

OUTCOME IMPACT OF HISTOPATHOLOGIC FACTORS REVIEW IN PATIENTS WITH RETINOBLASTOMA AT NATIONAL CANCER INSTITUTE – BRAZIL

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Background

Staging system and pathological consensus are decisive steps for adequate retinoblastoma(RB) management. Histopathologic Risk Factors(HRF) identification should be standardized by an experienced pathologist who is rarely available in low and middle-income countries. Histological divergences have been poorly characterized in RB and have significant clinical implications.

Objectives

This study reviewed histopathological findings and divergences impacting in outcome.

Methods

Retrospective cohort study including all unilateral RB primarily enucleated from 1997 to 2015. Cases were retrieved from National Cancer Institute, Brazil. The histopathologic review was based on the Consensus International Retinoblastoma Staging Working Group on the Pathology Guidelines from 2009.

Study variables included age, gender, clinical presentation, staging, lag time, optic nerve(ON), choroid and sclera invasion histopathological review and treatment. Low risk staging consisted of pre-laminar, isolated choroid and anterior segment invasion and high risk included: ON post-laminar, intra-scleral invasion and concomitant invasion of sclera and/or ON post-laminar and/or massive choroid (Figure 2).



Figure 1: Longitudinal anterior-posterior sections of the calotte are obtained from each calotte and then submitted one cassette per calotte and histological section of the ocular globe

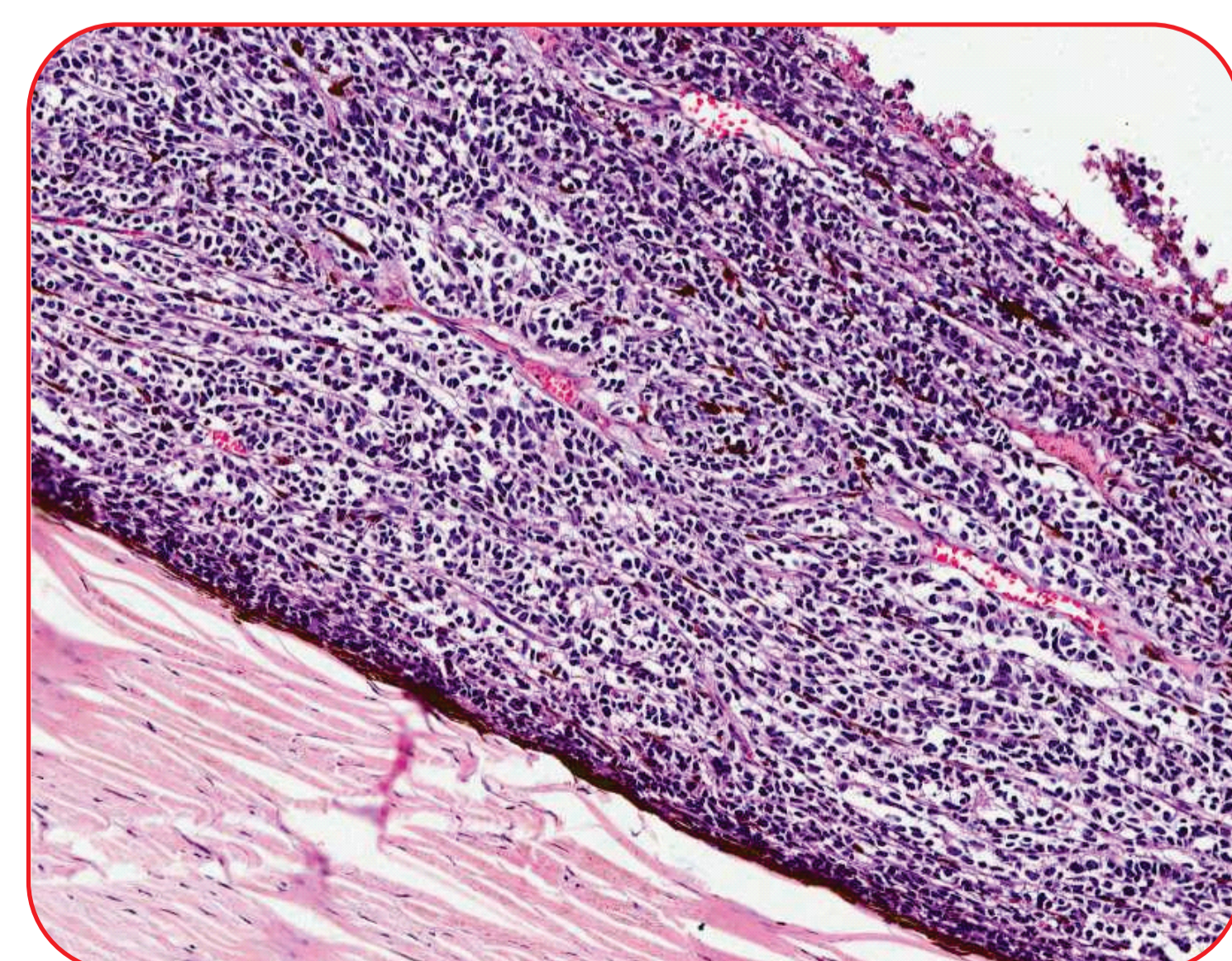
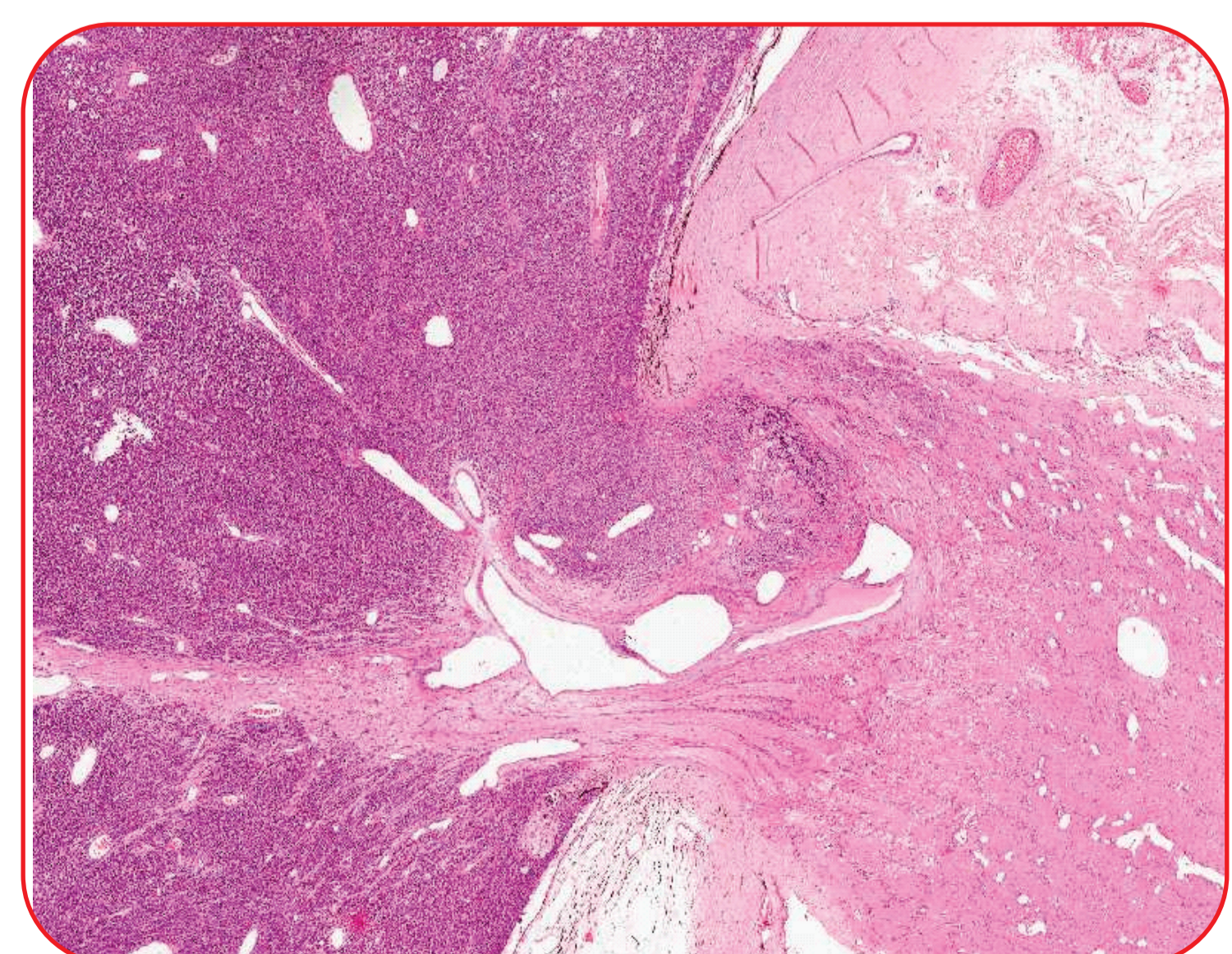


Figure 2: Retinoblastoma tumor invading through the lamina cribrosa (L.C.) into the retrolaminar optic nerve (postlaminar optic nerve invasion - PLONI) and massive choroidal invasion measuring more than 3 mm by tumor

Results

A total of 70/138 cases was evaluated (median diagnosis age 29.5 months, median lag time 7 months (range 0.4-31.6)); 52.9% female, 47.1% male; 92.8% leukocoria; 92.9% intraocular, 7.1% extraocular; 30% received chemotherapy and 7.1% radiotherapy). After pathology review, 69 cases were evaluable. Divergences were found in 52.8%. Minor divergences were those with minimal variation of tumor extent (41.3%) and major divergences which changed staging (11.5%) (Table 1). Two cases were restaged as low risk and are alive and disease-free. Six cases were restaged as higher staging. In 2/6 patients redefined as extraocular: one is alive and without evidence of disease and the other case relapsed with orbital and leptomeningeal disease and died. In 4/6 were redefined as high risk: 2 of them relapsed. One with orbital relapse is alive and disease-free and another one with bone, bone marrow and leptomeningeal disease and died. The overall five-year survival rate (OS) was 88.1% (SD = 78.4 years) (Figure 3).

Table 1: Divergences table

Divergences	Staging Pre Pathological Review	Staging Post Pathological Review	Adjuvant Treatment	Presentation and approach	Outcome
1	IRSS1 high risk (N2C0S0)	IRSS 2 (N2C2S2)	Yes (chemo)	Pseudocellulitis	Alive without disease
2	IRSS1 low risk (N1C1S0)	IRSS 1 high risk (N2C2S0)	No	Orbital relapse	Alive without disease
3	IRSS high risk (N2C0S1)	IRSS 2 (N3C2S0)	Sim (chemo)	Orbital and leptomeningeal relapse	Death by disease
4	IRSS 1 high risk (N2C0S0)	IRSS 1 low risk (N0C0S0)	No		Alive without disease
5	IRSS 1 low risk (N0C0S0)	IRSS 1 high risk (N2C2S0)	No		Alive without disease
6	IRSS 1 low risk (N1C1S0)	IRSS 1 high risk (N0C2S1)	Yes (chemo - CEV)		Alive without disease
7	IRSS1 high risk (N2C0S1)	IRSS 1 low risk (N1C0S0)	Yes (chemo - CEV)		Alive without disease
8	IRSS1 low risk (N0C0S0)	IRSS 2 (N0C2S2)	No	Orbital, BM and bone relapse	Death by disease

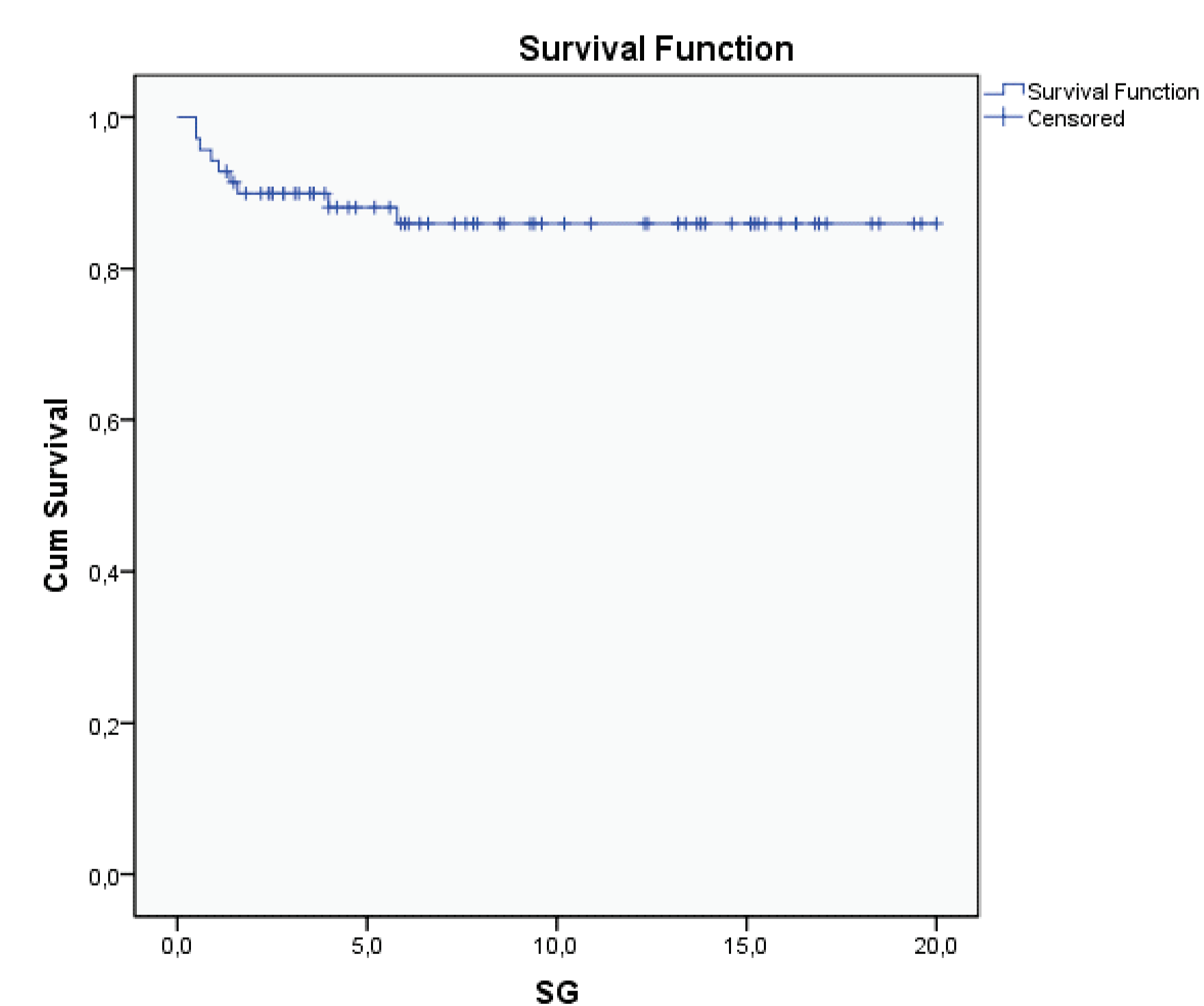


Figure 3: 5y OS (overall survival)

Conclusions

Histopathological risk factors(HRF) determination plays a crucial role in RB management predicting distant metastases development in intraocular disease. Pathological review show divergences which impacts outcome and can consolidate expertise in RB approach in a referral cancer center.