



ORIGINAL RESEARCH PAPER

Medical Science

SOLITARY FIBROUS TUMOUR OF ADNEXAE ASSOCIATED WITH HYPOGLYCAEMIA - A RARE EXTRA THORACIC CASE REPORT.

KEY WORDS: Solitary fibrous tumour, Extra-pleural, adnexal mass, benign tumour, vascular tumour.

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ABSTRACT A 60 year old female came with complaints of colicky, intermittent pain in the abdomen since 4 days, which was acute in onset, and present only on passing stools. Ultrasonography revealed mild enterocolitis, and a right adnexal mass lesion, most likely an exophytic uterine fibroid. She was operated in our hospital. Histopathological examination and immunohistochemistry revealed the lesion to be a solitary fibrous tumour, a rare neoplasm discovered at an extra-pleural location. Less than 100 cases of extrapleural solitary fibrous tumour have been reported till date. We discuss the clinico-histopathological findings of solitary fibrous tumour.

INTRODUCTION-

Tumours described originally as localized fibrous mesothelioma have come to be known as solitary fibrous tumours (SFT's), because they clearly are not of mesothelial origin(1-4). SFTs develop not only from pleura, but also near other serosal surfaces, such as the pericardium, peritoneum and the surface of the liver. SFTs belong to the category of fibroblastic tumours because some authors noted a histologic identity similar to that of previously reported breast tumours and perhaps the fibrous variant of spindle cell lipoma(5,6). The lipomatous hemangiopericytoma is now regarded to belong to the SFT group of tumours as well(7), and indeed, essentially all hemangiopericytomas are now considered SFTs(8). Regardless of the location, they are histologically identical to those in pleura, which are composed of non-descript bland and uniform spindle cells dispersed among elongated, thin, parallel collagen bands in a "patternless" pattern. The parallel arrangement of collagen bundles is a characteristic sign (9). The following markers are positive in SFTs : CD 34, BCL-2 and CD99. Most benign appearing SFTs behave in a benign fashion(10). It is important to identify these tumors as they may pose a diagnostic dilemma for the clinician and radiologist. We report a rare case of SFT presenting as painful mass in adnexae associated with hypoglycaemia.

CASE REPORT

A 60 year old female came with complaints of colicky, intermittent pain in the abdomen since 4 days, which was acute in onset, present only on passing stools. The pain exaggerated after 2 days and was associated with 2 episodes of vomiting. Patient was not a known diabetic or hypertensive. Patient was hypoglycemic at the time of admission. On physical examination a hard, non-tender mass was palpable deeply in the right lower abdomen. Auscultation of abdomen revealed normal bowel sounds. Ultrasonography revealed mild enterocolitis, and a right adnexal mass lesion, most likely to be an exophytic uterine fibroid.

Patient was a known case of poorly differentiated squamous cell carcinoma of cervix with reactive regional lymph nodes. Radical hysterectomy with bilateral salpingo-ophorectomy was done one and a half months back. The patient also had history of hypoglycaemic symptoms since four months. The patient was operated and the adnexal mass was sent for histopathological examination.

Grossly a brownish-white encapsulated lobular tissue mass measuring 8 cm x 6 cm x 4 cm was received (Figure 1). Cut-section showed dense white homogeneous areas (Figure 2).

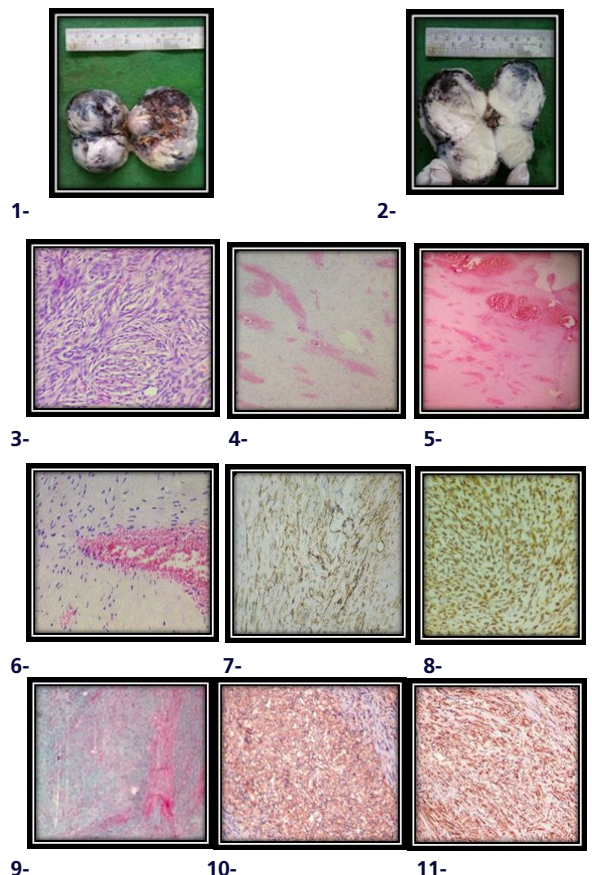
Histopathological examination revealed hypo cellular and hyper cellular areas along with few areas of hemorrhage. Hypocellular areas were composed of stellate type cells against a mildly myxoid

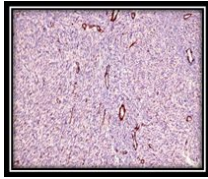
background. Hypercellular areas were comprised of spindle cells arranged in fascicles and storiform pattern. The individual cells were elongated, round to oval with indistinct cytoplasm. Also seen were thin strands of collagen interspersed between the cells. No evidence of atypia, mitosis or necrosis was found in the sections studied.

Immunohistochemistry was diffusely positive for vimentin and negative for S-100 and Actin. Also it showed uniform positivity for CD 34, CD 99 and BCL-2.

Thus a diagnosis of solitary fibrous tumour was made. The patient has been doing well post- operatively.

FIGURES:





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Figure 1 –Gross features- External surface showing an exophytic protrusion.

Figure 2 – Cut section showing dense white interior

Figure 3 –400x view- The thin parallel strands of collagen set this lesion apart. The spindle cells are bland and nondescript, but they may exist in storiform or pericytomatous patterns.

Figure 4 – 100x magnification showing dilated blood vessels.

Figure 5 – 400x magnification showing dilated blood vessels with hemorrhagic areas.

Figure 6 – 400x magnification showing thickened and dilated blood vessels surrounded by spindle cells.

Figure 7 – 100x magnification showing CD 34 positivity

Figure 8 – 100x magnification showing diffuse positivity for vimentin.

Figure 9 – 400x magnification showing Masson Trichome stain positive for collagen strands.

Figure 11- 100 x magnification showing BCL – 2 Positivity.

Figure 12- 100 x magnification showing Smooth muscle Actin-negative.

DISCUSSION:

Tumours described originally as localized fibrous mesothelioma have come to be known as solitary fibrous tumour (SFT's) because they are clearly not of mesothelial origin(1-4). SFTs develop not only from pleura, but also near the other serosal surfaces, such as the pericardium, peritoneum, and the surface of the liver. SFTs belong to the category of fibroblastic tumours because some authors note a histologic identity similar to that of previously reported breast tumours and perhaps the fibrous variant of spindle cell lipoma(5,6). The lipomatous hemangiopericytoma is now regarded to belong to the SFT group of tumours as well(7), and indeed, essentially all hemangiopericytomas are now considered SFTs(8). SFTs rarely express actin and they have (myo) fibroblastic ultrastructural features. Regardless of location, they are histologically identical to those in pleura, which are composed of non-descript bland and uniform spindle cells dispersed among elongated, thin, parallel collagen bands in a "patternless" pattern. The nuclei are small, and mitoses are difficult to find in the average case. Foci of storiform or hemangiopericytomatous growth are typical. Actually, the parallel arrangement of collagen bundles is a characteristic sign that is not seen in fibromatosis; the consistent CD 34 positivity is another feature distinguishing SFT from fibromatosis(9). Therefore, two markers distinguish between these two collagenized tumours- fibromatosis (SMA + / CD 34-) and SFT (SMA- / CD34 +). SFTs are also positive for BCL-2 and CD99. Most benign appearing SFTs are behave in a benign fashion(10). Sarcoma is a part of differential diagnosis, and needle biopsy specimens may be misinterpreted as fibrosarcoma. If an uncommon cellular tumour is encountered the following criteria developed for malignancy in pleural tumours are applicable in soft tissue(11,12): increase cellularity, necrosis, pleomorphism, and an increased mitotic rate (> 4 per 10 hpf). In rare cases, malignant SFTs appear to occur as fibro-sarcomatous progression next to benign – appearing SFTs. Significantly they may develop without an association to a serosal surface, such as in mediastinum, orbit, thyroid or nasal cavity; and now they are commonly reported in the soft tissues.

Virtually all solitary fibrous tumours contain a fusion oncogene, NAB2-STAT6, which has not been encountered in other soft tissue tumours and, therefore, appears to be diagnostically specific(13,14) NAB2 and STAT6 are adjacent genes in chromosome band 12q13, and the pathognomonic NAB2-STAT6 fusion results from a highly localized inversion event that is undetectable by standard G-banding karyotyping assays. Therefore, although the cytogenetic literature includes reports of

various non-recurrent chromosome aberrations in solitary fibrous tumour, the NAB2-STAT6 fusion was recognized only when next-generation sequencing methods were applied(13,14) The NAB2 protein functions normally as a repressor of transcription factors EGR1 and EGR2, but, in the context of the NAB2-STAT6 fusion, to which STAT6 contributes a transcriptional activation domain, NAB2 functions as an EGR activator, leading to upregulation of EGR-dependent genes such as IGF2 and FGFR1. NAB2 itself is an EGR-dependent gene, and, therefore, the NAB2-STAT6 oncogene positively regulates its own expression. Notably, NAB2-STAT6 appears to be ubiquitous in solitary fibrous tumour; therefore, other genetic mechanisms presumably account for the biologic and clinic variation within solitary fibrous tumours, including the clinically aggressive behaviour seen in approximately 10 % of cases.

Hypoglycemia has been reported in about 5% of SFT, most often those located in the pelvis and retroperitoneum, and may lead to symptoms of sweating, headache, disorientation, convulsions, and even coma. It is mediated through the production of insulin-like growth factors by the tumour(15-17). Insulin-like growth factors and insulin-like growth factor receptor mRNA can be identified in tumour cells even in the absence of clinical hypoglycaemia (18,19). Hypoglycemic symptoms abate with tumour removal. In addition, the insulin-like growth factors stimulate proliferation of tumour cells through an autocrine loop that can be abolished when the receptors are inactivated.

SFTs belong to the category solitary fibrous tumour is primarily a tumour of adult life that affects the sexes equally. It is located almost exclusively in deep soft tissues, particularly the thigh, pelvic fossa, retroperitoneum, and serosal surfaces. SFTs of pleural and extrapleural origin typically express CD34(80-90%), CD99 (70%), bcl2 (30%), and actin (20%). Desmin, cytokeratin and S- 100 protein are usually absent.

Variants of SFTs are lipomatous SFTs, meningeal SFTs, SFT with giant cells.

Differential diagnosis includes Fibrous histiocytoma, particularly its deep subcutaneous form, usually displays a more prominent, more uniform spindle-cell pattern than hemangiopericytoma, often with a distinct storiform arrangement of the tumour cells. Synovial sarcoma, in about 10% to 20% of cases, exhibits a distinctive but focal hemangiopericytoma-like pattern. This pattern usually occurs in high-grade round cell areas of the synovial sarcoma. Synovial sarcomas are almost always associated with distinct spindle cells, hyalinized-calcified areas, glands, and expression of cyto-keratin. CD34 expression is not seen in synovial sarcoma, a useful negative finding in cases where the differential diagnosis includes SFT with anomalous cytokeratin expression. Mesenchymal chondrosarcoma frequently shows a hemangiopericytoma-like vascular pattern in the closely packed small-cell areas but is readily recognizable by the presence of islands of well-differentiated cartilage or, much less frequently, bone. Ill-defined foci of immature cartilage may also be present in the small-cell component. Juxtaglomerular tumours that secrete renin and cause hypertension may also be misinterpreted as hemangiopericytomas, especially those rare lesions that occur in extrarenal locations such as the retroperitoneum(20). In most of these neoplasms, large epithelioid cells and thick-walled vessels are present, and some contain PAS-positive renin crystals. In the past, many phosphaturic mesenchymal tumours (PMTs) were erroneously labelled as hemangiopericytomas. Recognition of the distinctive matrix produced by PMTs and clinical investigation for associated osteomalacia should allow for the ready distinction of these two entities(20).

CONCLUSION:

In summary, CD34 is an important IHC marker in diagnosing SFTs as the tumours are vascular, however BCL-2 and CD 99 positivity aids in the diagnosis. Histopathology has a prominent role in distinguishing the types of adnexal masses which can be misdiagnosed radiologically at times.

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