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Hospital & Clinics

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Hematology/Oncology Referral Guidelines

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This information is designed to aid practitioners in making decisions about appropriate medical care. These guidelines should not be construed as dictating an exclusive course of treatment. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institutional type of practice.

E-CONSULT DISCLAIMER:

E-consults are based on the clinical data available to the reviewing provider, and are furnished without benefit of a comprehensive evaluation or physical examination. All advice and recommendations must be interpreted in light of any clinical issues, or changes in patient status, not available to the reviewing provider. The ongoing management of clinical problems addressed by the e-consult is the responsibility of the referring provider. If you have further questions or would like clarifications regarding e-consult advice, please contact the reviewing provider. If needed, the patient will be scheduled for an in-office consultation.

All URGENT consultations require provider-to-provider communication. If your patient has a medical emergency, please direct them to the closest emergency room for expedited care.

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ANEMIA

1. **Background**
    a. Types of anemia
        i. **Iron deficiency anemia**
            1. Common causes for iron deficiency are menorrhagia in females, occult bleeding in males
            2. Other causes: celiac disease, stool ova and parasites and chronic diarrhea
        ii. **Anemia of chronic disease**
            1. Anemia of chronic inflammation (disease) from co-existing illnesses is usually characterized by a low serum Fe,low TIBC, ferritin > 100 ng/ml, elevated C-reactive protein, Hct > 27, an inappropriately low Epo level, and a reticulocyte index (% retics x patient Hct/normal Hct) less than 3% in the context of an identifiable chronic disease.
        iii. **Vitamin B12 deficiency**
            1. Diagnosis made by elevated MMA and patients can have an elevated MCV and hyper-segmented neutrophils.

2. **Pre-referral evaluation and treatment**
    a. Testing
        i. CBC, with manual differential
        ii. Electrolyte panel to assess renal function
        iii. Liver function tests
        iv. Reticulocyte count
        v. Iron panel including a serum iron, TIBC, and serum ferritin
        vi. Serum methylmalonic acid (MMA)
        vii. Serum protein electrophoresis
        viii. Serum immunofixation test (IFE)
        ix. Serum erythropoietin level
    b. Management
        i. **Iron deficiency anemia**
            1. If female and menorrhagia identified, refer for Gyn eval
            2. If occult bleeding identified, refer for GI eval including colonoscopy and EGD
            3. Following diagnosis, treat with oral iron supplementation - Ferrous Sulphate, ferrous gluconate or liquid iron preparations.

a. If patients intolerant to one form of oral iron it can be switched to an alternative as they may tolerate them better.
b. Taking oral iron with something citric (eg orange juice) helps absorption and lowers the side effects
c. Intolerant response or sub-optimal response to oral iron after 6-8 weeks trial can be considered for IV iron therapy.

ii. **Anemia of chronic disease**
1. If hemoglobin 10 and above then no interventions.
2. If less than 10 then refer to hematology for consideration of erythropoietin

iii. **Vitamin B12 deficiency**
1. Treatment can be given via parenteral or oral routes.
a. Oral dose : Vit B12 1000-2000 mcg po daily
b. Parenteral Vit B12 dosing: Vit B12 1000 mcg subcutaneous daily for 5 days, followed by Vit B12 1000 mcg subcutaneous weekly for 4 weeks, followed by Vit B12 1000 mcg subcutaneous monthly
2. For patients with permanently decreased ability to absorb vitamin B12 (eg, pernicious anemia, total gastrectomy, surgical removal of the terminal ileum), life-long treatment is required.
3. If the cause of the vitamin B12 deficiency can been eliminated (eg, diet, drugs, reversible malabsorption syndrome(s)), treatment can be stopped when the vitamin B12 deficiency has been fully reversed and the cause eliminated.

3. Indications for referral

a. **Iron deficiency anemia**

i. Refer for:
1. Intolerant response or sub-optimal response to oral iron after 6-8 weeks trial.
2. Refer for IV iron

ii. Do not refer for primary investigation of the iron deficiency (e.g. gastroenterology or gynaecology)
1. Should be carried out by the appropriate referrals. Iron deficiency anemia by itself does not require a referral to the hematology clinic.

b. **Anemia of chronic disease**

i. Refer for:
1. Hct less than 35

a. May receive treatment with subcutaneous erythropoietin.
b. Doses of erythropoietin are commonly given in the range of 20-40,000 units either once a week or once every other week subcutaneously. A target Hct is dependent on coexisting morbidities but current QOL recommendations state that the hematocrit usually should be maintained between 30-35% with a follow-up CBC obtained at least once every 1-2 months while the patient is receiving erythropoietin
c. Once the appropriate teaching is done with the patient and their family and treatment with erythropoietin is initiated, the patient will be referred back to his or her primary care provider.

ii. Typically do not refer if the Hct is more than 35.

c. **Vitamin B12 deficiency**
   i. Do not refer - in itself does not need hematology evaluation.

4. **Please include the following with your referral**
   a. Results of pre-referral testing

LEUKOCYTOSIS

1. **Background**
   a. One can see mild stable leukocytosis without any other clinical symptoms of concern in patients who are obese, smokers, psych patients on psych medications.

2. **Pre-referral evaluation and treatment**
   a. Testing
      i. A peripheral smear will show relative neutrophilia
   b. Management
      i. As long as no immature cells are present, and the patient has a normal smear without any symptoms of concern, patients can be managed and watched closely in the PCP office

3. **Indications for referral**
   a. Worsening leukocytosis with B symptoms.
   b. Abnormal peripheral smear with immature cells, blasts, myelocytes, metamyelocytes, basophilia or monocytosis.

c. Leukocytosis with absolute lymphocytosis of over 4000.

LEUKOPENIA

1. **Background**
    a. Causes
        i. Ethnic neutropenia is an entity seen in patients of east African descent with normal hemoglobin and platelets and a normal WBC differential except for low ANC. It is a benign condition and patients are not symptomatic from this. Duffy antigen testing in these patients has shown that the patients are Negative for Fy(a) antigen, Negative for Fy(b) antigen.
        ii. White blood cell counts as low as 2500/mm3 can frequently be seen in the setting of chronic or end stage liver disease especially when accompanied by coexistent chronic hepatitis B, or hepatitis C infections, or in the presence of HIV infection and should not usually constitute a reason for referral.

2. **Pre-referral evaluation and treatment**
    a. Testing
        i. CBC with manual smear
        ii. Liver function tests
        iii. Hepatitis B surface antigen
        iv. Hepatitis C virus antibody
        v. HIV screening, if indicated
        vi. Anti-nuclear antibody test (ANA)

3. **Indications for referral**
        i. Neutropenia with anemia and thrombocytopenia without a def etiology (like liver disease as mentioned above)
        ii. Frequent infections, mouth sores, need for antibiotics, B symptoms

LYMPHOCYTOSIS

1. **Background**
    a. Lymphocytosis is defined as a lymphocyte count > 4 x 10^9/L.
    b. Causes
        i. A transient, reactive lymphocytosis is frequently seen in acute viral infection, particularly infectious mononucleosis.

ii. Chronic lymphocytosis is characteristic of chronic lymphocytic leukaemia (CLL), the incidence of which peaks between 60 and 80 years of age. In its early stages this condition is frequently asymptomatic with treatment only being required on significant progression or if any symptoms from the disease.

2. **Pre-referral evaluation and treatment**
    a. Testing
        i. Blood for flow cytometry
            1. Helps make a diagnosis of CLL and rule out reactive causes of lymphocytosis

3. **Indications for referral**
    a. Persistent lymphocytosis without active infection.
    b. B symptoms, presence of lymphadenopathy, should initiate referral

MACROCYTOSIS

1. **Background**
    a. Differential diagnosis of red cell macrocytosis (mean corpuscular volume >100fl) includes Vit B12 and folate deficiency, excess alcohol consumption, hypothyroidism, reticulocytosis and myelodysplastic syndrome.
    b. Macrocytosis is a normal physiological finding in pregnancy.
    c. Is seen routinely in patients taking either hydroxyurea (hydroxycarbamide), or certain anti-retroviral agents.

2. **Pre-referral evaluation and treatment**
    a. Testing
        i. B12 and folate levels (plus Intrinsic Factor Antibodies and coeliac screen)
        ii. Blood film examination and reticulocyte count
        iii. Liver and thyroid biochemistry
        iv. Immunoglobulins and protein electrophoresis, urine for Bence Jones proteins
    b. Management
        i. Alcohol history screening and appropriate lifestyle modification

3. **Indications for referral**
    a. Refer for:

i. Suspected myelodysplastic syndrome (based on blood film report) and involvement of white blood cell and platelets as well
ii. MCV > 100fl with accompanying cytopenia (excluding Vit B12 / folate deficiency)
iii. Persistent *unexplained* MCV > 105fl

4. **Please include the following with your referral**
    a. Results of pre-referral testing

MONOCLONAL GAMMOPATHY

1. **Background**
    a. Minor elevations in beta or alpha globulins on a serum protein electrophoresis do not constitute a monoclonal gammopathy.

2. **Pre-referral evaluation and treatment**
    a. Testing
        i. CBC
        ii. Electrolyte panel
        iii. Ionized serum calcium
        iv. Serum protein electrophoresis and Serum immunofixation
            1. If a band is not clearly delineated by the laboratory in the gamma region on serum protein electrophoresis, a serum immunofixation should be obtained to confirm that a monoclonal protein in fact is present in serum.
            2. Serum immunofixation is also necessary to confirm a suspected monoclonal gammopathy noted on protein electrophoresis and to identify the components of any M-protein.
        v. Urine protein electrophoresis
        vi. Spot urine for quantitative protein (urine protein/creatinine ratio)
        vii. Beta 2 microglobulin
        viii. Quantitative immunoglobulins (IgG, IgA, IgM).

3. **Indications for referral**
    a. Refer to hematology if a monoclonal protein is identified
    b. Do not refer:
        i. Referrals to haematology should **not** be made for patients with raised immunoglobulin levels in the absence of a monoclonal paraprotein band on serum electrophoresis. (IFE testing) Polyclonal gammopathy implies a non-specific

immune reaction and is not associated with underlying haematological disorders. It can be seen in patients with underlying rheumatologic problems and liver disease. There are no hematology interventions that need to be done in this setting.

THROMBOCYTHAEMIA

1. **Background**
    a. Thrombocythaemia / thrombocytosis is defined as a platelet count > 450 x 10^9/L.
    b. It may be due to a primary myeloproliferative disorder (essential thrombocythaemia) or is more commonly 'reactive': secondary to infection, inflammation, chronic bleeding or neoplasia.
    c. Very elevated platelet counts in the setting of myeloproliferative disorders carry risk of both thrombosis and abnormal bleeding (due to platelet dysfunction).
        i. Patients with Platelet count > 1000 x 10^9/L and Platelet count 600 – 1000 x 10^9/L in association with: recent arterial or venous thrombosis (including DVT / PE, CVA / TIA, MI / unstable angina, PVD) neurological symptoms abnormal bleeding age > 60 years.

2. **Pre-referral evaluation and treatment**
    a. Testing
        i. CBC
        ii. Blood film examination
        iii. Iron stores
        iv. CRP
    b. Management
        i. Investigate and treat iron deficiency
        ii. Look for and treat reactive causes: infection, inflammation, neoplasia

3. **Indications for referral**
    a. No reactive causes identified.
    b. Patients who are Jak 2 and BCR abl positive

THROMBOCYTOPENIA

1. **Background**

a. A platelet count over 100,000 is not associated with any excess risk of bleeding.
b. Causes
    i. Thrombocytopenia with platelet counts as low as 50,000 are commonly seen in the presence of chronic liver disease, particularly cirrhosis accompanied by chronic infection with either hepatitis B or hepatitis C virus and should not in and of itself constitute a need for referral to Hematology.
        1. Following thrombocytopenia the patients with underlying cirrhosis then go on to develop anemia and at later stages leukopenia.
    ii. Rheum disorders with positive ANA
    iii. Heavy alcohol intake
    iv. Medications including over the counter herbal meds/tonic water
    v. *H. pylori* infection in the gut

2. Pre-referral evaluation and treatment

a. Testing
    i. CBC
    ii. Liver function tests
    iii. Hepatitis B surface antigen
    iv. Hepatitis C antibody
    v. HIV screening if indicated

3. Indications for referral

a. Platelets less than 100,000 without above identifiable causes.
b. Thrombocytopenia with other cell lines involved should also prompt referral.

Revisions:

- April 2017, formatting
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