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CASE REPORT

Late and Distant Metastases of Retinoblastoma to Long Bones: A Purpose of a Case

Luis Willians MD*[1], Marthelena Acosta Marin MD[2]

[1] Orthopedic Surgeon – Orthopedic Oncologist
Associate of the Bone Tumors Service – Padre Machado Oncology Hospital. Caracas, Venezuela.
[2] Pathologist – Specialist in Musculoskeletal Pathology.
Leopoldo Aguerrevere Maternity Clinical Center-Marín Pathology Laboratory. Miranda State, Venezuela.

* Corresponding autor: luiswi16@gmail.com

SUMMARY
The case of a 13-year-old male patient is presented, with a history of Bilateral Retinoblastoma since he was 2 years old, undergoing enucleation of the right eye in June 2007, and salvage of the left eye by chemotherapy and radiotherapy, said patient 11 years after This episode presented metastasis in the distal end of the right radius, performing neoadjuvant treatment and subsequent wide oncological resection with healthy margins of the distal end of the radius plus reconstruction with the proximal end of the ipsilateral fibula and arthrodesis of the wrist. . It is important to point out that distant bone involvement and that of long bones are very few cases reported in the literature, therefore this case was a challenge for diagnosis and treatment, since a retinoblastoma was obtained that metastasized 12 years later. of the enucleation of the eye with the primary tumor and in turn performed it in the long bone (radius), it is emphasized that said patient was followed up free of disease for 2 years after surgery (wrist fusion). Given the limitations of knowledge of the genetics of retinoblastoma metastasis to long bones, not all alterations are currently known. It is considered that a genetic study should be done in patients diagnosed on time.

Introduction

Retinoblastoma is the most common malignant intraocular tumor in childhood (approximately 18 months of life), and it originates from primitive cells of the sensory retina[1,2,3,4]. The origin of retinoblastoma is found in the cells of the retina[5]. It represents around 1-3% of cancers in children and approximately 1% of all cancers[3,6,7].

It is a hereditary tumor that occurs in 25 to 30% of cases, characterized by a mutation in the germinal RB1 gene and may be associated with the bilaterality of the lesion, however, 75% of cases are associated with mutations. in the germinal development of the retina that are considered non-hereditary[8].

Its worldwide incidence is estimated to be one case for every 18,000 to 30,000 live births[2]. In Venezuela, the presentation rate is 25 to 30 new cases per year and is usually found in around 3% of all childhood cancers[9].

The most important clinical sign is leukocoria, which is observed as a white reflection in the pupil, another important sign is strabismus, which occurs when the macular area is involved. Inflammatory phenomena and glaucoma can also be observed, both secondary to the tumor that invades and collapses the lens diaphragm and the trabecular meshwork. Another characteristic sign is proptosis secondary to retrobulbar extraocular expansion, orbital cellulitis or evidence of distant metastasis[10,11].

Tumor invasion and metastases represent the most common causes of mortality[12,13] for which reason several studies have been carried out in order to determine the main risk factors for them. It is estimated that the development of metastatic disease occurs in less than 10% of affected patients[14,15].

Likewise, the local control of the disease consists of the enucleation of the affected eyeball, in stage V of retinoblastoma and possible metastatic disease should be considered in case of extraocular extension of the lesion such as: choroidal invasion, scleral or nerve compromise. that extends to the cribriform plate, in these cases there is a high risk of metastatic disease[16]. And its dissemination worsens the patient's life prognosis.

Metastatic retinoblastoma is rare in developed countries, with a reported range of 4.8% in the United States to 5.8% in the United Kingdom. However, the frequency in developing countries varies from 9% to 11% at the time of presentation. Mortality is very high due to late presentations, late diagnosis aggravated by socioeconomic factors. The management of metastatic retinoblastoma is evolving, but remains a challenge in pediatric oncology.

One of the affected areas in cases of distant metastasis is the bone marrow, evidencing infiltration of disseminated tumor cells in the blood[16,17]. These metastases can present as bone lesions and have to be carefully distinguished from other primary bone tumors.

Postmortem studies have shown that the cranial and orbital bones are the most common sites of extension and metastasis[6,11]. Mackay et al.[18] in their studies found that 35% of patients with metastases had only the brain and 65% the skull and distant organs. The tumor may spread to long bones, lymph nodes, and viscera (including liver, kidneys, pancreas, and gonads), and rarely to the lungs[6].

Generally, distant disease in patients with retinoblastoma can present between 6% and 20% of cases, regardless of whether it is unilateral, bilateral, or in cases known as trilaminar, and the most common metastatic spread is usually to the central nervous system (through the meninges) and bone jointly represented by 60% of metastatic cases. 90% of the affected bones are usually represented by bones of the orbit and cranial bones and only 10% in long bones[19].

As for the treatment options in extracranial metastatic retinoblastoma (specifically long bones), they include systemic chemotherapy followed by high-dose myeloablative chemotherapy with stem cell rescue, in combination with radiotherapy; however, extraocular disease, especially in older early is often associated with a poor prognosis[9].

Another option in terms of distant disease in long bones is local control through resection surgery, improving local cure rates, allowing the preservation and functionality of the limb, in other cases ablative surgery must be used above all in patients with late-onset metastases, after local ocular treatment[20].

Given the above, a case of Retinoblastoma Metastasis to the Distal Metaphysis of the Right Radius is presented, 12 years after the Enucleation or Recession of the Primary Tumor, being managed and studied multidisciplinary.

Case report

A case of Late Metastatic Retinoblastoma is

presented, which affected long bones, specifically the distal end of the right radius, the following data were evaluated: male patient, of mixed race, chronological age 13 years, native of Nueva Esparta state, Venezuela, No known family cancer history.

He presented Bilateral Retinoblastoma since he was 2 years old, performing enucleation of the right eye in June 2007 and salvage of the left eye by chemotherapy (6 cycles) + radiotherapy (21 sessions). It should be noted that said patient attends strict controls by Tomography Optical Coherence, (OCT), Cerebral Magnetic Resonance of the orbit and fundus, by the Oncological Ophthalmology treating service.

In the month of June of the year 2019, the patient reported an increase in volume in the right wrist, concomitant pain of moderate intensity and functional limitation, which was attenuated with non-steroidal analgesics (NSAIDs). He is treated by the Traumatology Service of his locality (Nueva Esparta State, Venezuela), requesting X-ray studies of the wrist in Anteroposterior and Lateral projections, the results show an alteration of the bone structure (Figure 1), with the presence of a lytic lesion, with periosteal reaction, therefore, he was referred to the bone tumor service of the former Padre Machado Cancer Hospital.

In October 2019, the patient was evaluated at the Bone Tumor Service of the Padre Machado Oncological Hospital, in the city of Caracas, where the alteration of the aforementioned bone structure was clinically and with imaging studies, and it was decided to perform an incisional biopsy.

Figure 1

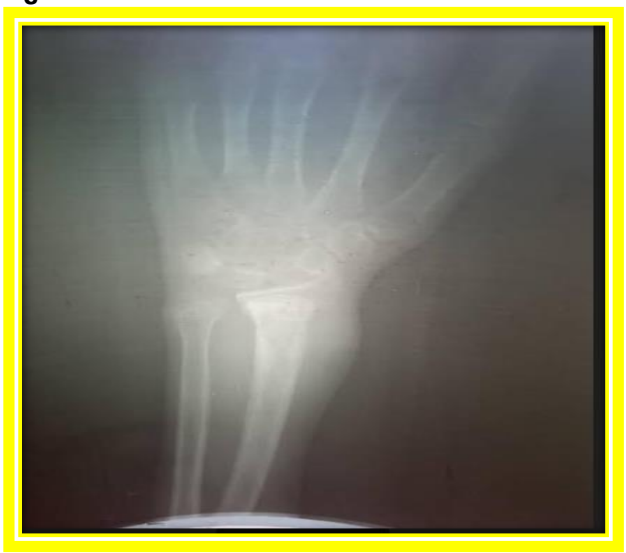
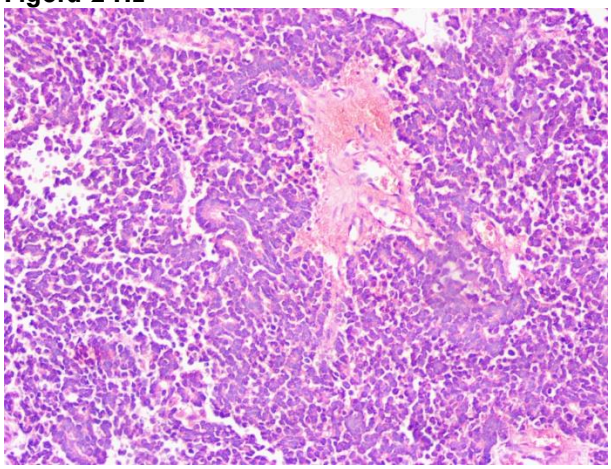
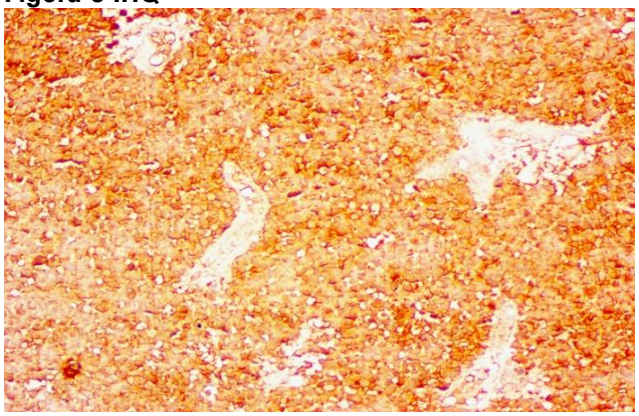


Figura 2 HE



Observing from the histological point of view the presence of densely cellular areas made up of round blue cells with little cytoplasm and moderate cytological atypia, without the presence of production of any type of osteoid or cartilage matrix, with a mitotic activity of 2 mitoses x 10 fields with a higher increase (mitotic activity was reported in 10 fields since to date the change suggested by the World Health Organization WHO 2020 did not exist), no vascular-lymphatic tumor embolism was seen, concluding as morphological findings compatible with malignant round cell tumor (Figure 2 Micro HE), for which an immunohistochemical study of the sample is indicated, yielding diffuse positivity for enolase (Figure 3) and synaptophysin (Figure 4), and on the other hand vimentin, cytokeratin AE1/AE3, common Leukocyte Antigen , CD34, CD99, Fli1 and protein S100 negative in tumor cells with a proliferative activity measured with ki67 of 85%, taking into account the known history of the patient.

Figura 3 IHQ



ENOLASA

A Metastatic Retinoblastoma is considered as the best diagnostic option. It should be noted that in developed countries retinoblastoma is more frequently diagnosed when the tumor is still

intraocular, in contrast to what This occurs in underdeveloped countries, where diagnosis is late and the tumor has the possibility of spreading to the optic nerve, orbit or even spreading, giving rise to metastasis 21, which is what is observed in the treated patient.

Sinaptofisina Figure 4

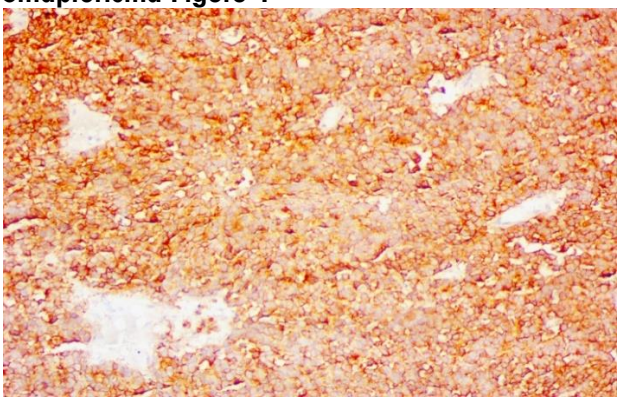
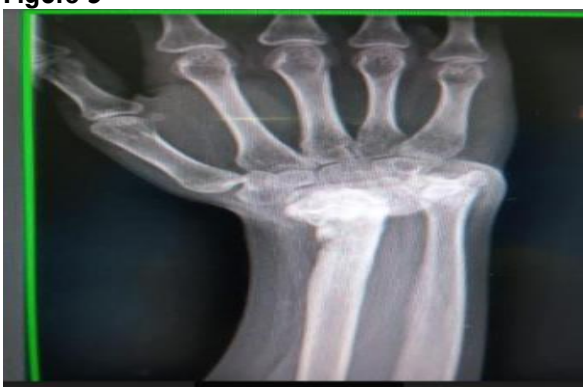


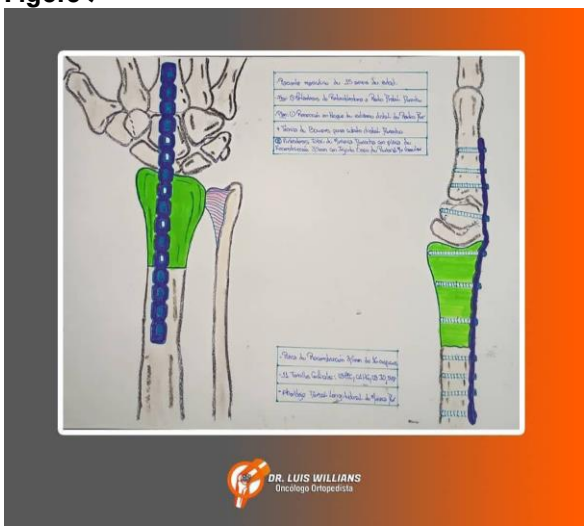
Figure 5



The patient is referred and treated at the Pediatric Oncology Service of the Luis Razetti Oncology Hospital, in the city of Caracas, in conjunction with the Radiotherapy Service at the José Manuel de los Ríos Hospital, where neoadjuvant therapy was performed using eight (8) Chemotherapy cycles plus ten (10) Radiotherapy sessions at a dose of 250 cGy each. Local and remote imaging studies (X-rays, Nuclear Magnetic Resonance of the right wrist, CT-PET) were again requested, where a fork-back deformity and marked limitation to wrist flexion extension were observed (Figures 5 and 6). In view of presenting only this oligometastasis, the decision was made, from a surgical point of view, to perform an en bloc oncological resection of the distal end of the right radius (metasoepiphyseal), plus the distal epiphysis of the ulna, the latter due to compartment contamination. reconstructing with proximal fibula autograft plus wrist arthrodesis in November 2020 (Figure 7).

Figure 6

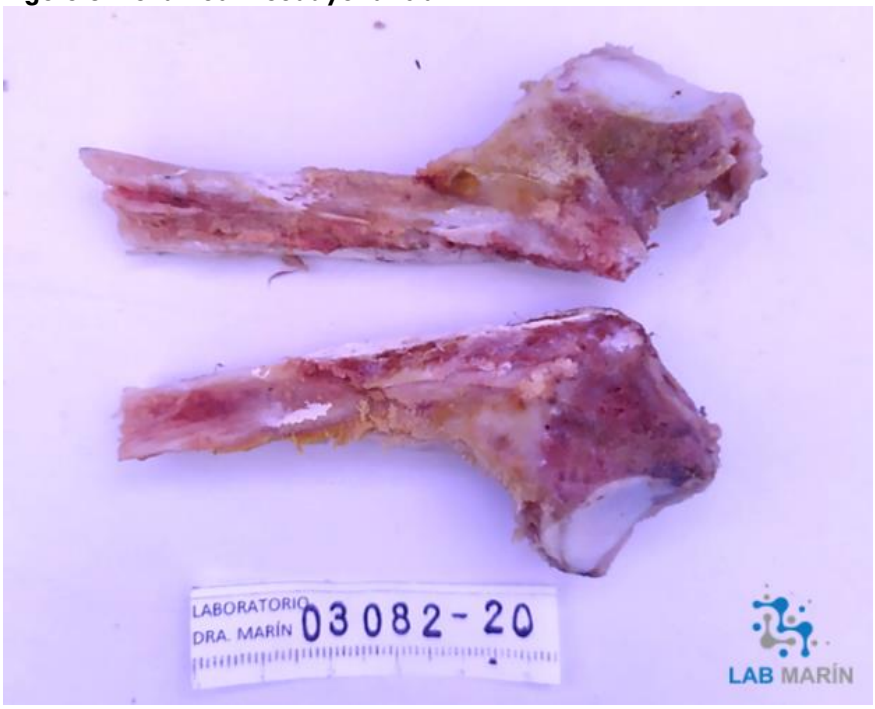
Figure 7



From the macroscopic point of view of the piece, a distal radius segment was received, measuring 8cm in length with variable diameters between 1.3 and 3cm (Figure 8). Radial cupula articular surface was identified without significant macroscopic lesions. The cortex was observed intact with areas of irregular appearance. The sagittal section of the piece identified increased consistency of medullary bone with calcified areas. The rest of the cancellous bone appears normal in appearance. Samples of

the entire bone surface were included with a post-neoadjuvant specimen protocol for definitive histological study and response evaluation. In the microscopic study of the piece, no residual tumor with reparative changes typical of neoadjuvant therapy was evident.

Figure 8 Pieza Post Neoadyuvancia



Total Wrist Arthrodesis

Total wrist arthrodesis is a basic operation whose objective is stable and painless radiocarpal and intercarpal fusion, with proper alignment and conservation of pronosupination mobility. (Figure 9 and 10) The surgical procedure that was carried out prior to surgical planning in this case was:

- SURGICAL TECHNIQUE

1. Under general anesthesia, after placing a tourniquet with emptying by gravity, asepsis and antisepsis of the right upper limb, a straight, longitudinal incision is made in the midmetacarpal area, centering between the second and third metacarpals. The incision passes through Lister's tubercle and ends on the dorsum of the distal radius.
2. The radial side of the incision is raised as a flap directly away from the dorsal surface of the retinaculum and contains the superficial branch of the radial nerve.
3. The distal radius is exposed subperiosteally and the incision is extended longitudinally into the periosteum distally through the capsule to the radial base of the third metacarpal.
4. A scalpel blade is used to elevate the two capsule flaps relative to the carpus.
5. The fourth extensor compartment is elevated subperiosteally from the radius and is reflected from its underlying capsule ulnarly over the distal radioulnar joint (DARC).
6. A resection of the distal radioulnar joint is performed in a block of approx. 7cm. and the dorsal cortices of the base of the third metacarpal and carpal bones are removed to provide excellent visual access to all joints to be included in the fusion. The articular cartilage is excised from the first proximal row and a nonvascularized bone graft is placed from the fibula.
7. It is fixed with a 3.5 mm reconstruction plate. 16-hole plate and center the plate directly over the dorsal aspect of the third metacarpal so that three screws (one metaphyseal and two diaphyseal) are placed in the metacarpal.
8. The hand is aligned with the forearm and the capitate is manually compressed against the unvascularized distal fibula.
9. With the plate aligned over the fibula and the hand, properly oriented, the second most distal screw is drilled into the fibula with a 2.5mm drill bit in compression mode and one 3.5mm cortical screw and the remaining 3.5mm cortical screws are inserted. Fibular holes are fixed with cortical screws.
11. The retained radial and ulnar blades of the previously opened third compartment (EPL) are used to close the capsule on the plate.
12. Subcutaneous plane closure and posterior skin closure is performed.

Figure 9

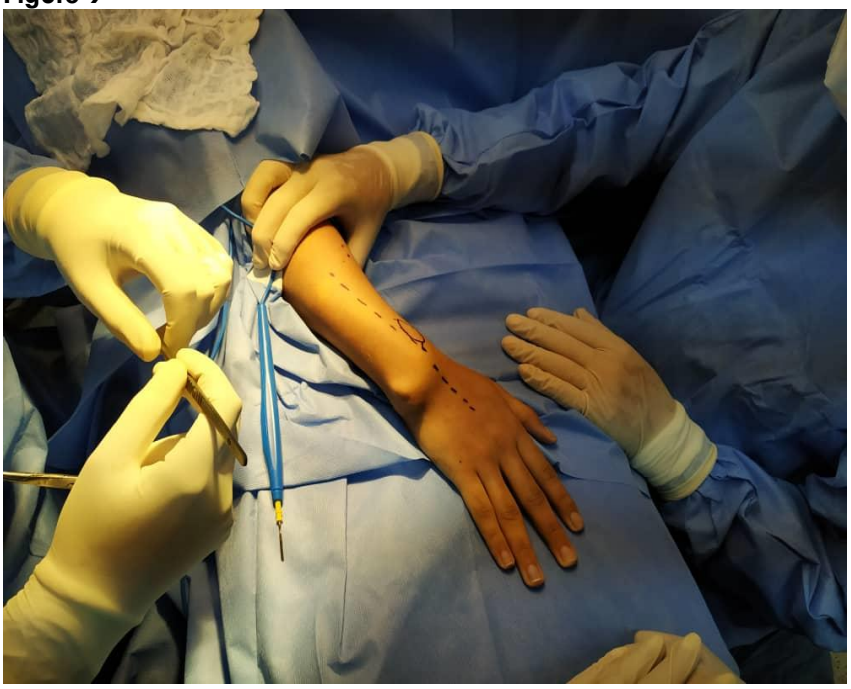
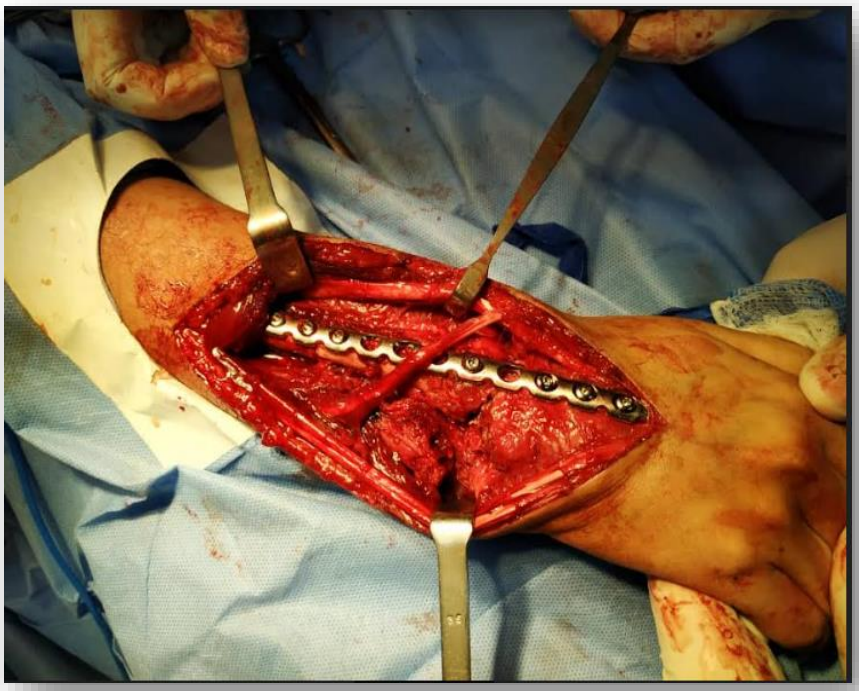


Figure 10



Resection and Interposition Arthroplasty

- BOWERS TECHNIQUE

1. The articular surface of the ulna is resected as it presents continuity with the removed radius tumor and a segment of soft tissue is inserted inside the radioulnar joint, preserving the triangular fibrocartilage.

2. Resection of the dorsal and articular portion is performed, preserving the ulnar styloid with capsular plasty that wraps the distal end of the ulna, and is subsequently reinforced with the extensor retinaculum.

With this technique, the stability of the Distal Radioulnar Joint (DRCD) is better achieved and it improves pronosupination while maintaining the length of the ulna.

Postoperative Treatment
- Brachiopalmar splint was placed for 06 weeks.
- At 10 weeks, full use of the hand was allowed.
- Bone consolidation was observed at 08 to 10 weeks.

Discussion

Children with retinoblastoma are at risk for three pathologic conditions: metastasis, intracranial neuroblastic tumor, and secondary cancer. This metastasis develops within the first year of diagnosis[22]. About 60% of cancer patients receive radiotherapy during the course of their disease[23]; Years after treatment, the development of a second neoplasia is possible (70% in the radiated area and 30% outside the area).

Metastases can occur despite having performed local control (enucleation), considering the possible metastatic disease in cases of extraocular extension of the lesion, such as: invasion of the choroid, scleral involvement or optic nerve that extends to the cribriform plate, in terms of secondary bone implantation, the most common bones affected are the bones of the face or the skull, it should be noted that everything depends on the type of retinoblastoma. It is important to point out that distant bone involvement and that of long bones are very few cases reported in the literature, therefore this case was a challenge for diagnosis and treatment, since a retinoblastoma was obtained that metastasized 12 years later. of the enucleation of the eye with a primary tumor and, in turn, performs it in the long bone (radius), it is emphasized that said patient was followed up free of disease for 2 years after surgery (wrist arthrodesis), this case and after reviews of many literatures, it breaks the walls of the natural history of the disease (metastatic retinoblastoma), and its diagnosis was possible with the new techniques of histopathology and immunohistochemistry, pending genetic tests due to economic limitations in our country.

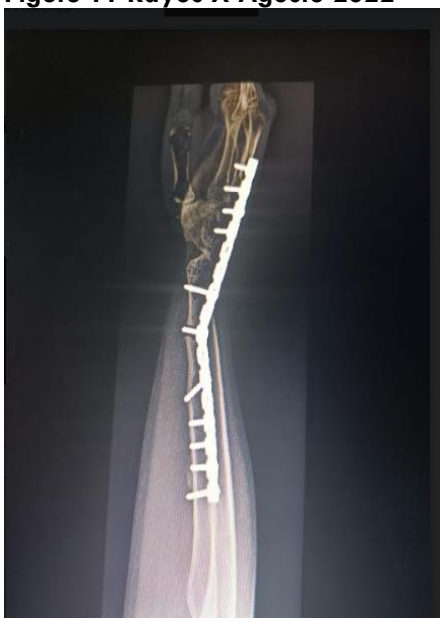
In their study Antillon and Esponda published two cases of sarcoma secondary to radiation in survivors of Retinoblastoma[24]; While Moll et al. evaluated the occurrence of second tumors in a series of 263 patients with Hereditary Retinoblastoma, finding that Hereditary Retinoblastoma conferred a higher risk of developing second tumors, particularly in patients whose neoplasms appeared outside the radiation field or were not dealt with her 28.

Conclusion

Given the limitations of knowledge of the genetics of retinoblastoma metastasis to long bones, not all alterations are currently known. It is considered that a genetic study should be done in patients diagnosed on time. Not all mutations have been identified, new studies and new analysis models must be investigated in order to have a better understanding of the disease, both in clinical and epidemiological aspects as well as in prognosis.

The patient under study has undergone an exhaustive follow-up for 19 months (from November 2020 to August 2022) in conjunction with the Pediatric Oncology and Oncological Ophthalmology service of the Luis Razetti Hospital, in the city of Caracas-Venezuela, using handheld x-rays. and forearm in Anteroposterior (AP) and lateral projections, Chest Tomography and CT-PET. In the evaluations, osseointegration of the fibula autograft was observed using the arthrodesis technique, the patient's wrist being functional (Figure 11, 12, 13). It should be noted that our patient continues in a physical medicine and rehabilitation plan to improve fine movements that help him with daily activities. From the oncological point of view, the patient does not present secondary implantation or metastatic lesion in the lung or other region of the body, he must continue with controls every 4 months for the first 2 years, observing his evolution. If there is a favorable improvement, the controls will be distanced every 6 months.

Figure 11 Rayos X Agosto 2022



It must be taken into account that Retinoblastoma is a curable disease if an early diagnosis and adequate therapy are carried out, since late consultation is correlated with the poor prognosis of the patient.

FIGURA 12 RAYOS X AGOSTO 2022

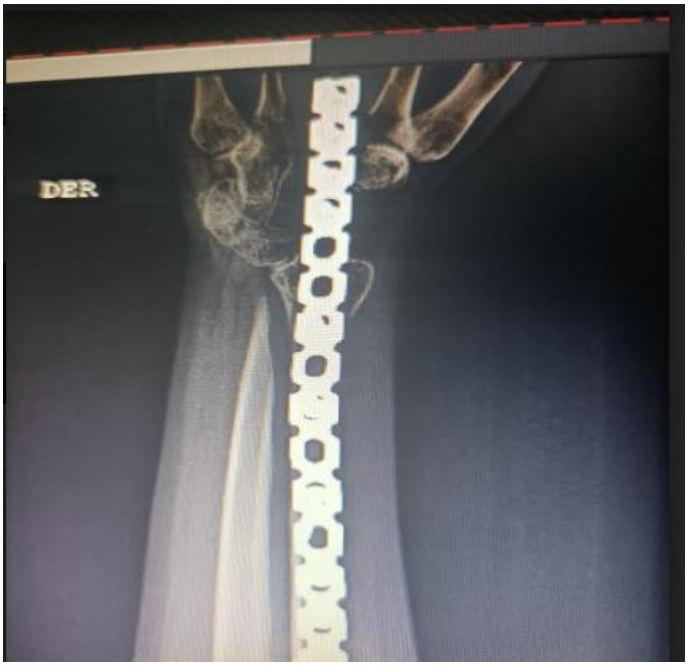
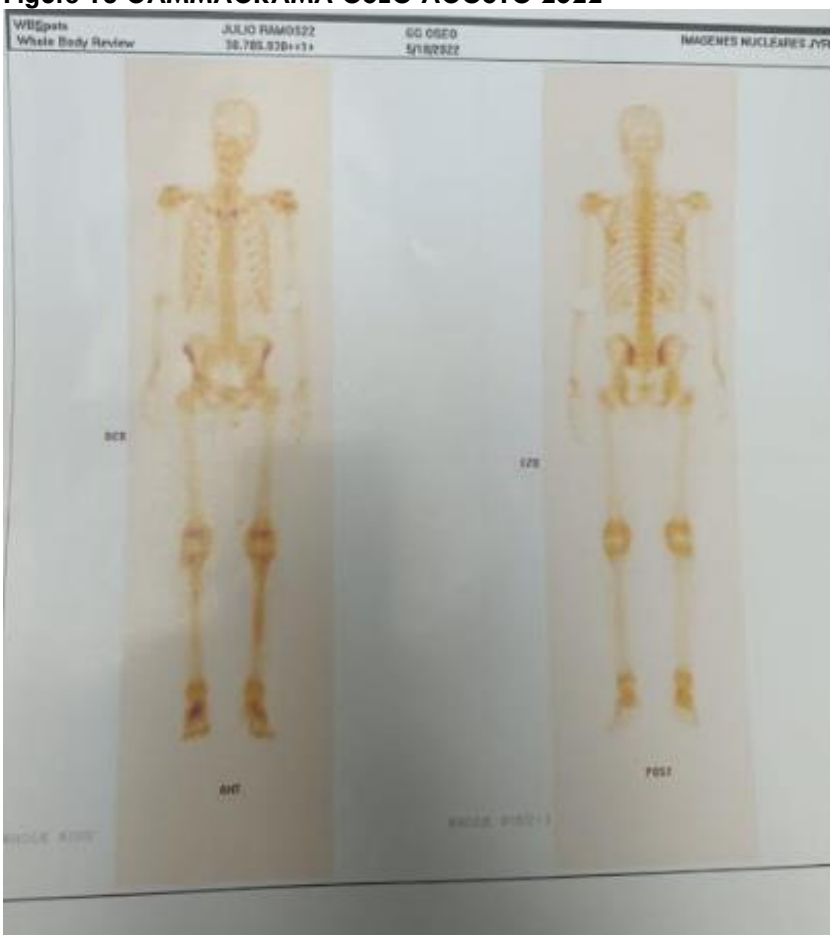


Figure 13 GAMMAGRAMA OSEO AGOSTO 2022



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