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REVIEWS

# Contarini's Syndrome: Bilateral Pleural Effusion, Each Side From Different Causes

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Bilateral pleural effusions usually have a single causative factor, such as heart failure or malignancy. Contarini's syndrome refers to the occurrence of bilateral pleural fluid accumulation which can be explained by a different cause for each side. Literature search finds, along with 5 new descriptions from our center, totaled 12 cases. A frequent combination is that of a parapneumonic effusion that triggers heart failure, which in turn produces a contralateral transudate. *Journal of Hospital Medicine* 2012;7:164–165.


The application of Ockham's razor, or the law of parsimony, to clinical reasoning implies selecting the competing hypothesis that makes the fewest new assumptions based on known factors. Thus, the prevailing hypothesis when confronting a patient with a bilateral pleural effusion would be that a single disease likely explains the accumulation of pleural fluid on both sides. Although the principle of diagnostic parsimony has become axiomatic for the differential diagnosis of diseases, it might not hold true for all cases. That is, the counterpart to Ockham's razor, known as Hickam's dictum, states that "patients can have as many diseases as they damn well please." An example is Contarini's condition. Francesco Contarini (1556-1624) died 1 year after he became the 95th Doge of Venice. The postmortem study revealed a right pleural effusion, probably due to heart failure and a contralateral empyema.[1] Since then, it became apparent that bilateral pleural effusions might have more than a single explanation. To improve knowledge of this entity, coined as Contarini's condition by Kutty and Varkey in 1978,[2] we systematically searched for cases from a large prospectively maintained pleural fluid database at the Arnau de Vilanova University Hospital (Lleida, Spain), a 470-bed general medical center serving a population of 400,000 inhabitants. An analysis of previously documented cases was also performed.

Information was gathered from all consecutive patients who have undergone pleural fluid aspiration and analysis during the last 16 years at our institution. Medical records were screened of those patients submitted to bilateral thoracentesis, during a single hospital admission, that resulted in pleural fluids with markedly different biochemical characteristics. Written informed consent was obtained from all patients to use their clinical data in future investigations. The local ethics committee approved this study. In addition, the Embase and PubMed databases were searched using the keywords "Contarini's condition," "Contarini's syndrome," and "bilateral pleural effusion" to identify all previously reported cases. Pleural effusion etiology and definition of transudate/exudate were established by standard criteria. Specifically, complicated parapneumonic effusion referred to those pneumonia-associated non-purulent effusions that needed a tube thoracostomy for resolution.

Of 2605 patients from our database, 546 (21%) had bilateral pleural effusions, mostly due to heart failure (286 patients) and malignancy (102 patients). There were only 5 (0.9%) patients who had bilateral effusions of different etiologies which, added to an additional 7 patients identified via literature review,[1-7] totaled 12 cases. Their characteristics are summarized in Table 1. However, it should be noted that 4 of the 7 previously reported cases were described as the concurrence of chylothorax and malignant effusion.[3-5,7] This combination may result from a common causative factor (ie, lymphoma or metastatic carcinoma), thus bringing into question their status as valid examples of Contarini's condition. Aside from these cases, bacterial infections (ie, parapneumonics and empyema) represent the most common coexisting disease in Contarini's cases, particularly in association with heart failure (50% of the cases). The reason behind this is that pneumonia may precipitate an acute decompensation of heart failure. In a recent study, 7.4% of 33,130 patients developed heart failure during hospitalization for pneumonia.[8]

Kalomenidis et al. studied 27 patients with bilateral pleural effusions who underwent bilateral

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**TABLE 1.** Clinical Characteristics of 12 Cases of Contarini's Syndrome, Previous and Present Reports

| Reports | Age/Sex | Characteristics of the Right-Sided Effusion | Characteristics of the Left-Sided Effusion | Right/Left-Sided Effusion Diagnoses | Notes |
|---|---|---|---|---|---|
| Reference | | | | | |
| Jarcho[1] | 68/M | Watery | Pus | Heart failure/empyema | The patient was named Francesco Contarini. Final diagnoses result from a retrospective interpretation of the autopsy study performed 3½ centuries earlier. |
| Kutty and Varkey[2] | 57/M | Lymphocytic exudate with negative culture | Neuthophilic exudate with positive culture for *S. aureus* | Probable malignant (leukemia)/empyema | No cytological or histological pleural studies were performed on the right side. |
| Lawton et al.[3] | 57/F | Straw-colored, positive malignant cytology | Chylous, positive malignant cytology | Malignant (SVC syndrome)/malignant chylothorax | The autopsy study showed tumor thrombosis of SVC and metastatic mediastinal lymphadenopathy from an ovarian adenocarcinoma. |
| Fred[4] | ND/M | Chylous with negative cytology | Bloody, with positive cytology consistent with lymphoma | Chylothorax/malignant | Lymphoma could have eventually explained both chylothorax and malignant effusion. |
| Brannen and Berman[5] | 48/F | Chylous with negative cytology | Straw-colored exudate with negative cytology | Chylothorax/probable malignant | A non-Hodgkin's lymphoma was responsible for the bilateral effusions. Pleural fluid triglyceride levels were not available on the left side. |
| Dixit et al.[6] | 23/M | Pus, positive culture for *S. aureus* | Lymphocytic exudate, smear positive for acid-fast bacilli | Empyema/tuberculosis | The patient tested positive for HIV infection. |
| Khan et al.[7] | 46/F | Serous, positive cytology | Milky, negative for malignancy | Malignant/chylothorax | The patient had metastatic ovarian carcinoma. |
| Current series | | | | | |
| Patient 1 | 79/M | Neutrophilic exudate with normal pH and glucose; negative cytology and culture | Transudate | Subphrenic abscess/hypervolemia due to perioperative excessive volume load | The patient had acute cholecystitis. |
| Patient 2 | 49/F | Transudate | Neutrophilic exudate with pH 7.1, glucose 1 mg/dL, and detection of pneumococcal antigen in pleural fluid | Pericardial disease/simple parapneumonic effusion | Pericardial involvement was considered secondary to pneumococcal disease. Left-sided effusion cured only with antibiotics. |
| Patient 3 | 73/M | Neutrophilic exudate with pH 7, glucose 9 mg/dL, and negative cultures and cytology | Borderline lymphocytic exudate with normal pH and glucose, and negative cultures and cytology | Complicated parapneumonic effusion/radiation pleuritis | The patient had a history of radiotherapy for a gastric adenocarcinoma. |
| Patient 4 | 57/M | Pus | Transudate | Empyema/heart failure | |
| Patient 5 | 76/M | Transudate | Neutrophilic exudate with pH 7.1 and negative cultures | Heart failure/complicated parapneumonic effusion | |

Abbreviations: HIV, human immunodeficiency virus; ND, no data available; SVC, superior vena cava.

thoracentesis to determine if the findings were the same.[9] They found that the main biochemical and cellular features on both sides were generally similar, except for 2 (7.5%) cases which had significantly different pleural fluid lactate dehydrogenase (LDH) levels. Although a plausible explanation for the latter was not given, this circumstance did not change the categorization of the effusions. The authors concluded that bilateral diagnostic thoracenteses were not necessary unless there was a specific clinical indication. The fact that most patients with bilateral pleural effusions are submitted to a unilateral thoracentesis may have resulted in an underestimation of the current prevalence of Contarini's syndrome. In our series, differing lung and pleural computed tomographic (CT) imaging characteristics between both hemithoraces was the primary reason for performing bilateral pleural taps in all 5 cases. After the dual diagnosis, the corresponding patients benefited from an additional therapeutic intervention, mainly treatment for heart failure. Therefore, the rationale to exceptionally consider a bilateral diagnostic thoracentesis is to avoid missing significant pathology by sampling the wrong pleural space (in particular, one caused by heart failure) and thus failing to properly diagnose contralateral exudative effusion with an attendant serious etiology.

In conclusion, Contarini's syndrome is a rare and distinct entity, but probably underdiagnosed. Although a bilateral pleural fluid aspiration is seldom justified in routine clinical practice, it should be considered if any of the following are met: unilateral parenchymal lung involvement, significantly disparate-sized effusions, markedly different attenuation values (Hounsfield units) or appearance (eg, unilateral pleural loculations or enhancement) on CT, atypical clinical findings (fever or pleuritic chest pain in the context of decompensated heart failure), resolution of pleural effusion only on 1 side, and the diagnosis of pleural diseases usually associated with unilateral effusions (eg, pneumonia). However, it should be stressed that these are expert, rather than evidence-based, recommendations.

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## References


1. Jarcho S. Empyema or hydrothorax in the ninety-five Doge of Venice. *Bull N Y Acad Med.* 1970;46:378–385.
2. Kutty CP, Varkey B. "Contarini's condition:" bilateral pleural effusion with markedly different characteristics. *Chest* 1978;74:679–680.
3. Lawton F, Blackledge G, Johnson R. Co-existent chylous and serous pleural effusions associated with ovarian cancer: a case report of Contarini's syndrome. *Eur J Surg Oncol.* 1985;11:177–178.
4. Fred HL. Contarini's condition. *South Med J.* 1992;85:33–34.
5. Brannen AL II, Berman EJ. Contarini's condition: paradise regained. *South Med J.* 1992;85:1153–1154.
6. Dixit R, Joshi N, Nawal CL. Contarini's syndrome in a HIV positive patient. *J Assoc Physicians India* 2004;52:841–842.
7. Khan Z, Miller A, Badhey K, Bachan M. Contarini syndrome resulting from ovarian carcinoma [abstract]. *Chest* 2007;132:703S.
8. Perry TW, Pugh MJ, Waterer WG, et al.Incidence of cardiovascular events after hospital admission for pneumonia. *Am J Med.* 2011;124: 244–251.
9. Kalomenidis I, Rodriguez M, Barnette R, et al.Patient with bilateral pleural effusion. Are the findings the same in each fluid? *Chest* 2003; 124:167–176.