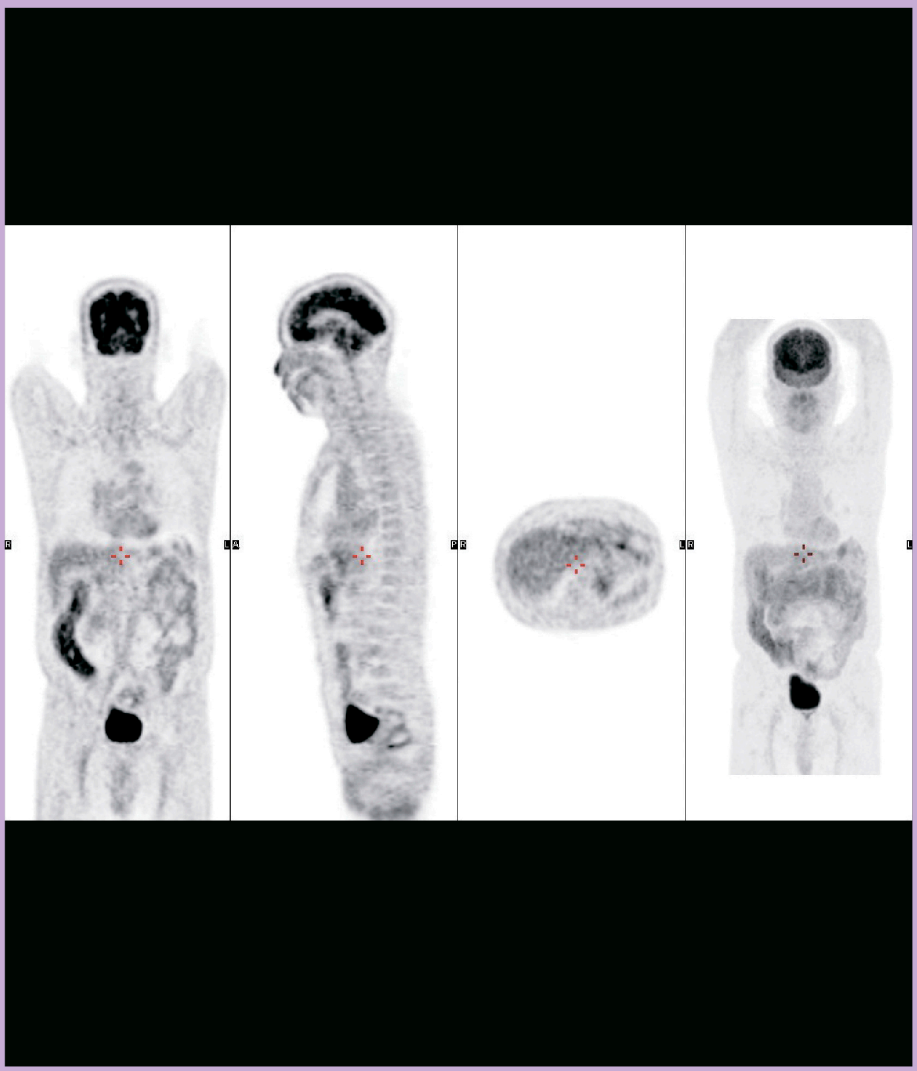
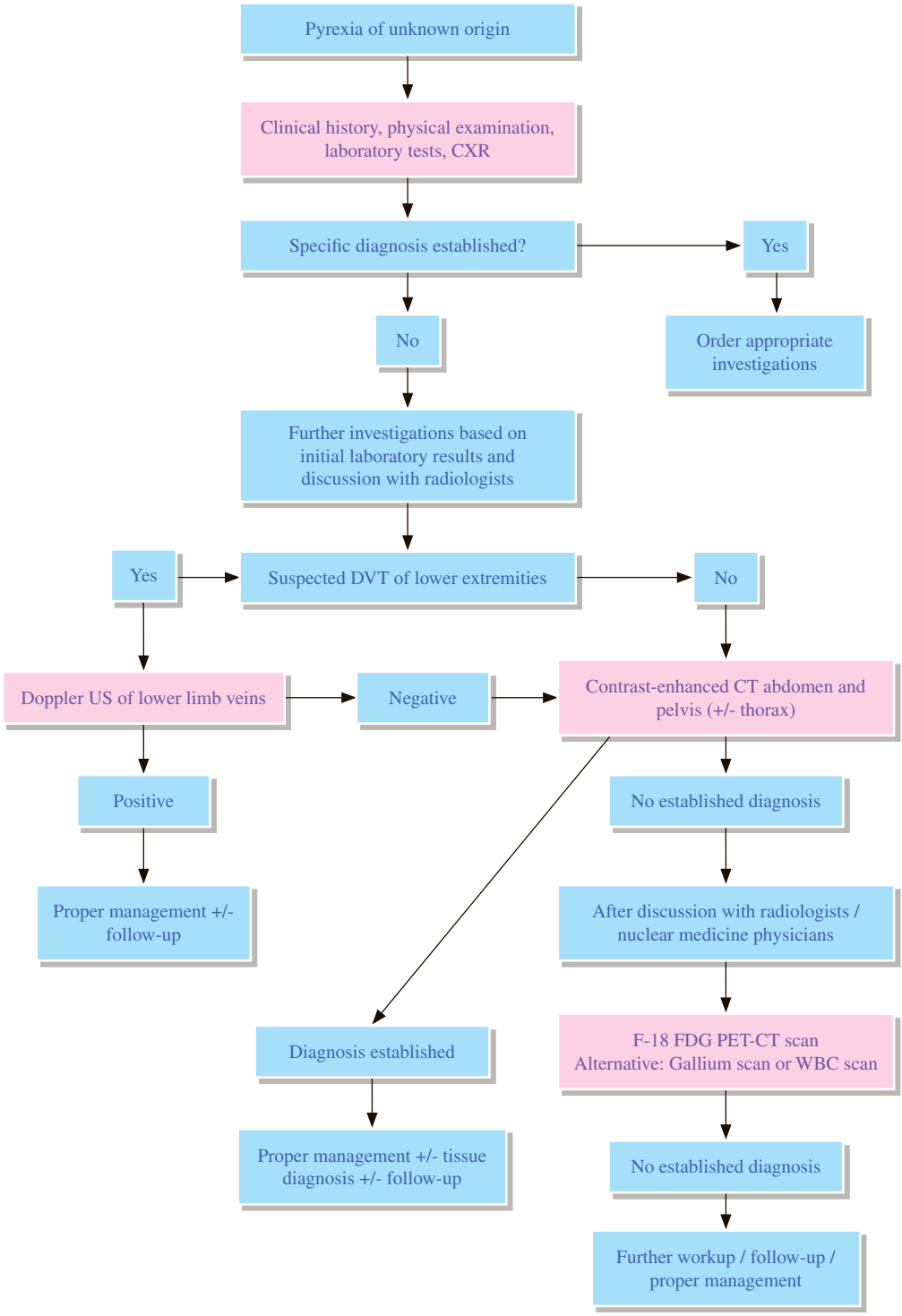
Miscellaneous



Hong Kong College of Radiologists


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
No established diagnosis
Proper management +/- follow-up
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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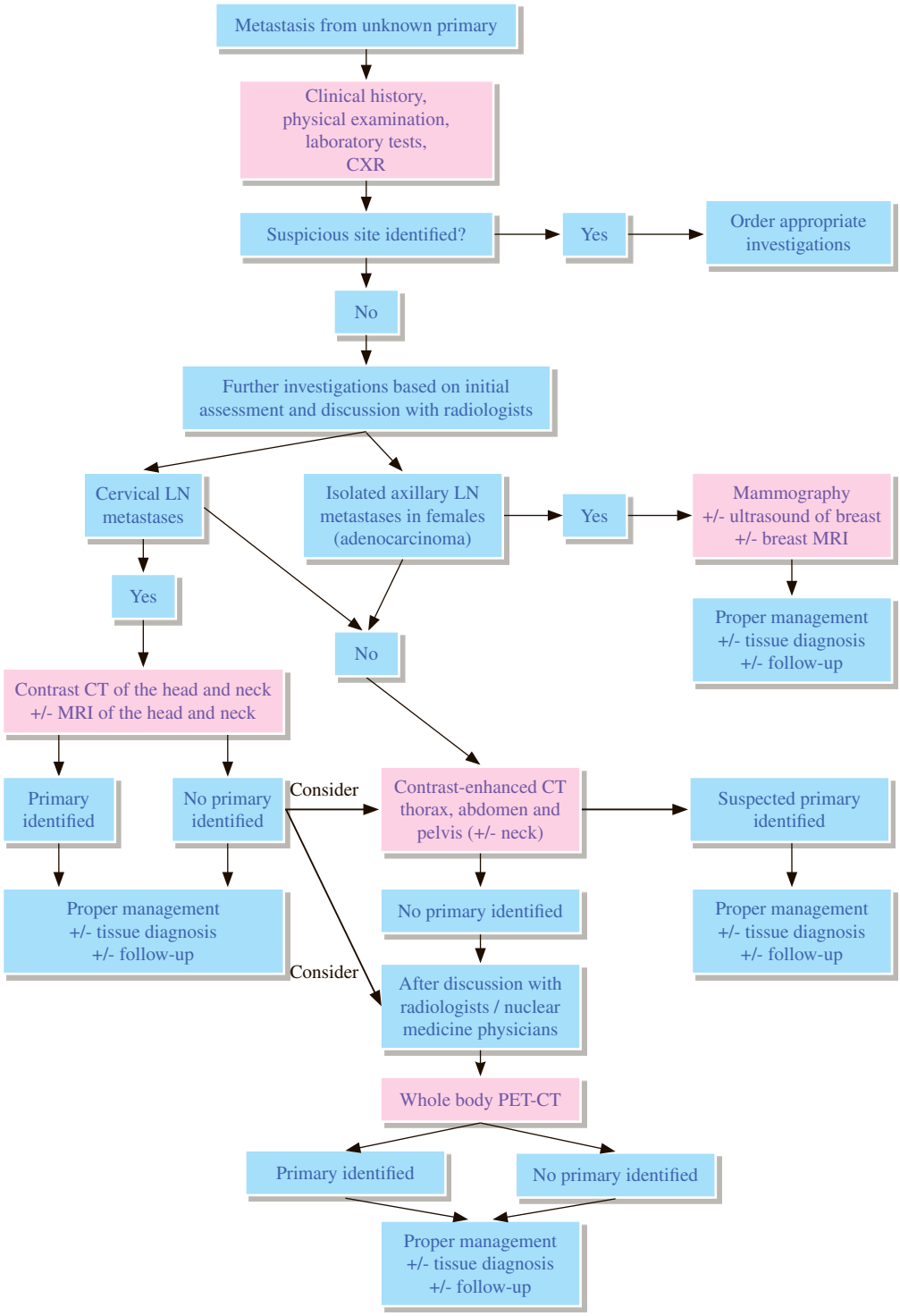
MC 2 Metastases from unknown primary



REMARKS

1 General

1.1 'Cancer of unknown primary' refers to a condition in which a patient has metastatic malignancy without an identified primary source, which is a very heterogeneous disease.[1]

1.1.1 Different terms have been used to differentiate patients at different stages of investigative pathway[1]

1.4.1.1 'Malignancy of undefined primary origin'—metastatic malignancy identified on the basis of a limited number of tests, without an obvious primary site, before comprehensive investigation

1.1.1.2 'Provisional carcinoma of unknown primary'—metastatic epithelial or neuroendocrine malignancy identified on the basis of histology/cytology, with no primary site detected despite a selected initial screen of investigations, before specialist review and possible further specialized investigations

1.1.1.3 'Confirmed carcinoma of unknown primary'—metastatic epithelial or neuroendocrine malignancy identified on the basis of final histology, with no primary site detected despite a selected initial screen of investigations, specialist review and further specialized investigations as appropriate

1.2 Incidence is about 3-5% of all cancers registered in the United Kingdom.[1,2]

1.3 Chest X-ray (CXR) and CT scan of the chest, abdomen and pelvis are among the initial radiological investigations offered to patients with malignancy of undefined primary origin, depending on patient's symptoms.[1,3]

2 Radiography

2.1 Lung Cancer is the most common cause of metastasis from unknown primary.[2,4] CXR is a cheap and very rapidly performed test to detect lung cancer.[2]

3 CT

3.1 CT of the thorax, abdomen and pelvis with the use of intravenous contrast material is a useful initial investigation.[1,2,3,5,6]

3.2 The recommendation of CT thorax is also based on its better detection of lung cancer than CXR.[5,7]

3.3 Contrast-enhanced CT of the head and neck is also useful for identification of primary tumour in patients with cervical lymph node metastases from unknown head and neck primary cancers.[8,9,10]

4 Breast Imaging

4.1 Do not routinely offer mammography to women with metastasis from unknown primary unless clinical or pathological features are compatible with breast cancer.[1]

4.2 Breast MRI should be considered in women presenting with isolated axillary adenopathy which is adenocarcinoma on histology and suspicious of breast primary, after negative initial mammography and ultrasonography.[1,2,5]

5 MRI

5.1 MRI has superior soft tissue contrast for head and neck imaging.[8,11]

6 PET scan

6.1 Whole-body Fluorodeoxyglucose (FDG) PET-CT may contribute to the management of patients with cervical adenopathies from occult primary and those with a single metastasis from occult primary. For other cases of metastases from occult primary, the role of FDG PET-CT is limited.[13]

6.2 FDG PET-CT is not recommended in routine systematic work-up for all cases of metastasis from occult primary.[13,14]

6.3 FDG PET-CT may be warranted in cases considered for local or regional therapy.[14]

7 Image-guided biopsy

7.1 It is recommended that needle core biopsy or surgical biopsy should be obtained for histological assessment for evaluation of metastasis from unknown primary.[1,2]

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