CASE REPORT

Intrapatellar tendon lipoma with chondro-osseous differentiation: detection of HMGA2-LPP fusion gene transcript

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A 54 year old man developed an unusual lipoma in the patellar tendon, consisting of a fibro-adipose component and a chondro-osseous component. The fibro-adipose component contained mature adipocytes, lipoblasts, and fibroblasts; the chondro-osseous component showed typical endochondral bone formation. Molecular analysis showed that the identical HMGA2-LPP fusion transcript—characteristic of lipoma, parosteal lipoma, and pulmonary chondroid hamartoma—was detectable in the both components.

Lipomas, which are benign adipose tissue tumours, are the most common tumours of mesenchymal origin in humans. They most often arise superficially in the soft tissue, but occasionally, as with parosteal lipomas, they are deep seated.¹ We present a case of an intrapatellar tendon lipoma with a fibro-adipose component and a chondro-osseous component. An identical HMG (high mobility group) A2-LPP (LIM containing, lipoma preferred partner) fusion transcript—characteristic of lipoma, parosteal lipoma, and pulmonary chondroid hamartoma^{2–5}—was detectable in the both tumour components.

METHODS

The fibro-adipose and chondro-osseous components were dissected from the tumour. Total RNA was extracted from each fibro-adipose component and chondro-osseous component of the lipoma using a standard method.⁶ Cultured parosteal lipoma cells with t(3;12)(q27;q13) or t(5;12)(q33;q15) were used as positive and negative controls for HMGA2-LPP fusion transcripts, respectively. cDNA was synthesised with random primers and was subjected to polymerase chain reaction (PCR) amplification of the HMGA2-LPP fusion transcript.⁵ A 452 base pair fragment of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) cDNA was also amplified as a control. The PCR products were separated by 1% agarose gel electrophoresis and were visualised by ethidium bromide. The identity of each band was confirmed by direct DNA sequencing.

The patient gave informed consent for the study, the protocol of which was approved by the local ethics committee.

CASE REPORT

A 54 year old man noticed a firm, painless mass on the anterior aspect of the right knee 10 years previously. The patient visited our clinic because the mass had grown during the past year. Physical examination revealed a firm immovable 3×3 cm mass just below the right patella (fig 1). The mass showed no tenderness, redness, or warmth. Plain film x ray showed a soft tissue shadow with punctuate curvilinear

Figure 1 A well circumscribed mass protruding from the anterior aspect of the right knee. Arrow indicates tumour; broken lined arrow indicates patella.

Figure 2 A radiograph of the right knee, lateral view. The tumour is located antero-inferior to the patella. Note the punctuate curvilinear mineralisations.

mineralisations (fig 2). Both T1 weighted and T2 weighted magnetic resonance images revealed a septated soft tissue mass with heterogeneous high signal intensity measuring 3×3×2 cm (fig 3). T1 weighted magnetic resonance images showed signal enhancement along the septa after gadolinium diethylene triamine tetra-acetic acid injection (fig 3).

A gallium scan showed no signal accumulation. The patient underwent marginal resection of the tumour, which proved to be well encapsulated within the patellar tendon (fig 4). Macroscopically, the tumour was lobulated with septa, and contained two distinct components: fibro-adipose tissue and chondro-osseous tissue (fig 5). Histologically, the fibro-adipose tissue contained mature adipocytes, lipoblasts, and fibroblasts (fig 6), and the chondro-osseous tissue showed typical endochondral bone formation (fig 6). Immunohistochemically, vimentin was diffusely positive and S-100 was positive within adipocytes and lipoblasts. CD34, desmin, smooth muscle actin, and p53 reactivity was negative and the MIB-1 labelling index was less than 1%.

Figure 3 Magnetic resonance images, sagittal view. T1 weighted (A) and T2 weighted (B) images show a septated soft tissue mass, with signal enhancement along the septa (C).

Figure 4 Photographs taken at the surgery. (A) The tumour was in the patellar tendon. (B) The tumour was marginally resected.

Figure 5 Macroscopic appearance of the tumour. The tumour contained both an adipose-like and a cartilage-like (chondroid) component. Scale bar = 3 cm.

Molecular analysis showed that the identical HMGA2-LPP fusion gene transcript, in which exons 1-3 of the HMGA2 gene were fused to exons 9-11 of the LPP gene, was detectable in the both tumour components (fig 7). The reciprocal LPP-HMGA2 fusion gene transcript was not detectable (data not shown). With the above information, this case was diagnosed as lipoma in the patellar tendon. The postoperative course was uneventful, and the patient has no evidence of the recurrence one year after the surgery.

DISCUSSION

A specific t(3;12) chromosomal translocation producing the chimeric HMGA2-LPP gene is detectable in some cases of lipoma, parosteal lipoma, and pulmonary chondroid hamartoma.²⁻⁵ The case presented here shares with parosteal lipoma and pulmonary chondroid hamartoma the findings of ectopic bone or cartilage formation. *HMGA2* encodes a member of the HMGA family architectural transcription factors, which is important for chromatin organisation and cell cycle regulation.⁷ LPP is a focal adhesion protein that is composed of an extensive proline-rich N-terminal region and three C-terminal LIM domains.⁸ Although HMGA2-LPP fusion gene transcript was detectable in the present case, the reciprocal LPP-HMGA2 transcript was not detectable, in keeping with previous reports.³ These findings suggest that the HMGA2-LPP fusion protein, in which the C-terminal part of HMGA2 is replaced by LPP, is responsible for lipomagenesis.

HMGA2 protein has been analysed in relation to adipogenesis.⁹ *Hmga2* knockout mice have a pygmy phenotype with a remarkable reduction of the adipose tissue,¹⁰ and disruption of *Hmga2* gene prevents obesity.¹¹ N-terminal, but not full length, HMGA2 induces neoplastic transformation in NIH3T3 murine fibroblasts.¹² In contrast to full length HMGA2, N-terminal HMGA2 transgenic mice develop a giant phenotype along with adiposity and show an abnormally high prevalence of lipomas.^{13 14} These observations indicate that the

Figure 6 Histological appearance of the tumour. (A) Haematoxylin-eosin (H&E) stain, low magnification. (B) H&E stain, high magnification of the chondro-osseous component.

Figure 7 Reverse transcription polymerase chain reaction detection of the HMGA2-LPP fusion transcripts. Lane 1, parosteal lipoma with t(3;12) (q27;q13); lane 2, parosteal lipoma with t(5;12) (q33;q15); lane 3, fibro-adipose component of the current case; lane 4, chondro-osseous component of the current case.

Take home message

- Evidence is presented that HMGA2-LPP fusion protein induces osteochondrogenesis as well as fibroadipogenesis. Functional analysis of HMGA2-LPP fusion protein could provide new insights into mesenchymal cell differentiation.

N-terminal part of HMGA2 is necessary for proliferation of adipocytes. On the other hand, involvement of C-terminal LPP in the genesis of lipoma is unclear.

In summary, we present an unusual lipoma with chondro-osseous differentiation. The mechanism of chondro-osseous differentiation in our case is unknown. However, detection of an identical HMGA2-LPP fusion transcript in the both fibro-adipose component and chondro-osseous component suggests that HMGA2-LPP fusion protein induces osteochondrogenesis as well as fibroadipogenesis. Functional analysis of HMGA2-LPP fusion protein would provide us with new insights into mesenchymal cell differentiation in general and the genesis of lipomas in particular.

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