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CASE REPORT

Echogenic lymph nodes in the differential diagnosis of pediatric sarcoidosis

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Abstract
We present a delayed diagnosis of sarcoidosis in an 11-year-old girl by demonstrating ultrasonographic imaging findings of granulomatous cervical and abdominal lymph node involvement. Pulmonary interstitial fibrosis in addition to multicompartmental enlarged echogenic lymph nodes could be considered sarcoidosis. Punctate echogenic foci in the cervical lymph nodes should be considered in the differential diagnosis of sarcoidosis.

Keywords Pediatric · Lymph node · Sarcoidosis · Lung

Introduction

Bilateral diffuse parotid enlargement in children can be seen in various infectious and inflammatory diseases. Chronic inflammatory diseases, such as Sjögren's syndrome and sarcoidosis, are the preferential differential diagnoses of chronic parotitis [1]. Childhood sarcoidosis is an extremely rare disorder with an incidence reported as 0.22–0.27 per 100,000 per year among Danish children younger than 15 years [2]. Parotitis as an initial presentation of sarcoidosis has been reported to be extremely uncommon [3]. We herein report cervical, mediastinal and periportal lymphadenopathy, asymptomatic pulmonary parenchyma involvement, and uveitis in an adolescent girl who presented with parotitis and was ultimately diagnosed with sarcoidosis.

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Case presentation

An 11-year-old girl previously diagnosed with bilateral parotitis based on an enlarged, heterogeneous, and hypoechoic parotid gland on ultrasound (US) examination presented with cervical lymphadenopathy. Whole blood count evaluation showed elevated red blood cell count (5.1 Tpt/l), and monocyte count and fraction (1.3/µl, 15%) with decreased mean corpuscular volume (64 fl). Biochemical analysis revealed elevated lactate dehydrogenase levels (LDH: 456 U/l) along with normal C-reactive protein levels (0.4 mg/l) and erythrocyte sedimentation rate (ESR: 8 mm/h). Cervical US examination was requested. On US examination, bilateral parotid glands were heterogeneous and enlarged, and a increased number of intraparotid lymph nodes were depicted without significant echogenic foci considered to be chronic parotitis. In addition, bilateral enlarged anterior cervical lymph nodes were revealed with ovoid shape and intact hilum but increased echogenicity due to multiple punctate echogenic foci within the cortex (Fig. 1). The thyroid gland was found to be normal; no mass formation suggestive of thyroid carcinoma was depicted. Posterior anterior chest radiography was performed to determine any accompanying mediastinal lymphadenopathy. On radiography, there were bilateral interstitial patterns in addition to hilar and paratracheal enlargement considered to be lymphadenopathy (Fig. 2). Intravenous contrast-enhanced chest tomography demonstrated bilateral hilar

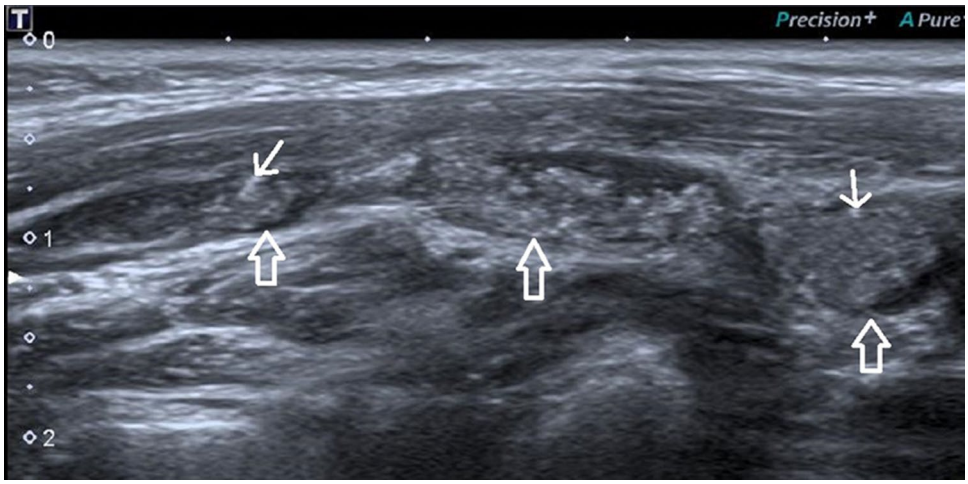

Fig. 1 Neck ultrasound examination shows multiple lymph nodes throughout anterior cervical lymphatic station with ovoid shape (closed arrow) and multiple millimetric echogenic foci within the cortex and also medulla. Most of the lymph nodes demonstrate central increased echogenicity with cortical echogenic foci. In the initial stages of sarcoidosis, histiocytic infiltration in lymph node sinus is seen

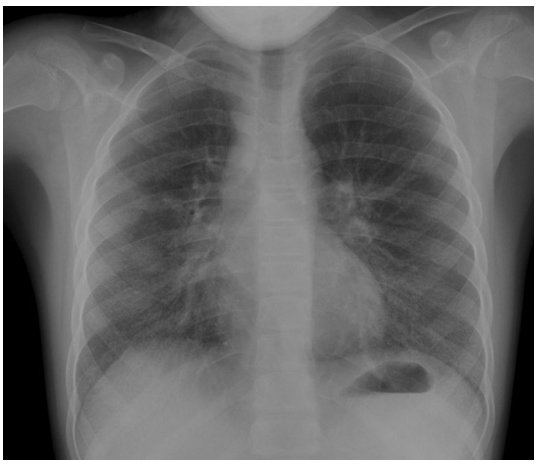

Fig. 2 Posteroanterior chest roentgenogram reveals bilateral hilar enlargement and reticulo-nodular interstitial pattern

and paratracheal pathological lymph nodes increased in size and number (Fig. 3). There was neither calcification nor necrosis. Parenchymal evaluation demonstrated bilateral ground glass opacification predominantly located in the basal and peripheral portion of the lungs along with subpleural sparing. There was interlobular septal thickening and tubular bronchiectasis considered to be interstitial fibrosis. Given the radiological findings, the main differential diagnoses were lymphoproliferative disease-associated interstitial pneumonia and granulomatous inflammatory diseases. Serum angiotensin-converting enzyme level was found to be elevated (168 U/L). Abdominal US revealed homogeneous liver and spleen with normal size. However, there were multiple echogenic and enlarged lymph nodes located in the periportal–perihilar region (Fig. 4). Based on the elevated LDH levels and lymphadenopathies, to exclude malignancy, cervical lymph node and salivary gland biopsy was planned. Histopathological examination confirmed non-caseating granulomas within the submandibular gland (Fig. 5). Histopathological lymph node evaluation revealed numerous homogeneously distributed uniform granulomas including epithelioid cells with scattered giant cells without remarkable necrosis. The patient was diagnosed with stage 3 sarcoidosis 5 years after the initial presentation with parotitis. Ophthalmological evaluation confirmed uveitis.

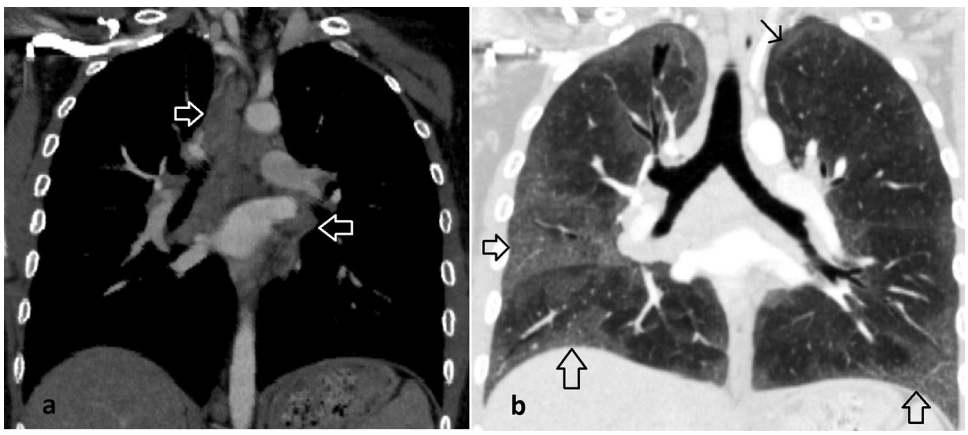

Fig. 3 Contrast-enhanced chest computed tomography with coronal reconstruction. **a** Mediastinum window; white arrows show mediastinal and bilateral lymphadenopathy. **b** Pulmonary parenchyma window demonstrating intralobular and interlobular interstitial thickening, and ground glass opacification (closed arrow) with subpleural sparing (open arrow) predominantly in the middle and lower zones

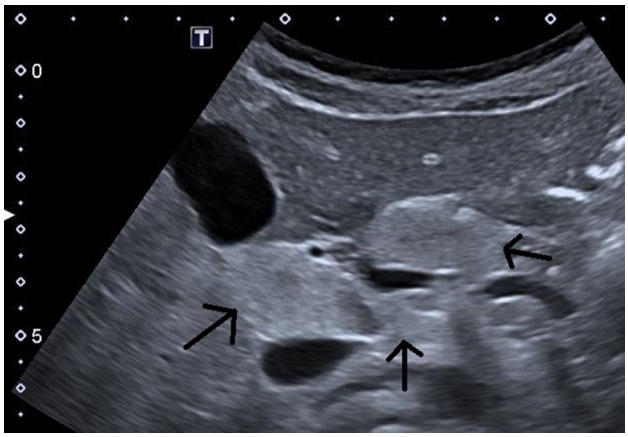

Fig. 4 Abdominal ultrasonography with a convex probe. Periportal and hilar echogenic and enlarged lymph nodes are depicted (arrow). Since we demonstrate the abdominal lymph nodes with a curved probe, the echogenic foci are seen as diffusely increased echogenicity in the lymph nodes because of limited axial resolution

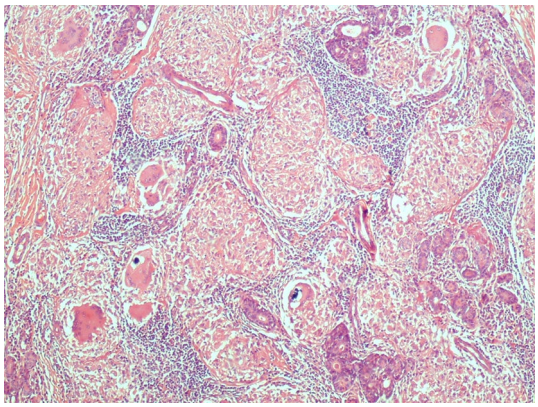

Fig. 5 Non-necrotizing granulomatous inflammation involving submandibular gland

Discussion

In the case presented, the diagnosis was achieved based on clinical presentation as chronic bilateral parotid enlargement; radiological findings, such as punctate echogenic granulomatous involvement of lymph nodes and interstitial lung disease; biochemical evaluation as elevated ACE levels; and histopathological evaluation revealing non-caseating granulomas devoid of any mycobacteria or fungi. Also, a tuberculin skin test was negative for tuberculosis contiguity. Granulomatous infections would be considered in cases with multi-compartmental enlarged lymph nodes. However, normal levels of white blood cells and C-reactive proteins along with negative staining for any microorganism eliminate infectious processes. LDH levels were elevated in this patient, and would normally be suggestive of malignant lymphoproliferative disorders, but they were ultimately considered to be caused by interstitial fibrosis. Elevated LDH levels have been observed in patients with fibrosing alveolitis [4], and sarcoidosis in advanced stages may resemble lymphoma based on elevated LDH levels [5]. ESR is more likely to be elevated in patients with sarcoidosis-associated arthritis [6]. Though the patient was ultimately diagnosed with multisystemic involvement with sarcoidosis, the accurate diagnosis was achieved 5 years after the initial presentation with parotitis. Though chest roentgenogram revealed pulmonary fibrosis, the patient was asymptomatic in terms of respiratory functions. Since most pediatric patients with sarcoidosis have been reported to be asymptomatic [2], sarcoidosis in childhood is often misdiagnosed or diagnosed late.

Hyperechogenic lymph nodes have been reported in cases of sinus histiocytosis, lymphoma, and metastatic lymph nodes [7]. We demonstrated intraabdominal echogenic lymph nodes with an 8-Mhz convex probe and punctate echogenic foci corresponding to granulomatous involvement depicted via a 12-Mhz linear array probe. This is the first report connecting echogenic lymph nodes to the diagnosis of sarcoidosis. In a few recent studies regarding sonographic features of benign lymph nodes, it has been reported that, in patients with sarcoidosis, a considerable percentage (88%) show homogeneous low echogenicity [8, 9], commonly do not include coagulation necrosis [10], and are generally hypoechoic followed by mixed echogenicity [11] presenting a granular appearance [12] and also clustered formation [13]. Lymph nodes in sarcoidosis are commonly reported to be hypoechogenic with a heterogeneous echotexture. According to a review of the literature, increased echogenicity was included within the heterogeneous category, and hyperechogenic foci have not been demonstrated. Histopathological diagnosis of the lymph nodes and salivary glands involved with sarcoidosis is made based on monotonous uniformity of the appearance of the non-caseating granulomas, small central foci of fibrinoid necrosis, and Schaumann bodies (calcium and protein inclusions inside of Langhans giant cells as part of a granuloma consistent with concentrically lamellated calcified nodules) [14]. Therefore, small echogenic foci in the lymph nodes and also salivary glands would correspond to fibrinoid necrosis and calcified nodules. A recent study has demonstrated the cutaneous involvement of sarcoidosis with high-resolution ultrasound [15].

Cervical lymph nodes presenting punctate echogenic foci would be suggestive of papillary carcinoma metastasis. The pathophysiology of the microcalcifications in lymph nodes with sarcoidosis has been reported to be caused by necrosis or hyalinized fibrosis that is seen in the late phase [16]. Hyalinized tissue is commonly associated with calcification of a duration that is different from the psammoma bodies

seen in the papillary carcinoma. In addition, the final state is replaced fibrous tissue undergoing calcification. On the other hand, a strong differential diagnosis in granulomatous involvement is tuberculous lymphadenopathy. When we compare granulomatous involvement due to sarcoidosis and tuberculosis, caseating necrosis is commonly seen in tuberculosis, whereas necrosis is not common or is limited in sarcoidosis. Also, granuloma formations tend to be compact, non-caseating, and presenting lymphocytic cuffing around the granuloma in sarcoidosis, and granuloma formations tend to be ill-formed while in tuberculosis including an intense inflammatory reaction [17]. Because of these differentiating microscopic features, non-homogeneously scattered micro- or coarse calcifications along with cystic and necrotic areas and contour lobulation in a lymph node would suggest tuberculous lymphadenopathy, and homogeneously involved lymph nodes with punctate echogenic foci corresponding to granulomas in the absence of necrosis would suggest inflammatory causes of granulomas such as sarcoidosis. Occult thyroid carcinoma with lymph node metastasis has been described in reports [18]. On the other hand, active granulomas are seen in some sarcoidosis cases, and most of the lymph nodes with epithelioid sinusoidal histiocytes without formation of granulomas may mimic reactive lymphadenopathies [19, 20]. It will be invaluable to obtain a histopathological picture of lymph nodes and to compare them with ultrasound images.

In the presented case, periportal lymph nodes were almost hyperechoic, cervical lymph nodes showed increased echogenicity in the lymph node hilum, and there were no echogenic foci within the numerous intraparotidal lymph nodes. Chest roentgenogram played a crucial role in this case by demonstrating bilateral hilar lymphadenopathy and pulmonary parenchyma involvement by sarcoidosis as the origin of echogenic foci. Therefore, sarcoidosis is a fascinating disorder requiring multisystemic, multidisciplinary, and multimodal evaluation.

Pulmonary involvement in sarcoidosis includes the sarcoid cluster sign corresponding to non-confluent perilymphatic or centrilobular distributed small nodules along with bilateral hilar lymphadenopathy [21]. In this case, since there was predominantly interlobular interstitial fibrosis in addition to subpleural sparing without nodule formations, lymphoproliferative disease-associated interstitial pneumonia could be considered in the differential diagnosis. However, lymph node histopathology revealed granulomas. This would be caused by delayed diagnosis of sarcoidosis as well as the pulmonary involvement because of the patient being asymptomatic. Pulmonary involvement in sarcoidosis is common in upper and middle lobes [21], but in this case, lower lobes were dominantly involved with interstitial pneumonia that was suggestive of Sjögren's syndrome [22]. In patients with chronic parotitis, prolonged pulmonary sarcoidosis may resemble involvement of lung parenchyma with Sjögren's syndrome. Furthermore, patients with sarcoidosis and also Sjögren's syndrome would see little impact on pulmonary functions [22] that would cause delayed diagnosis. Echogenic lymph nodes in this case along with bilateral hilar lymphadenopathy and interstitial lung disease were considered to be sarcoidosis rather than Sjögren's syndrome.

In conclusion, the presented case was unique for the initial presentation of sarcoidosis with parotitis. In addition, punctate echogenic foci within the cervical lymph nodes may have been misdiagnosed as papillary carcinoma metastasis. Pulmonary parenchymal involvement in corresponding interstitial fibrosis without perilymphatic nodules is extremely rare in childhood sarcoidosis.

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

Ethical statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

Informed consent Informed consent was obtained from all patients for being included in the study.

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