Pseudochylothorax, an Unknown Disease

To the Editor:

I congratulate Dr. Wrighton and colleagues on the excellent paper recently published in CHEST (October 2009) about their experience with six cases of arthritis-associated pseudochylothorax without pleural thickening and short duration of symptoms. I absolutely agree with them: The pathogenesis of pseudochylothorax has not been clarified yet. The very low incidence (around 190 cases reported) of this probably underdiagnosed disease has historically constituted, in my opinion, the major obstacle for the performance of randomized trials and the availability of clinical and research resources.

The authors state that “the medical literature has always emphasized that a hallmark of pseudochylothoraces is the presence of a grossly thickened (fibrotic) pleura…[and] that a pleural inflammatory process of at least 5 years is required for its development.”

Previously, almost all our knowledge about pseudochylothorax comes from case reports and retrospective descriptive reviews, so that definitive statements should be difficult to make. In our review of 174 cases published until 1999, we found a “remarkable association of pseudochylothorax with long-term effusions,” but we also pointed out that 16 patients (9%) had a pleural effusion of <5 years of evolution, one of them of 4 months, due to echinoceciosis, as had already been reported in 1975.

Pleur on pseudochylothorax presents most frequently as chronic inflammation and/or fibrous tissue, as revealed by performed biopsies, and seems to have a low yield for etiologic diagnosis (17% in tuberculous and 15% in nontuberculous cases in our review). On the other hand, as the authors comment, Hamm et al demonstrated a peak in the high-density lipoprotein region and a lack of low-density lipoprotein cholesterol in pseudochylo us fluid. They theorized that trapped cholesterol changed its lipoprotein-binding characteristics, possibly due to local metabolism, but could not rule out other mechanisms, so the precise pathogenic mechanism of cholesterol accumulation in pseudochylothorax remains unknown.

I find of great interest the experience of the authors on controlling or even diminishing the pleural fluid volume with disease-modifying antirheumatic drugs. In our experience, even successful treatment of an acute tuberculous pleurisy did not preclude the eventual development of pseudochylothorax, and we recommended to follow up closely residual effusions after appropriate treatment. As a final comment, it is in my opinion highly likely that TB will unfortunately remain the leading cause for pseudochylothorax during the next decades, due to the current high incidence of TB and the increasing problem of drug resistance, which could decrease the effectiveness of the antituberculous treatment.

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REFERENCES


Pseudochyle is defined by a high pleural fluid cholesterol concentration or cholesterol crystals. It has been implied, although not definitively proven, that pseudochyle might actually represent a common end point of a variety of disease pathophysiologic conditions; those associated with TB may arise from a separate mechanism from those associated with arthritis. Expansion of such a theory could provide a plausible explanation for the diversity in rates of formation of pseudochyle and other pathologic findings (such as degree of pleural thickening), as seen in our series.

Conventionally, pseudochylothorax is viewed as a single disease entity; this preconception should be challenged. The majority (54%) of the published cases of pseudochylothorax were associated with TB, followed by rheumatoid arthritis (9%). A large number of other conditions has also been implied, although each has been linked with very few cases of pseudochylothorax. Pseudochyle is defined by a high pleural fluid cholesterol composition (presence of cholesterol crystals on microscopic examination or cholesterol concentration > 200 mg/dL). This definition makes no assumption about the underlying pathogenetic mechanisms leading to pseudochyle formation. The previous literature has always associated pseudochylothorax with significant pleural thickening (a complication relatively common in TB) and assumed the fibrotic pleura plays a role in the accumulation of cholesterol within the pleural cavity. Our report of six cases of pseudochylothoraces—all associated with arthritis—without pleural thickening (a complication relatively common in TB) and without significantly thickened pleura contradicts such belief. Rather than one unifying mechanism resulting in pseudochyle formation, it is possible that pseudochyle actually represents a common end point of a variety of disease pathophysiologic conditions; those associated with TB may arise from a separate mechanism from those associated with arthritis. Expansion of such a theory could provide a plausible explanation for the diversity in rates of formation of pseudochyle and other pathologic findings (such as degree of pleural thickening), as seen in our series.

Differing pathogenetic mechanisms may also underlie the differing clinical outcomes. Regardless of underlying pathology, it would seem reasonable to propose better outcomes of pseudochylothoraces with nonfibrotic pleura, as seen in our cohort, over those with dense pleural thickening.

Like Dr Garcia-Zamalloa, we suspect that pseudochylothorax is underdiagnosed. Up to 20% of pleural effusions remain undiagnosed in routine clinical practice, and pleural fluid cholesterol concentration is infrequently evaluated, especially in the absence of extensive pleural thickening. A prospective study of pleural fluid cholesterol concentration (and cholesterol crystals) in undiagnosed pleural effusions will help determine the degree of underdiagnosis of this condition.

Specifically with regard to arthritis-associated pseudochylothoraces, our patients demonstrated pleural fluid volume control or reduction with intensified rheumatoid arthritis treatment. One could postulate that many patients with inflammatory arthritis may develop pseudochylothorax at some point during the evolution of their disease; the pseudochyle may remain uninvestigated and undiagnosed if subsequent intensification of arthritis treatment results in resolution of the pleural effusion.

Improved physician awareness of pseudochylothorax should improve rates of diagnosis. Cumulative knowledge may lead to new and testable hypotheses regarding the disease pathogenesis and, ultimately, much-needed studies on better treatment of pseudochylothorax.

To the Editor:

We thank Dr Garcia-Zamalloa for his comments regarding our case series of patients with arthritis-associated pseudochylothorax who did not have significant pleural thickening (October 2009). 1 We agree that the low number of reported cases has hitherto prevented a robust description of the pathogenesis and natural history of pseudochylothorax. Hopefully, our case series serves to add to our understanding of the disease.

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Solitary Fibrous Tumors of the Pleura: An Estimation of Population Incidence

To the Editor:

Primary tumors of the pleura present as either diffuse malignant mesotheliomas or localized solitary fibrous tumors of the pleura (SFTPs), the majority of which are benign. We have used nationwide registries in Iceland to study SFTP and establish an age-standardized incidence rate ([ASR] world standard population), which has not been previously reported. All patients diagnosed with histologically proven SFTP in Iceland from 1984 to 2007 were identified through a centralized pathology registry. For comparison, information on mesotheliomas was obtained from the population-based Icelandic Cancer Registry.

Eleven patients were diagnosed with SFTP (mean age 60 years; eight women) compared with 33 with mesothelioma (mean age 68 years; four women) (Table 1). The ASRs for SFTP and mesothelioma were 1.4 and 4.0 per million (95% CI, 0.54-2.2 and 2.6-5.4), respectively. All cases of SFTP had a benign histology. Only three cases were symptomatic (dyspnea, pneumonia, pleuritic pain), with eight incidentally detected. Apart from one case diagnosed at autopsy, all patients with SFTP were treated with complete surgical resection of the tumor. Average tumor diameter was 6.5 cm (range, 1.3-20 cm) and weight was 130 g (range 5-3,260 g), with eight of the tumors arising from the visceral and parietal pleura (SFTPs), the majority of which are benign. We have used nationwide registries in Iceland to study SFTP and establish an age-standardized incidence rate ([ASR] world standard population), which has not been previously reported. All patients diagnosed with histologically proven SFTP in Iceland from 1984 to 2007 were identified through a centralized pathology registry. For comparison, information on mesotheliomas was obtained from the population-based Icelandic Cancer Registry.

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