HISTOPATHOLOGIC REVIEW AND PROGNOSTIC FACTORS OF PRIMARILY ENUCLEATED UNILATERAL INTRAOCULAR ADVANCED RETINOBLASTOMA AT NACIONAL CANCER INSTITUTE – BRAZIL

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BACKGROUND / OBJECTIVES

Retinoblastoma(RB) is the most common intraocular malignancy of childhood. In advanced intraocular disease,enucleation is the treatment of choice.Recently a consensus staging system and pathological guidelines were relevant steps to standardize histopathologic factors which can predict relapse risk.The objetive of this study was to review the histopathologic risk factors from primarily enucleated eyes and analyse the overall(OS)/event-free(EFS)survival and prognostic factors in patients with unilateral RB.

METHODS

Retrospective study from primarily enucleated unilateral RB cases at National Cancer Institute-Rio de Janeiro/Brazil,from 1997 to 2015.All eyes were submitted to histopathological review by an expert pathologist describing optic nerve,scleral and choroidal invasions.High-risk intraocular features definition: intrascleral and/or post-laminar optic nerve(PLONI)invasion.Demographic and clinical characteristics and treatment outcomes were obtained from medical charts.

RESULTS

Of 215 patients with RB admitted during this period,138(64%)were unilateral and 70(51%)primarily enucleated.Median age at diagnosis was 39 months.Median lag time was 6 months and 37(53%)were female.Standard risk was identified in 46(66%)cases.Isolated choroidal invasion found in 14 patients (8 massive and 6 focal)did not receive adjuvant therapy,are alive and disease free.Intraocular high risk cases in 19(27%) and 5(7%) extraocular disease. In 29(41%)cases,two or more ocular coats invasions were observed. On univariate analysis,cut end optic nerve invasion,PLONI,two or more ocular coats invasions, high risk intraocular and extraocular disease were found to be associated with a poor survival outcome (p<0.001).After histopathological review,8(11%) patients were reclassified and 2/8 from intraocular standard to high risk,both did not receive adjuvant treatment and relapsed(one had orbital/systemic relapse and died).All of twelve relapsed cases had two or more ocular coats invasions and eight among them died of disease and one of secondary leukemia.

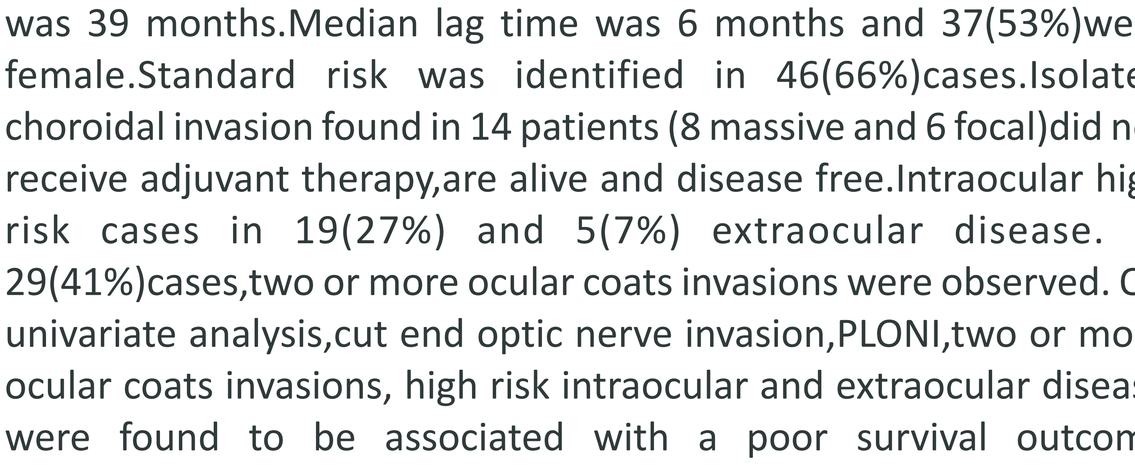

Figure1 A) Probability of OS was 88% and 86% at 5 and 10y and EFS,82%,at 5 and 10y,respectively.B) Probability of OS according to IRSS staging (IRSS 1 low risk/IRSS high risk and IRSS 2).

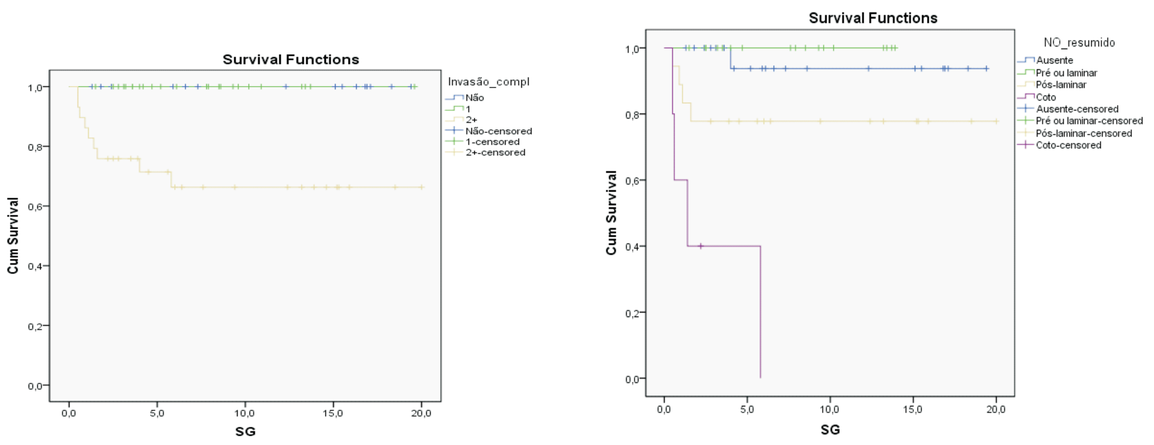

Figure 2 A) Probability of OS according to number of ocular invasions and B) Probability of OS according to Optic Nerve(ON) Invasions (None, Prelaminar/Laminar, PLONI and Cut End ON)

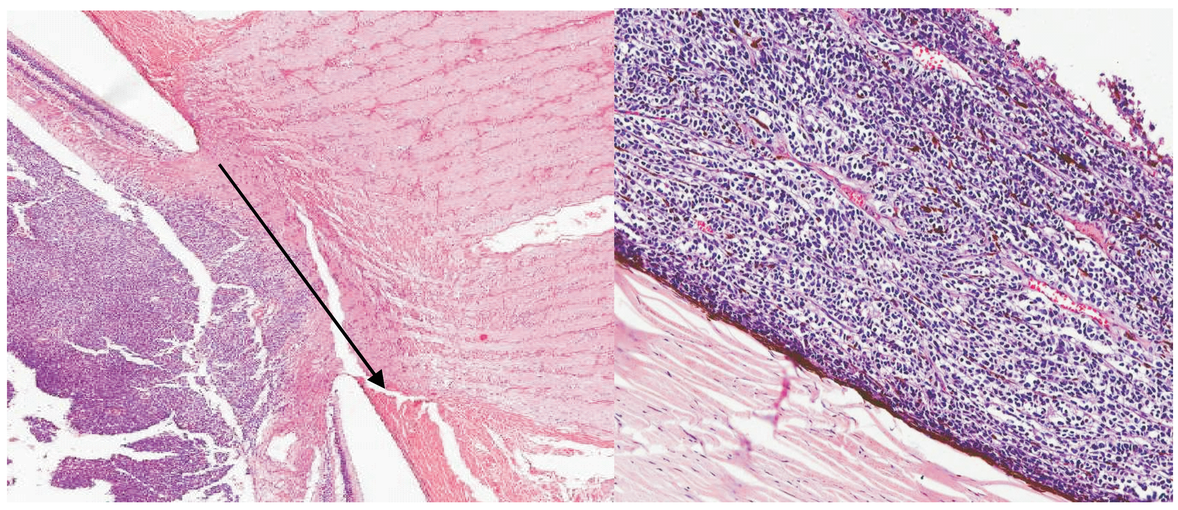

Figure 3: A) Poslaminar optic nerve invasion B) Massive choroidal invasion

Relapse	Review Histopathological	Risk Factors	Adjuvant Treamer*	Sites	Outcome
Case 1	IRSS1 low to high risk	PLONI+ Massive Choroid	No	Orbital	Alive without dise
Case 2	IRSS1 high risk to IRSS 2	Cut end ON + Massive Choroid	Yes (Chemo LA protocol + RT)	Leptomeningeal	Dead (disease)
Case 3	IRSS 2 (N3C0S0 to N3C2S0)	Cut end ON+ Massive Choroid	Yes (Chemo LA protocol + RT)		Dead (AML)
Case 4	IRSS 2 (N3C0S2 to N3C2S2)	Cut end ON+Trans-escleral+ Massive Choroidal)	Yes (Chemo CEV + RT)	CNS/CSF	Dead (disease)
Case 5 (glaucoma+pseudocelulitis)	IRSS2 (N3C2S1 to N3C2S0)	Cut end ON+ Massive Choroid	Yes (Chemo LA protocol + RT)	LCR	Dead (disease)
Case 6	Pathology Not Evaluable		No	Orbital	Alive without dise
Case 7 (initial abdonment)	IRSS1 high risk	PLONI+ Focal Choroid	Yes (Chemo CEV)	CNS	Dead (disease)
Case 8	IRSS1 low to high risk	Trans-escleral+ Massive Choroidal	No	Orbital/BM/Bone	Dead (disease)
Case 9	IRSS1 high risk(N2C0S1 to N2C2S1)	PLONI+ Massive Choroid+ Focal Sclera	Yes (Chemo CEV)	CSF	Dead (disease)
Case 10	IRSS1 high risk	PLONI+ Massive Choroid	Yes (Chemo CEV)	Orbital	Dead (disease)
Case 11	IRSS1 high risk (N2C0S0 to N2C2S0)	PLONI+ Massive Choroid	Yes (Chemo CEV)	CNS/CSF	Dead (disease)
Case 12	IRSS 1 low risk	Peroperative rupture	Não	Orbital	Alive without dise

Table 1: Relapsed cases and its patterns/approachs/outcomes (IRSS: International Retinoblastoma Staging System; Chemo: chemotherapy; RT: radiotherapy; LA protocolo: Latin American protocol, CEV: carboplatin, etoposide and vincristine)

CONCLUSIONS

Consensus in pathological evaluation is crucial to standardize risk classification predicting relapse and death.Its use may improve prognostic risk factors identification improving RB patients' management.

Projeto Gráfico: Setor de Edição e Informação Técnico-Científica / INCA