Seminars in Diagnostic Pathology 33 (2016) 358–366

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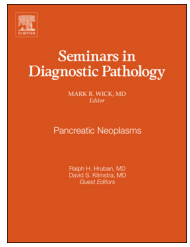

Inflammatory myofibroblastic tumour

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ARTICLE INFO

Keywords:
Inflammatory
Myofibroblastic
Tumor

ABSTRACT

While initially controversial, the proposal that a subset of inflammatory pseudotumours were myofibroblastic neoplasms is now acknowledged. Inflammatory myofibroblastic tumour is a spindle cell neoplasm of intermediate biological potential that may arise in a wide range of anatomic sites but has a particular propensity for the lung and abdominal soft tissues. Depending on its location, IMT may present with a variety of clinical symptoms and it may also express a variable pathologic phenotype, leading to a broad range of clinical and pathological differentials. Recent discoveries about the molecular signatures of IMT not only provide additional tools to assist in their diagnosis, they also point to possible therapeutic interventions that may transform the management algorithms for patients with this condition.

Introduction

The past 20 years have seen a profound evolution in our understanding of inflammatory myofibroblastic tumours (IMT). In the 1990s, IMT as we now recognise it, was still lost amidst the noise of inflammatory pseudotumours, an umbrella term that encompassed an array of infectious, reactive and reparative processes.[1] However, astute clinico-pathologic observation, led by Pepper Dehner and colleagues suggested that in the midst of this confusing melee, a discrete subset existed that could be defined as true myofibroblastic neoplasms, despite the presence of a conspicuous inflammatory background.[2] While initially controversial, this proposal was ultimately confirmed as evidence of clonal aberrations was detected in this subgroup at the turn of the century.[3] Recognition that these genetic anomalies frequently involved translocations of the ALK gene soon followed and we now know that a whole host of translocations involving a range of kinases underpin this tumour.[4] These revelations have not only identified molecular signatures that can assist in diagnosis, they have also provided therapeutic targets for specific drug interventions that have already impacted on lives of patients with this condition.[5] The speed and extent of this progress has been breath-taking. As such, IMT provides a paradigm for the rapid benefits that may ensue from thoughtful collaborative exploration of any rare disease. As is the case with many paediatric tumours, Pepper's insights were critical to the early steps in this evolution and he has continued to contribute to the literature in the area. Furthermore, many of the seminal observations made over this time period have come from pathologists who trained under and subsequently worked alongside Pepper who, no doubt, both piqued their interest in this once enigmatic tumour and then provided them with the skill set to unravel the biological mystery at its heart.

Site and clinical presentation

IMT is uncommon, afflicting no more than 150–200 children in the USA.[6] While most commonly arising in the lung and deep intra-abdominal soft tissues, IMT has been reported at a wide variety of body sites including skin, heart, mediastinum H&N intracranial liver, GIT, skin testis and bone. The most commonly involved intra-abdominal site is the mesentery, comprising 34% of all extra-pulmonary lesions and 60% of soft tissue cases.[2,7] Omental and retroperitoneal sites are also common and, given a significant overlap, it is perhaps more appropriate to regard these

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http://dx.doi.org/10.1053/j.semdp.2016.08.007
0740-2570/

as a single disease location in which case they comprise almost half of extra-pulmonary IMTs.[7] Other less common sites include the pelvic soft tissue, subcutaneous tissue, skeletal muscle and even bone.[2,7,8] The mediastinum can be involved as a primary site or by extension from a pulmonary lesion and direct invasion of chest wall from pulmonary lesions is also recognised.[2]

Not surprisingly, the range of clinical presentations reflects these different locations and a potentially bewildering array of symptoms may potentially be attributable to IMTs arising in particular body sites. Thus pulmonary IMT may be associated with cough, dyspnoea and chest discomfort, while the rare cardiac IMT often presents with dyspnoea, syncope or angina.[2,9–11] Meanwhile, soft tissue IMT are most frequently identified as asymptomatic abdominal masses although they may also induce abdominal pain, bowel obstruction and jaundice.[7]

One of the more intriguing aspects of this neoplasm is the propensity for paraneoplastic constitutional symptoms that can provide an important clinical clue to the diagnosis. While rare in lung IMT, up to one-third of patients with extra-pulmonary IMT exhibit a characteristic syndrome of intermittent fever, malaise and weight loss with or without night sweats.[12] Laboratory evaluation frequently detects corresponding abnormalities including hypochromic, microcytic, or normochromic anaemia, and an elevated sedimentation rate. In up to 10% of cases, serum immunoglobulin levels may be increased.[2] These systemic symptoms have been attributed to cytokines produced or triggered by the IMT, in particular interleukin 6 and there is evidence to support this contention.[13] Recrudescence of these constitutional symptoms may herald a recurrence of the IMT that gave rise to them.[14,15]

Age

IMT has been reported in patients of all ages, from new-born to the elderly.[16] However, it is most frequently a disease of children and young adults. Extra-pulmonary IMT presents at a younger age than its pulmonary counterpart, with average age 9.7 years as opposed to 29.6 years in two large series.[2,7] There is no obvious gender predilection.

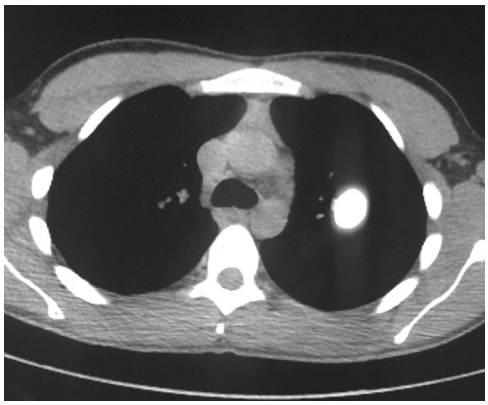

Fig. 1 – PET CT showing discrete high signal lesion within the pulmonary parenchyma.

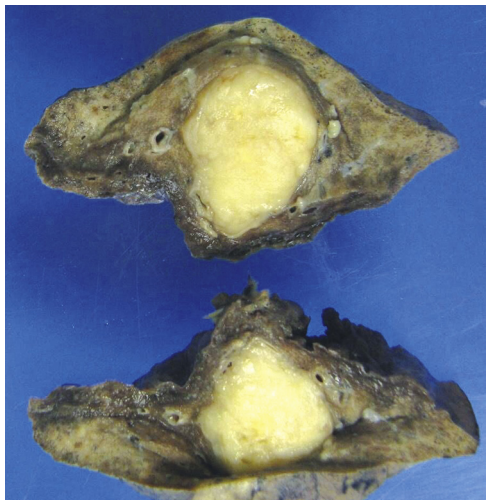

Fig. 2 – Gross image of discrete, firm pulmonary parenchymal IMT.

Radiological findings

The wide range of potential sites, varying gross appearance and the absence of specific radiological features mean that a confident diagnosis of IMT is rarely possible on imaging alone (Fig. 1). However, imaging studies are obviously critical to the localisation of these lesions and the documentation of their extent. Nonetheless, when a mass lesion in a child or young adult in any location is associated with the typical constitutional symptoms, it is incumbent upon the radiologist to include IMT in the differential diagnosis.[7,17]

Pathologic features

Pulmonary lesions may present as endobronchial masses or isolated, circumscribed but not encapsulated coin lesions or irregular masses that infiltrate chest wall or mediastinum (Figs. 2 and 3).[7] They tend to be relatively small, averaging 4 cm at presentation but larger lesions are recognised.[2]

Visceral lesions may be polypoid projections into the lumen or infiltrative masses within the wall of an organ.[18,19] Macroscopically, IMT in deep soft tissue are usually bulkier than those seen in the lungs, and may extend up to 17 cm.[7] Lesions in more accessible other locations may present when quite small.

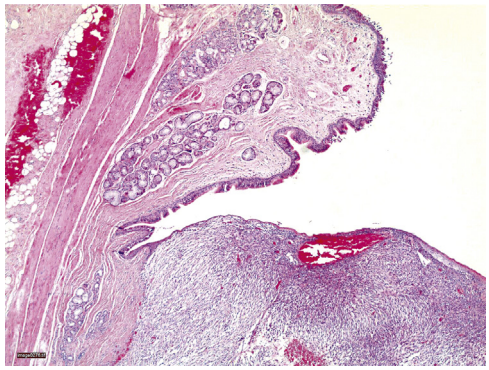

Fig. 3 – Polypoid, endobronchial IMT.