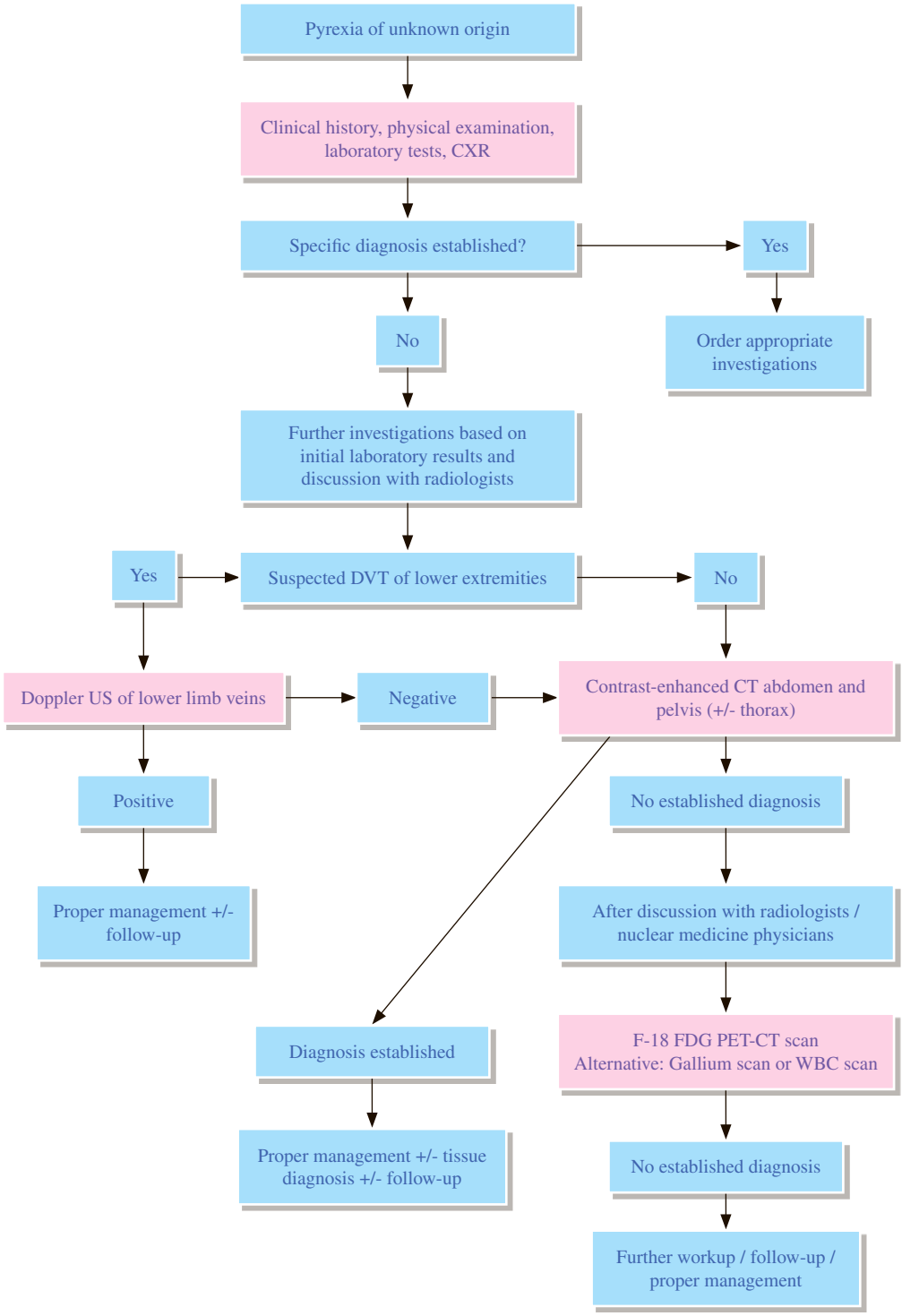
Pyrexia of unknown origin
Clinical history, physical examination, laboratory tests, CXR
Specific diagnosis established?
Yes
Order appropriate investigations
No
Further investigations based on initial laboratory results and discussion with radiologists
Yes
Suspected DVT of lower extremities
No
Doppler US of lower limb veins
Negative
Contrast-enhanced CT abdomen and pelvis (+/- thorax)
Positive
Proper management +/- follow-up
No established diagnosis
After discussion with radiologists / nuclear medicine physicians
Diagnosis established
F-18 FDG PET-CT scan
Alternative: Gallium scan or WBC scan
Proper management +/- tissue diagnosis +/- follow-up
No established diagnosis
Further workup / follow-up / proper management

REMARKS

1 General

1.1 Definition of pyrexia of unknown origin[1]

1.1.1 Pyrexia of unknown origin was first defined as an illness of greater than 3 weeks' duration with a temperature higher than 101°F (38.3°C) on several occasions and an uncertain diagnosis after 1 week of study in the hospital.

1.1.2 The requirement of 1 week in-patient evaluation has been recently modified and only evaluation of 3 out-patient visits or 3 days of in-hospital evaluation are stated in some articles.[2-4]

1.2 Classifications based on patient's subtypes include: classic, nosocomial, immune deficient and human immunodeficiency virus (HIV) associated, which may require different investigations pathway.[2,3]

1.2.1 The classic pyrexia of unknown origin excludes patients with known immunodeficiency or HIV infection.[2]

1.3 Causes of pyrexia of unknown origin[3-5]

1.3.1 Infectious, oncologic, inflammatory and miscellaneous/unknown are the four main categories.

1.3.2 There is an increasing trend of pyrexia of unknown origin in which the cause remains unknown.[4,6,7]

1.3.3 Infection is the most common cause. However, many factors may affect the implementation of study results to clinical practice due to different geographic locations, different subgroups of patients and different types of institutions.[3]

2 Radiography

2.1 Some articles have listed out the minimum diagnostic evaluation to qualify as pyrexia of unknown origin. Chest X-ray (CXR) is among one of the first investigations.[6,8]

3

The decision to obtain any further diagnostic studies should be based on abnormalities found in the initial laboratory work-up.[3] Further diagnostic studies should be performed after discussion with radiologists/nuclear medicine physicians.

4 CT

4.1 For further diagnostic workup, CT of the abdomen should be one of the first investigations since it has a high diagnostic yield, with reported yield rate being 19%.[6,9]

4.2 No definite evidence to support CT thorax for evaluation of pyrexia of unknown origin. Consideration of the investigation should be based on patient's clinical history, physical examination, laboratory test and initial chest radiographic findings.

5 Nuclear Medicine

5.1 Gallium scan and white blood cell (WBC) scan

5.1.1 Conventional scintigraphic methods are Ga-67 citrate scintigraphy, In-111 labeled or Tc-99m labeled WBC scintigraphy. These techniques have their disadvantages and limitations, such as handling of potentially infected blood products (labeled WBC scintigraphy), and the relatively long time span between injection and diagnosis.[14]

5.2 F-18 FDG PET-CT

5.2.1 Compared with conventional scintigraphy, advantages of FDG PET-CT include higher resolution, higher sensitivity in chronic low-grade infections, higher accuracy in the central skeleton, as well as shorter time period between injection of the radiopharmaceutical and the imaging procedure. Furthermore, FDG shows an increased vascular uptake in patients with vasculitis.[14]

5.2.2 Beside, FDG is accumulated in various types of malignancy, which can be a cause of pyrexia of unknown origin.

6 US

6.1 Venous thrombosis is a cause of prolonged fever. Studies revealed that it is a cause of pyrexia of unknown origin in 2-6%.[6,13] Although deep vein thrombosis (DVT) accounts for a small percentage of pyrexia of unknown origin, Doppler US is a safe method to identify the treatable cause.[6]

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