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ONLINE CASE REPORT

Follicular Dendritic Cell Sarcoma

Cytogenetics and pathological findings

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ساركومة الخلية التغصنية الجريبية

الوراثة الخلوية و النتائج المرضية

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ABSTRACT: Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm with a non-specific and insidious presentation further complicated by the difficult diagnostic and therapeutic assessment. It has a low to intermediate risk of recurrence and metastasis. Unlike other soft tissue sarcomas or histiocytic and dendritic cell neoplasms, cytogenetic studies are very limited in FDCS cases. Although no specific chromosomal marker has yet been established, complex aberrations and different ploidy types have been documented. We report the case of a 39-year-old woman with FDCS who presented to the Sultan Qaboos University Hospital in Muscat, Oman, in February 2013. Ultrastructural, immunophenotypical and histological findings are reported. In addition, karyotypic findings showed deletions of the chromosomes 1p, 3q, 6q, 7q, 8q and 11q. To the best of the authors' knowledge, these have not been reported previously in this tumour. Techniques such as spectral karyotyping may help to better characterise chromosomal abnormalities in this type of tumour.

Keywords: Chromosomal Aberrations; Cytogenetics; Follicular Dendritic Cell Sarcoma; Fine Needle Aspiration; Karyotyping; Case Report; Oman.

الملخص: ساركومة الخلية التغصنية الجريبية هو ورم نادر تكون أعراضه غير واضحة وظهوره قد يكون بصورة غير متوقعة. تشخيص المرض يكون صعبا جدا لعدم وجود طفرة وراثية محددة يمكن الكشف عنها عن طريق التنميط النووي و الفحوصات الجينية الأخرى. يحمل هذا المرض نسبة اختطار بسيطة إلى متوسطة من رجوعه والنقيلة. يختلف هذا الورم عن بقية أنواع ساركومة الأنسجة الرخوية و الأورام النسيجية والتغصنية بقلة فحوصات الوراثة الخلوية فيه ولكن تم تسجيل عدد من الزيغ المعقد و أنواع مختلفة من الصيغة الصبغية لهذا المرض. نعرض هنا حالة امرأة عمرها 39 عاما تم تشخيصها بساركومة الخلية التغصنية الجريبية في مستشفى جامعة السلطان قابوس بمسقط، سلطنة عمان في شهر فبراير من عام 2013، حيث تم الاعتماد على التحليل الجزيئي والفحص باستخدام المضادات والتشخيص النسيجي. بينت فحوصات الوراثة الخلوية وجود حذف في الصبغيات، 11q و 8q، 7q، 6q، 3q، 1q. حسب أفضل معرفة للمؤلفين لم يتم عرض هذا سابقا في هذا الورم. الفحوصات التقنية مثل التنميط النووي الطيفي قد تمكن من التشخيص الدقيق للتغيرات في هذة الصبغيات.

مفتاح الكلمات: زيغ الصبغي؛ الوراثيات الخلوية؛ ساركومة الخلية التغصنية الجريبية؛ خزعة مشفوطة بالإبرة؛ التنميط النووي؛ تقرير حالة؛ سلطنة عمان.

Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm; although it is classified under histiocytic and dendritic cell neoplasms, FDCS is typically nodal, with extranodal involvement occurring in approximately 30% of cases.[1] The major hurdle in treating FDCS cases is misdiagnosis, due to similarities in presentation to lymphoma. Cytogenetic data on FDCS are very scarce, with the first description appearing in 2008.[2,3] This report presents a FDCS patient with a complex karyotype and pathological findings.

Case Report

A 39-year-old woman presented to the Sultan Qaboos University Hospital in Muscat, Oman, in February 2013 with a swelling on the right side of her neck. On examination, a firm, non-mobile, non-tender supraclavicular swelling was found. Magnetic resonance imaging showed a mass involving the sternocleidomastoid muscle and the compression of the internal jugular vein with an intact carotid [Figure 1A].Surgical excision of the tumour revealed a globular nodular firm grey mass measuring 7 x 6 x 2.8 cm [Figure 1B].

For the cytogenetic analysis, a fine needle aspirate (FNA) was collected under sterile conditions. The FNA was distributed into three culture flasks and cultured in Roswell Park Memorial Institute media at 37 °C with 5% carbon dioxide. Both 24-hour and long-term cultures were set up. When sufficient growth was observed under an inverted microscope

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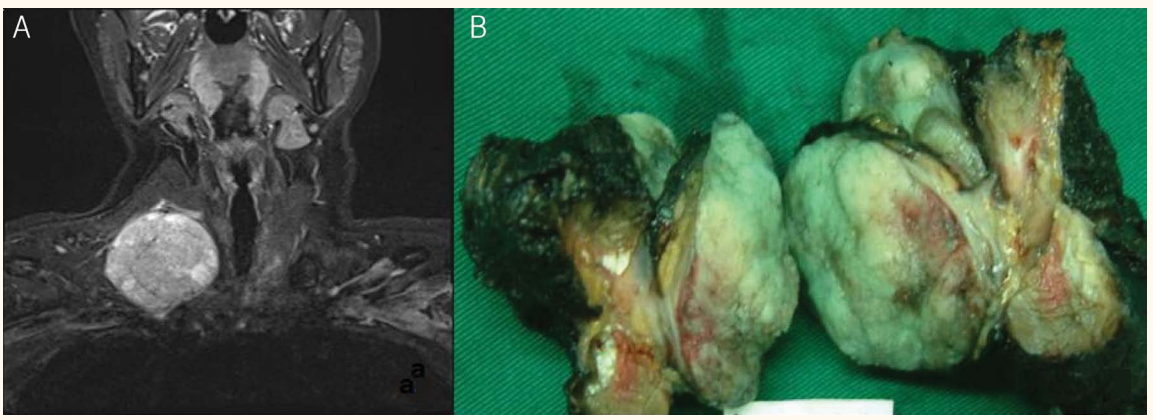

Figure 1A & B: A: Magnetic resonance image showing the follicular dendritic cell sarcoma tumour mass involving the sternocleidomastoid muscle. **B:** Photograph showing a gross specimen of the globular nodular tumour after excision (7 x 6 x 2.8 cm).

on the fourth day, 50 µL of colcemid at 10 µL/mL of Gibco™ (Life Technologies, Thermo Fisher Scientific Corp., Carlsbad, California, USA) was added for 30 minutes, followed by hypotonic treatment (0.075 M of potassium chloride) for 45 minutes. The cell pellet was fixed using Carnoy's fixative solution and slides were prepared and G-banded the following day.

Microscopic findings showed a relatively well encapsulated neoplasm, composed of nodules separated by thick fibrous septae which contained multiple foci of lymphoid aggregates. The nodules were composed of sheets of pleomorphic spindle cells and epithelioid cells with indistinct cytoplasmic borders; the nodules exhibited a moderate amount of acidophilic cytoplasm, vesicular nuclei and prominent nucleoli. These cells were arranged in short fascicles or whorls or exhibited a storiform pattern. Abundant mitotic figures (24 mitoses/10 high-power fields) and apoptotic bodies were present and foci of necrosis and haemorrhage were also noted [Figure 2A].

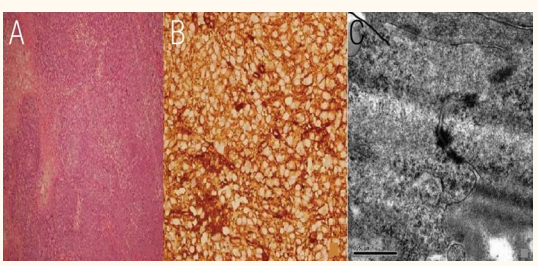

Figure 2A–C: Haematoxylin and eosin histopathology section showing (**A**) neoplastic nodules composed of sheaths of spindle cells exhibiting vesicular nuclei, prominent nucleoli and indistinct cytoplasmic borders at x40 magnification, (**B**) tumour cells showing strong membranous positive staining for cluster of differentiation 21 at x400 magnification and (**C**) several well-formed desmosomes firmly joining the cytoplasmic process of contiguous neoplastic cells at x25,000 magnification. This favoured a diagnosis of follicular dendritic cell sarcoma.

Immunohistochemical staining showed strong positivity of neoplastic cells for clusters of differentiation (CD) 23, CD35 and CD21 via membranous staining [Figure 2B] and focal positivity for CD99. Markers for CD34, human melanoma black 45 and CD68 were negative. The Ki-67 protein cell proliferation index was high (80%). Electron microscopy findings showed elongated nuclei with cytoplasmic invagination. Abundant desmosomes with no evidence of Birbeck granules were also observed [Figure 2C], favouring a diagnosis of FDCS. Intranuclear pseudo-inclusions were not visible on morphology. The nodular grey tumour mass on the sternocleidomastoid muscle compressed the internal jugular vein.

Of the 20 karyotypes, 19 showed complex abnormal karyotypes and one showed a normal karyotype. The chromosome numbers ranged from 72 to 80. Structural aberrations, such as deletions, were observed on chromosomes 1p, 3q, 6q, 7q, 8q and 11q. Additional material of unknown origin was observed on both copies of 16q and 19q. The loss of chromosome 21 was obvious in the majority of the metaphases. Other common missing chromosomes were 8, 9, 13, 14 and 22. Various marker chromosomes were present in all of the abnormal metaphases. As the range of chromosomes were in the hypertriploid category, a composite karyotype was interpreted as per the International System for Human Cytogenetic Nomenclature (2013).[4] These were as follows: 72~80<3n+>,XXXX,-1,del(1)(p32)x2,-3,del(3)(q24),-4,del(6)(q13)x2,-7,del(7)(q11)x2,-8,-8,del(8)(q22)x2,-9-9-9,del(11)(q13),-12,-13,-13,-14,-14,-14,add(16)(q24)x2,-18,add(19)(q13)x2,-20,-21,-21,-21,-21,-22,-22,-22,+mar1,+mar2,+mar3,+mar4,+mar5[19][cp11]/46,XX[1] [Figure 3].

Discussion

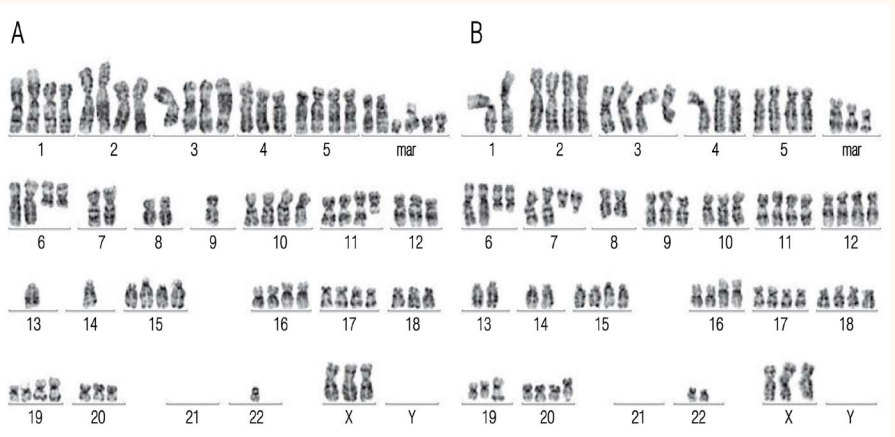

Figure 3A & B: Representative complex karyotypes showing structural abnormalities such as del(1p), del(3q), del(6q), del(7q), del(8q), del(11q), add(16q) and marker chromosomes in a patient with follicular dendritic cell sarcoma.

Although FDCS is pathologically well characterised, there are very few cases described cytogenetically. Thus far, only six case reports are available in the literature with chromosomal findings.[2,3–7] To the best of the authors' knowledge, this is the first report from a Middle Eastern Arab population. The results of the current case yielded a good mitotic index and morphology of chromosomes by culturing the FNA of the tumour, which is often difficult to obtain. In sarcomas, even though the cytology of FNA material may not be of much diagnostic use, the cytogenetic benefits are substantial.[6] Hence, the authors of this report endorse FNA as the best technique for obtaining ideal samples for solid tumour cytogenetics, as per current and past experiences with soft tissue sarcomas.[8]

Table 1: Comparative analysis of the ploidy status, frequently involved chromosomes and structural aberrations in follicular dendritic sarcoma cases in the literature

Author and year of case report	Ploidy status (chromosomes involved)	Structural aberrations
Jones *et al.*[5] 2001	Hypertetraploidy (93–103)/hyperdiploidy (47–57)/pseudodiploidy	Xp-, 21p+
Della Porta *et al.*[9] 2003	Hypotriploidy (62–71)	14q+, 15q-
Sander *et al.*[7] 2007	Hypodiploidy (35–45_/ pseudodiploidy	3q+,7p+, 8p-, 8q+, 9p-, 9q+, 10p-, Xp-
Suzuki *et al.*[2] 2008	Diploidy (46)	21q+
Wang *et al.*[6] 2010	Diploidy (46)	Normal karyotype
Perry *et al.*[3] 2013	Hypodiploidy	15p+, 16q+, 17p+
Present case	Hypertriploidy (72–80)	1p-,3q-, 6q-, 7q-, 11q-, 16q+, 19q+

Immunophenotypic comparisons of the positivity of CD21 and CD35 markers vary among patients. In the current case, CD21 was strongly positive and the tumour cells were also positive for CD23 and CD35; similar results were reported by Wang *et al.* in a previous report.[6] However, in another report of FDCS by Jones *et al.*, all these markers were negative.[5]

The current patient had hypertriploidy in all of the abnormal metaphases ranging from 72 to 80. Earlier reports of FDCS have shown hypodiploidy and diploidy in two cases;[3,7] furthermore, two cases had hyperdiploidy along with pseudodiploidy.[5,7] Della Porta *et al.* reported a patient with hypotriploidy and Jones *et al.* reported a patient with hypertetraploidy.[5,9] Notably, two reported cases showed the involvement of chromosome Xp.[5,7] No involvement of chromosome X was observed in the current patient.

Add(16q) has been reported in previous cases and the current patient had similar additional material of unknown origin on 16q.[3] Add(21q), add(21p), add(15p) and add(17p) were reported by Suzuki *et al.*, Perry *et al.* and Jones *et al.*[2,3,5] The patient in the current report study also had add(19q) and did not have any involvement of chromosomes 14, 15, 17 or 21. Marker chromosomes were seen in two earlier cases reported by Perry *et al.*, which were also observed in the patient in the current report in all of the abnormal metaphases.[3]

Cytogenetic observations in the current patient showed novel aberrations, such as the deletion of chromosomes 1p, 3q, 6q, 7q, 8q and 11q, which were not reported earlier [Table 1]. These novel findings are an addition to the literature already available on FDCS. Material of unknown origin was observed in both copies of chromosome 16 and 19 in the current patient, in contrast to the gains observed in earlier reports

for chromosomes 3, 7, 8 and 9.[7] Hence, observations from the current patient confirm the heterogeneity of chromosomal findings in FDCS proposed by Perry *et al*. in their two cases.[3]

Great variation has been observed among the ploidy statuses and structural alterations in FDCS cases. Use of the latest technologies, such as spectral karyotyping, is recommended for the complete characterisation of chromosomes. Single nucleotide polymorphism arrays and next generation sequencing should also be utilised in future studies investigating the genes responsible for FDCS.

Conclusion

FDCS is a rare tumour which is difficult to diagnose based on its non-specific presentation. Unlike other soft tissue sarcomas, cytogenetic studies are very limited in FDCS cases. Cytogenetic observations of the current patient with FDCS showed novel aberrations, such as the deletion of chromosomes 1p, 3q, 6q, 7q, 8q and 11q; to the best of the authors' knowledge, these have not yet been reported. The cytogenetic characterisation of rare tumours is important so as to establish chromosomal markers. This aids in the diagnosis of patients and enables a precise classification in order to predict prognosis. However, further research is needed before a conclusion can be drawn. Spectral karyotyping is recommended for the complete characterisation of chromosomes for this type of tumour. Moreover, FNA is deemed the best technique for obtaining samples for cytogenetic analyses of solid tumours.

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