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Case Report

A case report of sclerosing thymoma of the anterior mediastinum: an exceedingly rare morphology

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Abstract: The morphology of thymoma is diverse, although 5 basic subtypes are recognized in the World Health Organization classification system. Sclerosing thymoma was first documented in 1994 and to date only 13 cases have been reported. Sclerosis itself is considered to be an ancient change and can occur in various histological subtypes. Herein, we present a case of a 62-year-old woman incidentally found to have an anterior mediastinal mass, 31 × 24 × 17 mm in size, without an associated autoimmune disease such as myasthenia gravis. The mass was finally diagnosed as sclerosing thymoma derived from type A thymoma. Intraoperative pathological examination using a limited amount of sample did not allow a definitive diagnosis of thymoma in this case. When dealing with fibrous lesions observed in limited samples such as biopsy and intraoperative frozen specimens, recognizing sclerosing thymoma is important since there are several disease entities accompanying fibrosis in the anterior mediastinum.

Keywords: Sclerosing thymoma, anterior mediastinum, type A thymoma

Introduction

Thymoma is the most common neoplasm arising from thymic epithelial cells [1]. Its histological classification was proposed by the World Health Organization (WHO) in 2004 [2]. According to this classification, thymoma can be categorized into 5 subtypes: A, AB, B1, B2, and B3. In addition to these basic subtypes, other variants, such as micronodular thymoma with lymphoid stroma [3] and metaplastic thymoma [4] are well described. Other rare variants include microscopic thymoma [5], thymolipoma [6], lipofibroadenoma [7], and sclerosing thymoma [8, 9].

Sclerosing thymoma was first documented by Kuo in 1994, who reported 2 cases. The second report was presented by Moran et al. in 2004, and included 10 cases. There has been only one subsequent report of a single case, which was published in Japanese in 2006 and indexed in PubMed [10]. Three cases were associated with myasthenia gravis [8, 9].

Herein, we present an additional, exceedingly rare case of sclerosing thymoma occurring in a 62-year-old woman. It was incidentally found and the patient had no clinical symptoms and no complicated autoimmune disease, such as myasthenia gravis. Intraoperative pathological examination did not allow a definite diagnosis due to massive fibrosis. We further discuss tumors of the anterior mediastinum that include abundant fibrous tissue, as this could help pathologists avoid making an incorrect diagnosis based on biopsy or intraoperative frozen specimens.

Clinical summary

A 62-year-old woman was referred to our hospital owing to an anterior mediastinal mass incidentally found on a chest x-ray film taken at the time of her regular check-up. She had no clinical symptoms related to the mass, and laboratory tests revealed no abnormality. Computed tomography revealed a well-circumscribed anterior mediastinal mass, measuring 31 × 24 × 17 mm (**Figure 1A**) that showed moderate contrast-enhancement (**Figure 1B**). Thymoma was suspected for which a thymectomy was performed. A definitive diagnosis of thymoma could

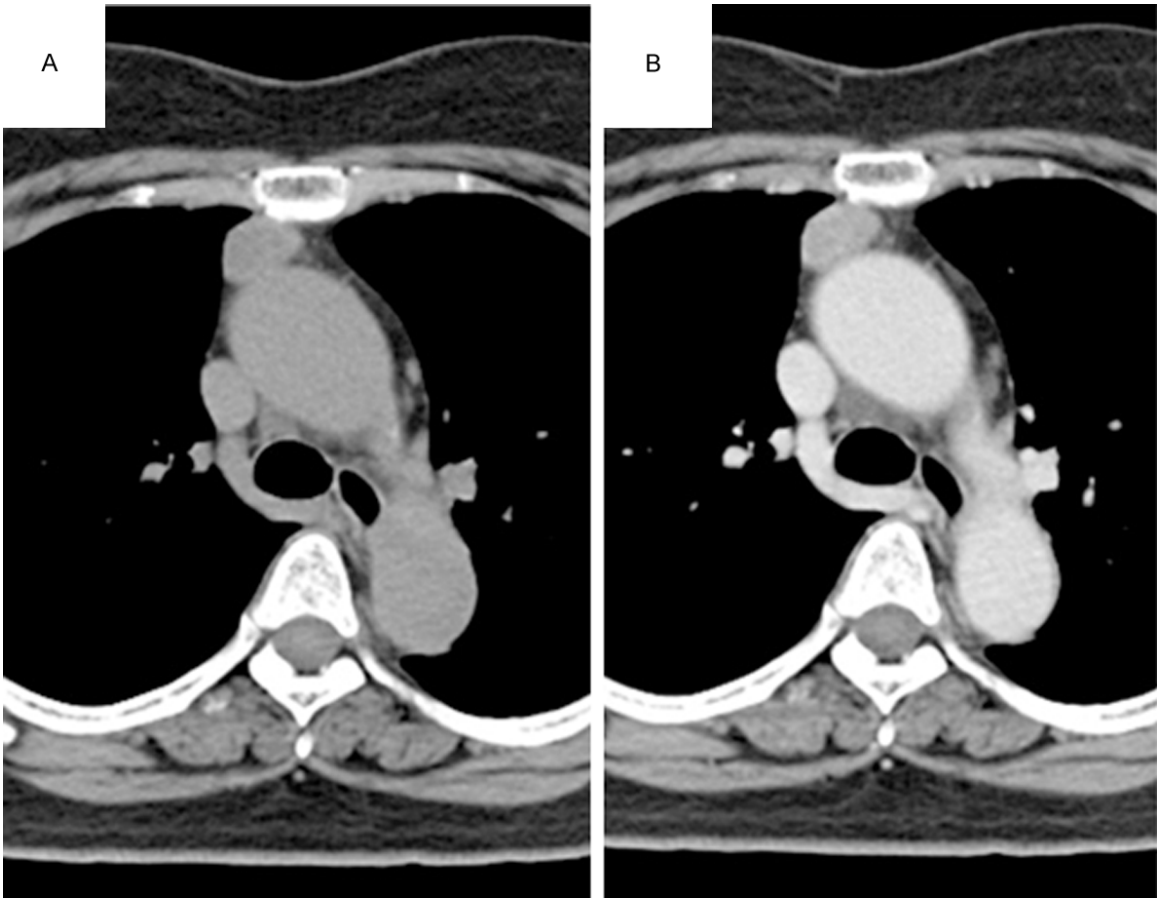

Figure 1. Computed tomography scan. A. A well-circumscribed anterior mediastinal mass was identified, measuring 31 × 24 × 17 mm. B. The mass was moderately contrast-enhanced.

Figure 2. Gross findings of the surgically resected specimen. A well-circumscribed mass was found containing an incision from which sampling was performed during the operation. The cut surface of the mass showed a mosaic pattern of predominantly whitish fibrous areas together with light yellowish areas.

not be made based on the intraoperative pathological examination findings owing to the presence of extensive fibrous tissue with only scant areas of proliferating spindle cells. Her postoperative course was uneventful.

Pathological findings

The surgically resected specimen revealed a well circumscribed mass with an incision from which sampling was performed during the operation. The cut surface of the mass showed a mosaic pattern composed predominantly of whitish fibrous areas, in addition to lightly colored yellowish areas (**Figure 2**).

Histopathologically, fibrous tissue accounted for 70% of the mass. Areas of spindle cell proliferation were observed intermingled with the

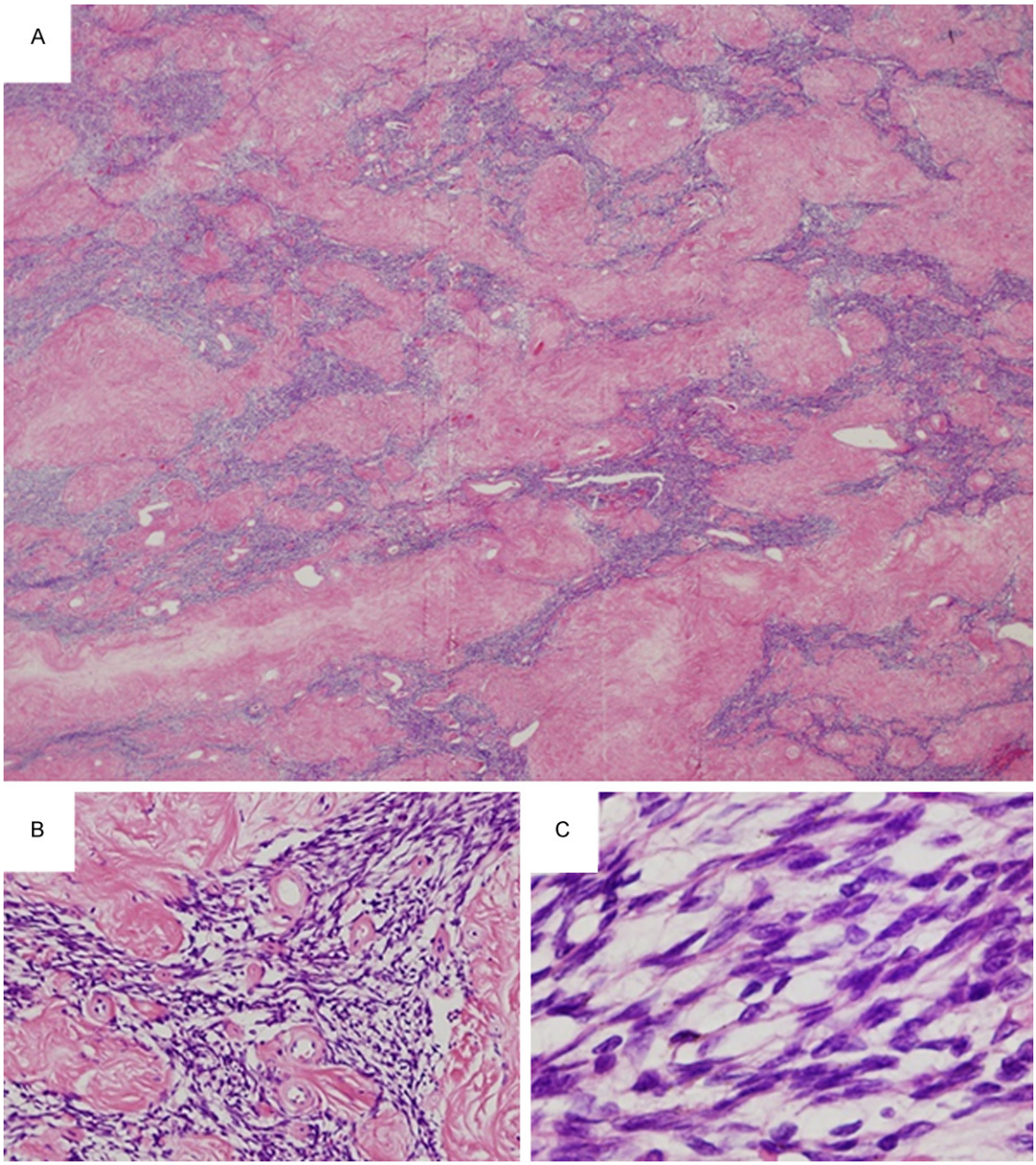

Figure 3. Microscopic findings. A. Fibrous tissue accounted for 70% of the mass, and contained areas of spindle cell proliferation (30%) (× 20). B. There were abundant capillaries inside the areas of spindle cell proliferation, which showed some hyalinization of the vessel walls (× 200). C. Spindle cells showed no apparent nuclear atypia or mitosis, and were sparsely intermixed with lymphocytes (× 400).

fibrous tissue (30%) (**Figure 3A**), which contained numerous capillaries with some hyalinization of the vessel walls (**Figure 3B**). Spindle cells showed no apparent nuclear atypia or mitosis, with sparse admixed lymphocytes (**Figure 3C**).

Upon immunohistochemistry (IHC), spindle cells were found to be diffusely positive for a pan-cytokeratin marker (AE1/AE3, 1:100; Dako, Glostrup, Denmark) (**Figure 4A**), and negative for CD34 (QBEnd 10, 1:100; Dako). No lymphocytes positive for TdT (EP266, 1:100; Dako) were found (data not shown). Cytokeratin-positive spindle cells were also present, predominantly at the periphery of the fibrous tissue, adjacent to the areas of spindle cell proliferation (**Figure 4B**). Based on the WHO classifi-

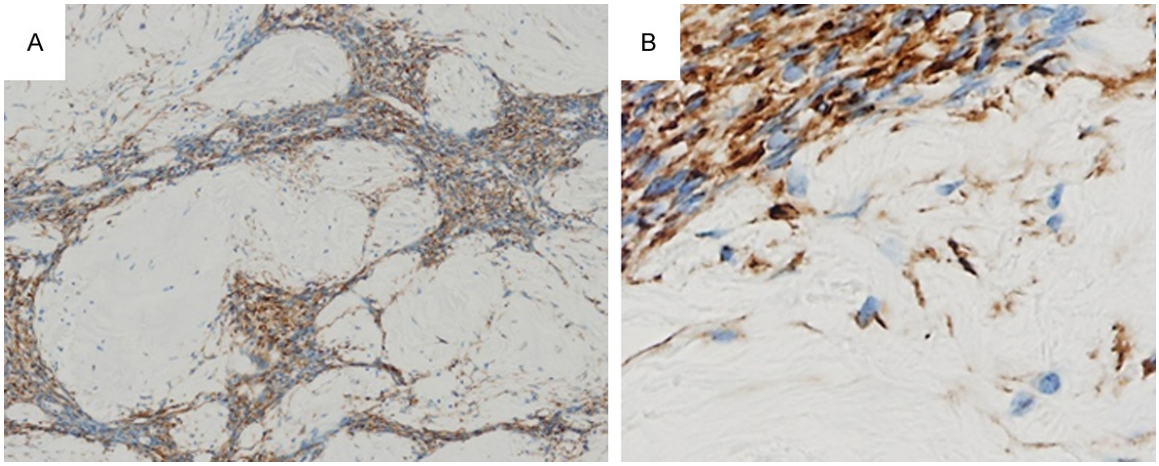

Figure 4. Immunohistochemical findings. A. Spindle cells were diffusely positive for a pan-cytokeratin marker (AE1/AE3) (× 40). B. Cytokeratin (AE1/AE3)-positive spindle cells were found predominantly at the periphery of the fibrous tissue, adjacent to the areas of spindle cell proliferation (× 400).

cation, a diagnosis of type A thymoma with extensive fibrosis was made. The surgical margin was free of tumor.

Discussion

When compared to the basic subtypes of thymoma defined in the WHO classification [2], the tumor in this case could be considered unusual on the basis of its composition that was an extensively fibrosing variant of type A thymoma. Moran et al. suggested that extensive fibrosis may reflect an ancient change [9]. This is supported through our case by the presence of capillaries with hyalinized walls; capillaries are usually abundant in type A thymoma [11]. Hyalinization of the vessel wall is one of the characteristics more often encountered in ancient schwannoma [12], and its presence is generally supposed to be associated with tumors that have undergone an ancient change. The fibrocollagenous bands commonly seen in thymomas are presumed to coalesce over a long period of time [9], and extend into the areas previously occupied by tumor cells. This results in the replacement of tumor cells with fibrous tissue. The presence of cytokeratin-positive cells within the fibrous areas and their absence from the innermost parts of the fibrous areas indicates that this process also occurred in the case that we report here. We recognized the importance of this unique and rare modification within the pre-existing tumor, and categorized this thymoma as sclerosing thymoma in accordance with previous studies [8-10]. It is noteworthy that the ancient change could be seen in a variety of histological subtypes of thymoma, including both type A and type B [9].

Focusing on the extensive fibrosis irrespective of thymoma subtype is also important for achieving an accurate diagnosis with small samples such as biopsy or intraoperative frozen specimens. Several disease entities might be considered in the differential diagnosis, such as solitary fibrous tumor [13], sclerosing mediastinitis [14], and lymphoma with sclerosis [15, 16]. These could not be confidently distinguished if the sampled specimen mostly contained fibrous tissue, and in such a case, thymoma, especially sclerosing thymoma, should be included in the differential diagnosis.

Due to the limited number of reported sclerosing thymoma cases, its prognosis is not well established. However, it is most likely that it would follow a benign clinical course since ancient change has initiated and biological activity is therefore likely to have lessened. In fact, no unfavorable events related to tumor recurrence have been reported after resection of sclerosing thymoma [8-10].

In conclusion, this is the 4th study of sclerosing thymoma and the 14th reported case. Sclerosis is probably due to ancient change and the prognosis of sclerosing thymoma would thus be expected to be favorable. When dealing with limited samples such as biopsy and intraoperative frozen specimens obtained from anterior mediastinal lesions, the presence of extensive

fibrosis may complicate differential diagnosis as several disease entities that often exhibit fibrosis would need to be included. In this context, sclerosing thymoma should also be included in the differential diagnosis.

Disclosure of conflict of interest

None.

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