CASE REPORT

Case Report: Sarcoidosis with azygos vein enlargement mimicking metastatic cancer [version 1; peer review: awaiting peer review]

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Abstract

Sarcoidosis is a systemic disease with heterogeneous clinical manifestations that is characterized histologically by the presence of noncaseating granulomas in the affected organs. It can be a diagnostic challenge, especially when mimicking malignancy or fungal infections. Previous case reports of sarcoidosis presenting with multiple masses are highly suggestive of infectious or malignant etiology. In this case, our patient presented with enlarged lymph node and was found to have innumerable nodules in the mediastinum, lungs, and liver. Azygos vein enlargement was also seen on radiological imaging, and malignancy was highly suspected; hence, an extensive workup was conducted, including laboratory, radiology and biopsy evaluation, which were diagnostic of sarcoidosis. Our case showed the importance of correlation of the history, physical examination, radiological and histopathologic studies in confirming the diagnosis and the need to rule out other serious infections and malignancies, especially with azygous vein enlargement, which can sometimes be missed in chest radiograph.

Keywords
Sarcoidosis, Malignancy, Liver mass, Azygous vein
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Introduction
Sarcoidosis is a systemic inflammatory condition of unknown etiology that is characterized histologically by the presence of noncaseating granulomas in the affected organs. It is called the ‘great mimicker’ because it can present in various ways similar to other diseases. It can affect multiple organ systems, but most commonly involves the lungs and the lymph nodes. Other less commonly involved organs include the eyes, skin, liver, spleen, bone marrow, heart and brain. The age adjusted annual incidence of sarcoidosis in the United States is 35.5 per 100,000 for African Americans compared with 10.9 per 100,000 for Caucasians, according to a five-year cohort study. We present a case of asymptomatic cervical lymph node enlargement, multiple liver lesions and azygos vein enlargement, which were suggestive of malignant or infectious etiologies. However, investigations resulted in the diagnosis of the ‘great mimicker disease’ sarcoidosis.

Case presentation
A previously healthy 53-year-old Caucasian man on no regular medication presented to his primary care provider complaining of a painless slowly growing cervical lump that he noticed one month prior to presentation. Review of systems were negative for fever, weight loss, night sweat, fatigue, loss of appetite, cough, chest pain, hemoptysis, or shortness of breath. Family history was significant for lymphoma. The patient never smoked, and was not exposed to any chemicals at work. Physical examination showed normal vital signs and enlarged right cervical lymph nodes. The rest of the physical examination were unremarkable. Initial laboratory workup showed normal complete blood cell count and basic metabolic panel. (Table 1). A decision to proceed with fine needle aspiration was taken, which showed a non-necrotizing inflammatory reaction. Therefore, a core biopsy was recommended to rule out lymphoma and he was referred to the rheumatology clinic for possible sarcoidosis.

Three months after the initial presentation, he was seen in the rheumatology clinic; further workup was ordered, including an angiotensin-converting enzyme level which was normal, and chest radiograph (CXR), which showed azygos vein enlargement and thus a high suspicion of malignancy (Figure 1). Next, computed tomography (CT) scan of the chest was done and it showed pathologic lymph node enlargement within the thoracic inlet and mediastinum, innumerable bilateral small pulmonary nodules, and multiple liver cystic lesions concerning for metastatic disease. (Figure 2–Figure 4). Further metastatic workup with CT abdomen/pelvis showed multiple hepatic cysts without any other organ involvement (Figure 5). At the same time, histoplasma antigen/antibody were negative, and his erythrocyte sedimentation rate was within normal limit (Table 2). One month later, the patient was referred to the pulmonary clinic and underwent general surgery for an excisional biopsy on the most accessible lymph node, which showed non-caseating granulomas without evidence of malignancy, fungal or mycobacterial infection, and confirmed the diagnosis of sarcoidosis. The patient was subsequently started on tapered prednisone (40 mg for two weeks then 20 mg for two weeks then 10 mg for one month). Three months later, he had repeated imaging which showed the same lesions in the lungs and the liver that are of the same size. Therefore, as he was completely asymptomatic, a decision to discontinue prednisone with 1-year radiology imaging follow-up was taken.

Table 1. Complete blood count and blood chemistry.

<table>
<thead>
<tr>
<th>Component (latest reference range, units)</th>
<th>On first presentation</th>
<th>3 months after first presentation</th>
<th>5 months after first presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (70–100 mg/dl)</td>
<td>88</td>
<td>102 (High)</td>
<td>119 (High)</td>
</tr>
<tr>
<td>BUN (6–24 mg/dl)</td>
<td>11</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Creatinine (0.60–1.30 mg/dl)</td>
<td>0.84</td>
<td>0.91</td>
<td>1.06</td>
</tr>
<tr>
<td>Sodium (125–145 mmol/l)</td>
<td>139</td>
<td>140</td>
<td>142</td>
</tr>
<tr>
<td>Potassium (3.7–5.1 mmol/l)</td>
<td>4.8</td>
<td>4.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Chloride (96–110 mmol/l)</td>
<td>102</td>
<td>106</td>
<td>109</td>
</tr>
<tr>
<td>Calcium (8.5–10.5 mg/dl)</td>
<td>9.4</td>
<td>9.4</td>
<td>9.4</td>
</tr>
<tr>
<td>Total Protein (6.0–8.4 g/dl)</td>
<td>8.2</td>
<td>7.8</td>
<td>8.2</td>
</tr>
<tr>
<td>Albumin (3.5–5.0 g/dl)</td>
<td>4.5</td>
<td>4.2</td>
<td>4.0</td>
</tr>
<tr>
<td>Aspartate transaminase (10–40 U/l)</td>
<td>26</td>
<td>29</td>
<td>38</td>
</tr>
<tr>
<td>Alkaline phosphatase (33–138 U/l)</td>
<td>118</td>
<td>103</td>
<td>96</td>
</tr>
<tr>
<td>Bilirubin, total (0.0–1.5 mg/dl)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Alanine transaminase (12–78 U/l)</td>
<td>39</td>
<td>50</td>
<td>65</td>
</tr>
<tr>
<td>White blood cells (4.0–12.0×10^9/µl)</td>
<td>6.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red blood cells (4.30–5.90×10^12/µl)</td>
<td>5.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (13.5–17.5 g/dl)</td>
<td>16.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit (39.0–55.0%)</td>
<td>50.1</td>
<td></td>
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</tbody>
</table>
Figure 1. Chest x-ray showing right paratracheal soft tissue prominence (arrow) with ill-defined medial border consistent with mediastinal origin. Possibly Azygous vein enlargement.

Figure 2. Sagittal (A) and coronal (B) images in lung window showing multiple nodules in centrilobular (white arrowheads) and subpleural (black arrowheads) location consistent with peri lymphatic distribution that can be seen in cases of sarcoidosis. Incidental liver cysts are also noted.
Figure 3. CT chest scan showing enlarged mediastinal lymph node measuring 4.5 cm.

Figure 4. CT image showing the enlarged mediastinal lymph node and the hepatic nodules.
Table 2. Laboratory analysis for granulomatous disease markers.

<table>
<thead>
<tr>
<th>Component (reference, units)</th>
<th>3 months after first presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin converting enzyme (14–82 U/l)</td>
<td>30</td>
</tr>
<tr>
<td>Sedimentation rate (0–15 mm/h)</td>
<td>8</td>
</tr>
<tr>
<td>Histoplasma antibody (negative)</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Discussion

The clinical manifestations of sarcoidosis vary and can range from asymptomatic disease detected incidentally on imaging studies to the presence of constitutional symptoms and symptoms attributed to the organ system involved, to multiorgan failure. The diagnosis of sarcoidosis requires fulfillment of certain criteria, which include existence of typical clinical and radiological findings, histopathological evidence of noncaseating granulomas, and exclusion of other causes of granulomatous inflammation.

The azygos vein is formed by the union of the ascending lumbar vein and the right subcostal vein. It is usually too small to be seen on chest x-ray. The enlargement of the azygos vein on chest x-ray can be seen in multiple diseases, such as congestive heart failure, inferior vena cava thrombosis, and intrathoracic malignancy.

In this report, we present a patient with asymptomatic cervical lymph node and azygos vein enlargements, with innumerable lung bilateral nodules, hilar, para-esophageal and mediastinal lymph node enlargement and multiple liver nodules which were highly suspicious for malignancy or fungal infection. However, histological evaluation was consistent with sarcoidosis. To our knowledge, this is the first reported case of sarcoidosis and azygos vein enlargement. Hence, we conducted a systematic review of the literature for studies published from 1960 to October 2019 in PubMed, Scopus, Web of Science, and Cochrane Central databases. The following search terms were used: “sarcoidosis”, “azygos vein enlargement” and “malignancy”. Our search was limited to individuals aged 18 years and older. Our search revealed a total of three patients. None of the cases showed azygos vein enlargement.

Our findings were similar to previous cases reported by Oketani et al. who were among the first to report a case of sarcoidosis mimicking metastatic cancer. They reported a case of a 49-year-old female who was found to have mediastinal and intraabdominal lymphadenopathy on radiologic imaging, in addition to presence of space occupying lesions in the liver and the spleen, which raised suspicion for metastatic hepatocellular cancer. However, histologic examination of liver biopsy specimen showed evidence of noncaseating epithelioid granulomas suggestive of sarcoidosis, which responded to treatment with steroids. Giovinale et al. reported another case of a 55-year-old female who presented with weight loss and abnormal liver function tests. Imaging revealed the presence of abdominal lymphadenopathy, as well as hepatic and splenic lesions, which were thought to be related to metastatic cancer, as the patient has family history of colorectal cancer. However, histological examination of specimens obtained during exploratory laparotomy showed chronic granulomatous inflammation, and the
work up for neoplasia was negative. Finally, Jafari et al. reported a case of a 39-year-old male who was found to have hilar lymphadenopathy and a hepatic nodule on radiologic imaging, which were initially thought to be related to metastatic cancer; however, biopsy confirmed chronic granulomatous inflammation and a diagnosis of sarcoidosis was made after ruling out tuberculosis.

**Conclusion**
Azygous vein enlargement is a commonly missed finding on chest radiograph which can be a sign of underlying malignancy. However, it can also be seen in sarcoidosis. Further appropriate tests are required to confirm the underlying etiology.

**Data availability**
All data underlying the results are available as part of the article and no additional source data are required.

**Consent**
Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/parent/guardian/relative of the patient.

**References**

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