Chapter 2
Initial Management of New Diagnosis

Katrin Scheinemann

Keywords Compression syndrome • Electrolyte supplements • Febrile neutropenia • Flow cytometry • Hemorrhage • Hyperleukocytosis • IV hydration • Leukapheresis • Leukostasis • Lymphadenopathy • Pancytopenia • Rasburicase • Renal failure

Initial Contact

While solid tumors and brain tumors often get referred to pediatric surgery and neurosurgery, children with pancytopenia, blasts on peripheral smear, or lymphadenopathy are often referred directly to pediatric oncology.

As these referrals are made by family physicians or pediatricians who potentially have never seen such a case before, guidance is needed for the initial contact.

The following points should be considered:

1. Patient's name and contact information.
2. Age of the patient.
3. History of current illness.
4. Recent blood work:

   Date?
   Exact values?
   Peripheral blood smear?
   Chemistry available?

K. Scheinemann (✉)
Division of Hematology/Oncology, McMaster Children's Hospital,
1200 Main Street West, 555 University Avenue, Hamilton, ON, Canada L8N 3Z5
e-mail: kschein@mcmaster.ca

K. Scheinemann and A.E. Boyce (eds.), *Emergencies in Pediatric Oncology*,
DOI 10.1007/978-1-4614-1174-1_2,

5. When was the patient last seen (delay between taking blood sample and reporting from the outside laboratory)?
6. Last clinical exam?
7. Any other additional test performed? X-ray, etc.?

Upon obtaining this information, a decision has to be made as to how quickly (immediately vs. the next day(s)) and where (ER vs. outpatient clinic vs. direct admission to the inpatient ward) the patient needs to be seen. It is the responsibility of the referring physician to inform the parents about the potential diagnosis of a malignancy and provide information about the next step including the contact person of the referring hospital.

Arrival and First Steps in the Hospital

Upon arrival in the hospital, it is important that the patient/family will be seen as soon as possible by a pediatric oncologist. First, it will help to start a good and trustful relationship as families will have many questions which can only be answered by pediatric oncology. Second, it will help to get the necessary investigations ordered in a timely manner without delays or misses. Third, a quick clinical assessment will help facilitate the further care of the patient and decrease early morbidity.

The following blood work should be ordered:

1. CBC, including differential
2. Peripheral blood smear – to be reviewed by the lab technician and the hematopathologist and/or pediatric oncologist
3. Reticulocyte count
4. Dependent on the white cell count, flow cytometry from peripheral blood should be ordered (not possible with low counts)
5. Electrolytes (Na, K, Cl, PO_4, Mg, Ca)
6. Kidney function test (BUN, creatinine)
7. Bilirubin and liver function test (AST, ALT)
8. Tumor lysis blood work (uric acid, LDH) [please see Chap. 3 for further information]
9. Coagulation screen (PTT, INR) – important for further procedures
10. CMV serology – important to know patient's status prior to the first blood product transfusions

The patient should be started on IV hydration – important to use only normal saline as IV solution. The amount of fluid will be determined by the patient's clinical status and the blood work results. If the patient is febrile, blood cultures should be taken, and the patient should be started on broad spectrum antibiotics as per the institutional febrile neutropenia protocol. Other culture samples such as urine culture or NPS should only be considered with clinical symptoms.

The clinical exam should include at least the following points:

1. Heart – listen for murmurs due to anemia, cardiac effusion
2. Respiratory system/chest – infection, respiratory distress with positioning, pleural effusion
3. Skin – for signs of bleeding including mouth, nose, and ears
4. Abdomen – hepatosplenomegaly, other palpable masses
5. General lymphadenopathy
6. Male patients' testes – for possible malignant infiltration
7. Hydration status
8. Any signs of sepsis without fever – peripheral perfusion and pulses, extremity temperature
9. Other sites of infection – cut, bitten, ingrown toenail, teeth
10. Other "lumps and bumps" – e.g., chloroma in AML
11. Neurological status including fundoscopy
12. Joints and bones – if there was history of joint or bone pain.

Please keep in mind that most of these patients are quite sick and are not feeling well – so please be as gentle and thorough at the same time. Explain to the patient and parents what you are looking for throughout the exam.

Additional testing besides clinical exam and blood work is needed:

1. Chest X-ray, two views – Is there mediastinal mass or infection?
   Please do not lay the patient flat if there are any concerns about respiratory distress prior to the chest X-ray [please see Chap. 4 for further information]
2. U/S testes if concern about malignant infiltration
3. U/S abdomen – hardly necessary, clinical hepatosplenomegaly does not need to be confirmed
4. CNS imaging – only necessary with clinical symptoms/concerns
5. Bone/joint X-ray – dependent on clinical symptoms

With all of these results, the immediate management and risk of the patient will be determined.

The following points should be considered until final diagnosis (bone marrow aspiration/biopsy) is made:

1. IV fluids with normal saline – at least at one-and-a-half at least fluid maintenance, but needs to be increased depending on total white cell count and hydration status
2. No electrolyte supplements should be added unless patient has clinical symptoms
3. Adequate balance monitoring including weight
4. Repeat blood work – frequency will be determined by previous results
5. Blood product transfusion – please consider the need for blood product transfusion carefully as PRBC will increase viscosity and with this morbidity. Blood products should only be transfused either for procedures or for clinical symptoms, e. g., bleeding or signs of acute cardiac failure
6. NPO orders for procedure
7. Consents for procedure and tissue samples
8. Treatment of hyperuricemia [please see Chap. 3 for further information]

Management of Hyperleukocytosis

A high initial white cell count will require immediate intervention and careful monitoring. A white cell count over 100×10^9 per L is defined as hyperleukocytosis. Hyperleukocytosis is more often observed in AML (up to 25%) compared to ALL (10%) and can be seen quite often in infants [1]. The early morbidity (20–40%) and mortality risk with an increased white cell count is higher in AML compared to ALL as the blasts are bigger in size and "stickier" to each other and the endothelium [2]. This phenomenon together with leukostasis is considered as the underlying pathomechanism.

Clinically, the following presentations are possible:

1. Neurologic (stroke, headache, blindness, altered level of consciousness)
2. Respiratory (hypoxia, dyspnea)
3. Hemorrhagic (CNS, GI, pulmonary)
4. Renal failure
5. Metabolic (tumor lysis syndrome)

Patients with symptomatic hyperleukocytosis have a higher risk of morbidity and mortality.

Treatment principles can be summarized as the following:

1. Close observation and monitoring (consider ICU admission)
2. Fluids should be increased to 1.5–2× maintenance with close monitoring of output
3. Correct coagulopathy (plt > 30–50×10^9 per L, FFP and cryoprecipitate as needed)
4. Avoid PRBC transfusion – if necessary due to clinical symptoms, use a dose of 5 mL/kg
5. Tumor lysis precaution/treatment
6. Reduce white cell count:
   - Early start of chemotherapy
   - Leukapheresis

Leukapheresis

As leukapheresis is a resource-intense procedure with a lot of risks, the decision to proceed has to be made early including all considerations. As all evidence is based on retrospective studies, no clear guidelines are established. Also, with the implementation of rasburicase, the value of leukapheresis is under discussion. Certainly, in patients with symptomatic hyperleukocytosis, it should be considered. The goal is to reduce the total white cell count by 50% or $<100 \times 10^9$ per L [3].

As the implementation requires some planning, the decision has to be made as early as possible:

1. PICU admission for close monitoring and central line
2. Pheresis nurse on call
3. Blood bank – volume needed should be calculated prior to contact, platelet transfusion

The needed blood volume needs to be calculated and ordered by the pediatric oncologist – pheresis nurse can help if no institutional guidelines are available

Blood volume calculation:

1. Reconstituted whole blood (with FFP) matches to hematocrit of the patient
2. Close monitoring of platelet count will require repeat transfusions
3. "Double blood volume processing:"

- Infants: 100 mL/kg
- 1–10 years: 80 mL/kg
- >10 years: 70 mL/kg

As leukapheresis is a risky procedure, careful monitoring of the side effects is necessary. Despite the fact that the patient is in the PICU, regular visits from the pediatric oncologists through the procedure are required:

1. Electrolyte imbalance
2. Hemorrhage
3. Respiratory failure
4. Renal failure
5. Allergic reaction to blood product
6. Bleeding from central line site

Depending on the reduction of the white cell count, more than one round of leukapheresis is needed. Diagnosis should not be delayed through the procedure as with the high-white-cell/blast-count flow cytometry and molecular cytogenetics can be performed from peripheral blood. Diagnostic lumbar puncture should wait until the completion of leukapheresis, adequate platelet count, and no coagulopathy.

Solid Tumors/Brain Tumors

As previously mentioned, patients with a suspicion of a solid or brain tumor are often referred to the pediatric surgeon and neurosurgeon. As diagnosis in almost all cases is pathology dependent, the first step is to get a tissue sample plus/minus tumor removal as soon as possible.

Pediatric oncology is getting involved earlier or later depending on the underlying tumor type. Early involvement will have the advantage of closing the gap

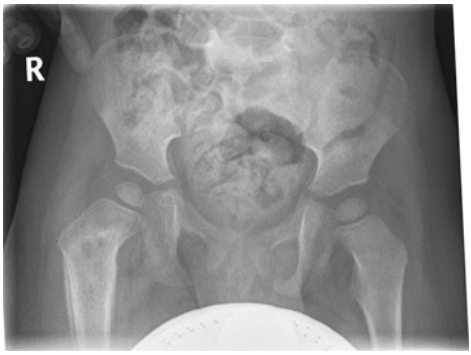

Fig. 2.1 Initial X-ray: Lytic lesion in the right femur

between the biopsy and when the pathology results are available. Further staging investigations or basic organ function tests could be performed throughout the waiting time. Also, patients and their parents will greatly benefit from early involvement of a pediatric oncology social worker to decrease the stress and to implement any paperwork that may be needed (i.e., for financial assistance).

The risk of tumor lysis syndrome is much lower, but still an assessment is necessary. On the other hand, the risk of compression syndrome is higher and will require adequate monitoring. Depending on the patient's clinical status and the underlying malignancy, a discharge between the initial surgical procedure and the disclosure meeting is possible.

Case 1
A 23-month-old boy was brought in with a 4–5-week history of difficulty in weight bearing, wherein the boy only crawled and refused to walk. Admitted to the hospital with right hip pain and fever, X-ray showed a lytic lesion, and he was started on antibiotics. Upon referral to orthopedic surgery, a biopsy of the lytic lesion was performed which revealed a negative gram stain but lots of small round blue cells. Subsequently, a bone marrow aspiration was done which established the diagnosis of pre-B-ALL (Figs. 2.1 and 2.2).

Case 2
A 34-month-old boy presented with lymphadenopathy, on left site of his neck. A course of antibiotics did not decrease the size; instead it was increasing. A referral to an ENT surgeon was made, who performed a biopsy. As the pathology revealed small round blue cell tumor, patient was referred to pediatric oncology. Following re-biopsy and staging investigations, patient was diagnosed with stage IV neuroblastoma (Fig. 2.3).

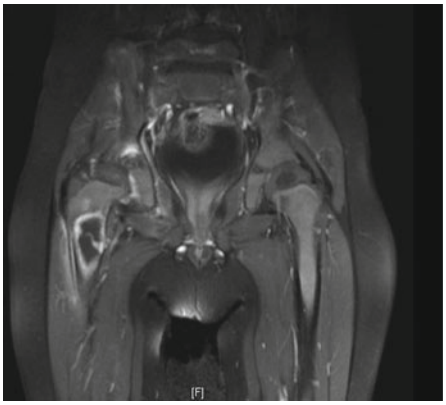

Fig. 2.2 MRI pelvis: Enhancing mass lesion in the proximal diaphysis of the right femor, associated with periostitis surrounding soft tissue edema and enhancement of the adjacent femoral muscles

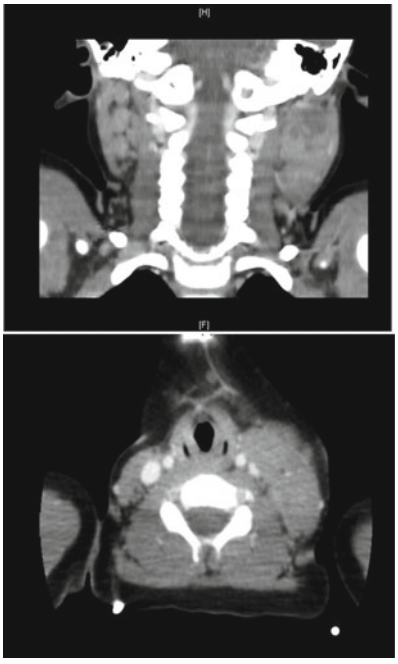

Fig. 2.3 CT neck: Large inhomogeneous mass left side of the neck with lymphadenopathy displacing the left jugular vein. Irregular calcifications within the mass

References

1. Eguiguren JM, Schell MJ, Christ WM, Kunkel K, Rivera GK. Complications and outcome in childhood acute lymphoblastic leukemia with hyperleukocytosis. Blood 1992; 79: 871–875
2. Porcu P, Farag S, Marcucci G, Cataland SR, Kennedy MS, Bissell M. Leukocytoreduction for acute leukemia. Therapeutic apheresis 2002; 6 (1): 15–23
3. Haase R., Merkel N., Diwan O., Elsner K., Kramm CM. Leukapheresis and exchange transfusion in children with acute leukemia and hyperleukocytosis. A single center experience. Klinische Paediatrie 2009; 221: 374–378

http://www.springer.com/978-1-4614-1173-4

Emergencies in Pediatric Oncology
McMaster University Health Sciences, A.P.K.S.; Boyce, A.E. (Eds.)
2012, XI, 185 p. 66 illus., 31 illus. in color., Softcover
ISBN: 978-1-4614-1173-4