

A RARE PEDIATRIC CASE WITH THREE MALIGNANCIES

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CASE PRESENTATION

THE PATIENT

- A 9-years old male
- Referred to the hospital around July 2019
- Referred with fever which had been lasted for nearly 1.5 months
- The main cause of his refer was pain, swollen foots and pale.

FAMILY HISTORY

- He was a first child of a non-familial marriage
- without any history of familial malignancies
- The parental grandfather had a history of diabetes mellitus
- there was a report of Multiple Sclerosis (MS) in the uncle of his mother.

PHYSICAL & CLINICAL EXAMINATIONS

July 2019

PHYSICAL & CLINICAL EXAMINATIONS

- The patient had 2-3 lymph nodes two sides of the neck
- There was splenomegaly (the size of spleen: 124 × 55 mm) too.

- The results of laboratory tests at that time were as:

✓ WBC: 6300 cells/ μ L;

✓ Hgb: 7.9 g/dL;

✓ Plt: 83000 cells/ μ L;

✓ SGOT: 116 units/L;

✓ SGPT: 160 units/L;

✓ LDH: 1485 unit/L;

✓ uric acid: 1.6 mg/dL;

✓ ESR: 88 mm/hr.

BONE MARROW AND FLOW-CYTOMETRY EVALUATIONS

- Bone marrow aspiration report showed hypo cellularity and was in compatible with **Acute Lymphoblastic Leukemia** (ALL).
- Analysis of CD markers by flow-cytometry was in favor of **Pre-B ALL**
 - CD19: 53.9%;
 - CD20: 54.2%;
 - HLA-DR: 82.9%

TREATMENT FOR ALL

CHEMOTHERAPY (JULY 2019)

- According to the Children's Oncology Group (COG) protocol, the patient was in **average risk group**.
- with **Pre B-Cell ALL: BFM protocol 2009** started from 1 July 2019.

DAY 14 & DAY 33

- At day 14: the bone marrow aspiration was hypo cellular
- At day 33: hypo cellular bone marrow aspiration
- The flow cytometry immuno-phenotyping analysis at the day of 33 was 4% mononuclear population that mainly composed of mature T-lymphocytes.

CONTINUING REGIMEN (AUG & SEP 2019)

- Consolidation phase started from 10 Aug 2019 with
 - CPA 1000 mg, 6MP 50 mg and Mesna 400 mg/m² and continued based on the protocol.
- The M protocol started at 28 Sep 2019 for the patient.
 - For starting the maintenance phase, the bone marrow aspiration revealed 10% mononuclear population mainly of mature T-lymphocytes and it was in complete remission.

AT THE FINAL DAYS OF M PROTOCOL

- Three months after the maintenance phase, the patient had pain and swollen knees.
- Because of a lytic lesion on left distal femur, so the patient referred to a pediatric orthopedic specialist for making a consultation.

THE SECONDARY MALIGNANCY

Dec 2019

DIAGNOSIS

- The core needle biopsy of left femur soft tissue mass done after orthopedic consultation.
- The diagnosis based on the pathology report at 10 Dec 2019 was malignant neoplasm compatible with **osteosarcoma, conventional type**.

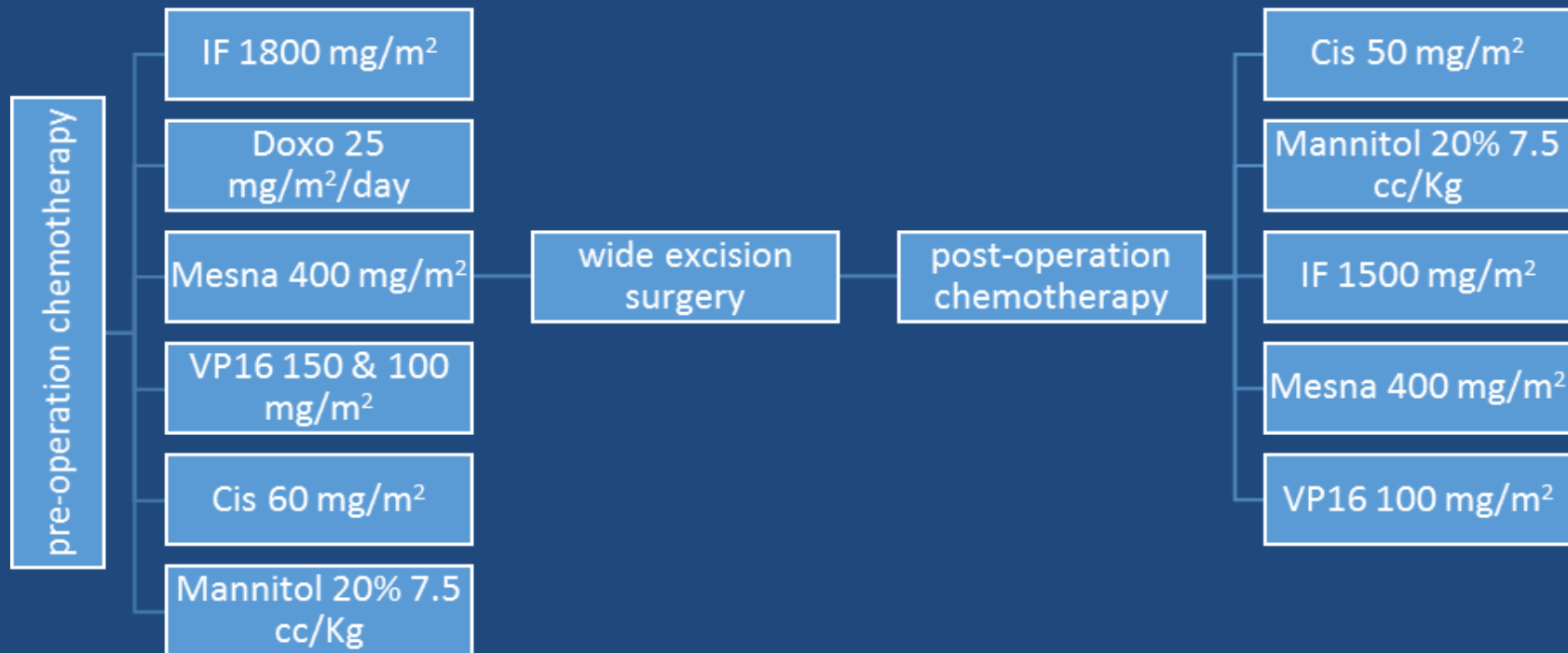
TREATMENT FOR OSTEOSARCOMA (DEC 2019 UP TO NOV 2020)

- The neo-adjuvant chemotherapy administered from 22 Dec 2019 according to the osteogenic sarcoma protocol through 5 cycles.
- At 6 June 2020, the patient had surgery.
- After surgery the adjuvant chemotherapy continued with 7 cycles and the **therapy finalized for the child at 8 Nov 2020.**

PATHOLOGY EVALUATION DURING THERAPY

- At 6 June 2020, the pathology evaluation from the
- wide excision of left distal femur revealed
 - completely (100% necrosis) we had chemotherapy effect.
 - All surgical margins were tumor free.

OSTEOGENIC SARCOMA PROTOCOL



4 MONTHS AFTER FINALIZING TREATMENT

Apr 2021

SIGNS & SYMPTOMS

- the patient referred to the emergency ward with **seizure and fever**.
- The **COVID-19 PCR test was positive** for the child and the other laboratory tests were as below:
 - ✓ WBC: 12000 cells/ μ L;
 - ✓ Hgb g/dL: 14.1;
 - ✓ Plt: 226000 cells/ μ L;
 - ✓ CRP: 2 mg/L;
 - ✓ ESR: 4 mm/hr.
 - ✓ O₂ saturation was 95%.

TREATING FOR SYMPTOMS

- Phenytoin was administered for controlling the seizure
- supportive care with oxygen therapy were done for treating COVID-19.

CT SCAN & MRI

- The CT scan of brain showed a clinical tumor in the right basal ganglia
- MRI of total region with and without contrast was normal
- At 25 May 2021, the MRI showed abnormal enhanced tumoral mass in the central part of the brain with bithalamic involvement and extension through the corpus callosum.

THIRD MALIGNANCY

May 2021

BIOPSY

25 MAY 2021

- The stereotactic biopsy from brain lesion in the right basal of ganglia was done.
- The biopsy samples evaluated by IHC and the results were as:
 - Positive GFAP
 - Negative CD20 & CD30
 - 9-10% of Ki67
- Finally, the report of IHC was in favor of **astrocytoma grade 3**.

SECOND LOOK EVALUATION

02 JUNE 2021

- The paraffin block sent for the second look diagnosis at 2 June 2021 through molecular genetic study. The results were as:
 - Negative IDH-1 (R132H)
 - Negative H3K27m
 - Retained ATRX
 - More than 50% of mutant P53
 - Wild type of BRAF-V600E
 - Intact nuclear expression of MLH-1, MSH2, MSH6, PMS2
 - Negative mutation of EGFR

MOLECULAR STUDY

- the P₅₃ was mutant,
- BRAF-V600E was wild type
- EGFR was wild type,
- MGMT methylation was positive for nearly 20% of all CPG islands.

FINAL DIAGNOSIS

- At last the final diagnosis of the second opinion was compatible with diffuse high grade pediatric type glioma; H3 wild type; WHO grade 4.

TREATMENT

- For treating the third malignancy, the radiotherapy was planned to start for the child.
- Unfortunately, at 29 June 2021 the patient had seizure and decreased level of consciousness before starting the radiotherapy
- Glasgow Coma Scale (GCS): 8.
- In this regard the child hospitalized in ICU ward and intubated.

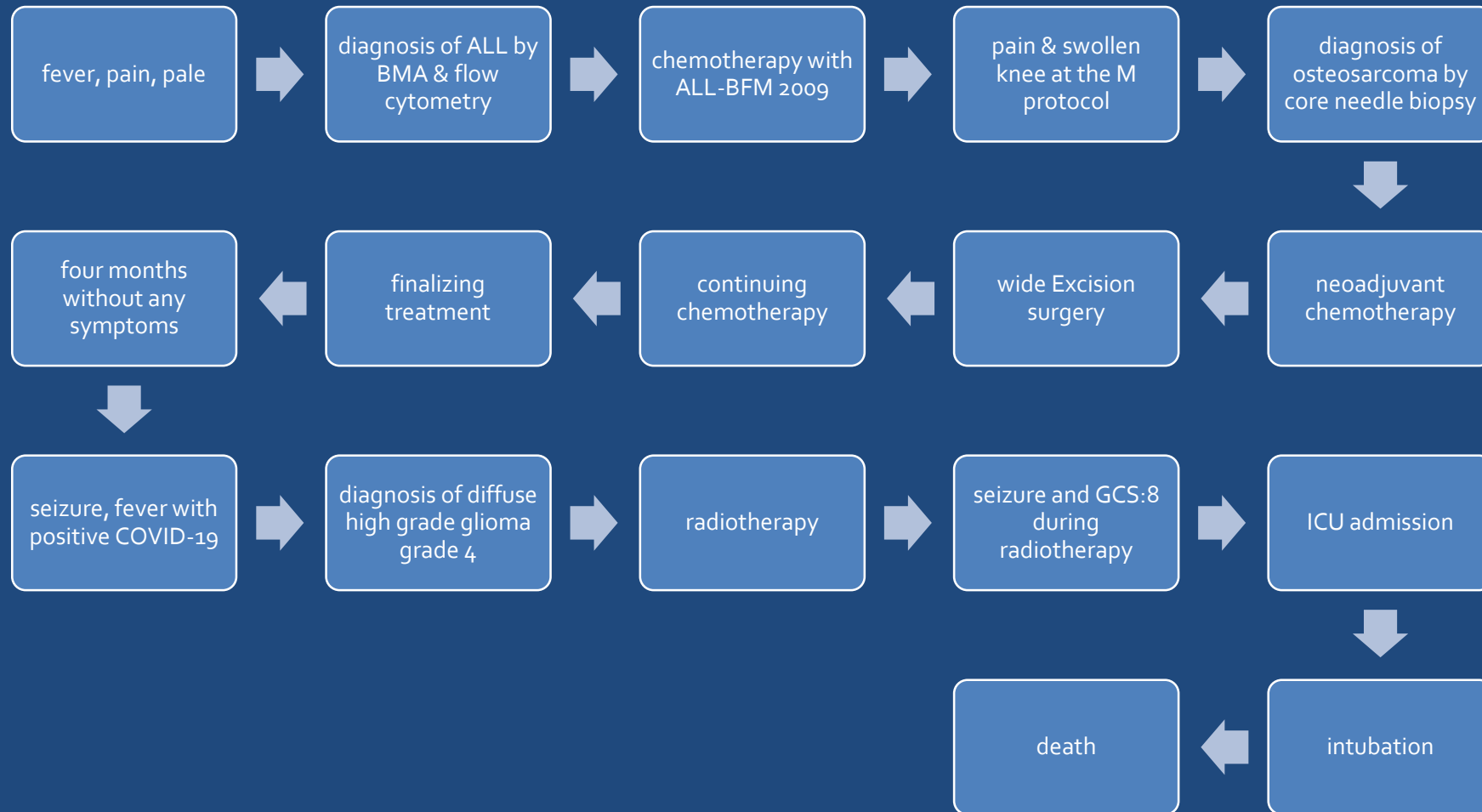
CT-SCAN

- Spiral CT scan of brain without contrast showed
- a heterogenous (65 × 55 mm) lesion involvement, right thalamus obliterating 3rd ventricle was in favor of the pathology report.
- Also there was resultant active moderate 3 ventricular hyper cephalus, and similar smaller sub cortical lesion in both sides.
- Another finding was hyper dense foci in one of the lesions that was in favor of hemorrhage.

FINAL SITUATION

- The consultation by the surgeon announced that there was not the indication of surgery for the child.
- After two weeks the GCS became 3, and unfortunately two weeks later at 25 July 2021 the child died.

THE PATIENT IN SUMMARY





Thank
you!