follow up period of 3.3 years was 97 %.

CONCLUSION

- Orbital rhabdomyosarcoma commonly presents as proptosis in the first or second decade of life.
- Presentation of advanced rhabdomyosarcoma was seen in majority of cases.
- Embryonal followed by alveolar variant was common subtype found in our series.

- Multimodal treatment including initial surgery, followed by multi-drug chemotherapy and stereotactic radiotherapy provides excellent chance of local tumour control (86% primary control, 100% secondary control) and life salvage (97%) in cases of advanced rhabdomyosarcoma.

Thank you!

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