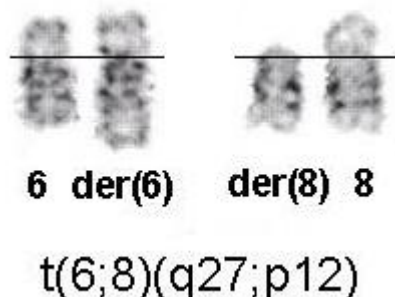


t(6;8)(q27;p12)

Identity



G-band analysis. Partial karyotype showing the t(6;8)(q27;p12); courtesy José Luis Vizmanos.

Clinics and Pathology

Disease	BCR-ABL negative chronic myeloproliferative disease associates with 8p11 chromosomal rearrangements and a clinical entity named " 8p11 myeloproliferative syndrome " (EMS) or "stem cell leukemia/lymphoma" (SCLL) syndrome. These chromosomal rearrangements fuse FGFR1 (a receptor tyrosine kinase gene) with other genes resulting in new chimeric genes which are translated in constitutionally activated FGFR1-like proteins. This is a multilineage disorder with combined occurrence of myeloid malignancy and T- cell NHL , or myeloid metaplasia .
Phenotype / cell stem origin	The same t(6;8)(q27;p12) is found both in the bone marrow and in the lymph node: the multilineage involvement suggests the malignant transformation of a primitive hematopoietic stem cell.
Epidemiology	Rare, very few cases described with this translocation (eight until date, four female and four male). A higher number have been described with other FGFR1 fusions, mainly t(8;13) and ZNF198-FGFR1 fusion.
Clinics	This is a myeloproliferative aggressive disease; complex picture of myeloid hyperplasia progressing to myelodysplasia and T- lymphoma, and acute non lymphocytic leukemia ; enlarged lymph node infiltrated by myeloid blast cells; blood data: high WBC (median 40 X 10 ⁹ /l); myelemia; monocytosis and eosinophilia. The clinical phenotype at presentation may vary between different partner genes involved in the FGFR1 fusion and, furthermore, between individuals. Only eight cases with the t(6;8)(q27;p11) have been reported. Four of these patients had features at presentation and/or a clinical course typical of EMS: malignant T-cell lymphoma and CML , AML/myeloproliferative disease, CML-like disease with eosinophilia that progressed rapidly to AML, and primary AML that evolved to EMS following chemotherapy. Two cases presented with polycythemia vera (PV) , one of them progressed to AML after a period of 5 years and the other one progressed to an EMS-like myeloproliferative disorder. The remaining case reported showed a B-ALL at presentation. This phenotype has been also described in the transformation phase of some cases with other FGFR1 fusions.
Treatment	EMS or SCLL seems to be refractory to conventional chemotherapy and some good results have been reached with allogeneic stem cell transplantation. Imatinib is not effective against constitutional activated FGFR1, but this disease could be responsive to specific FGFR1 inhibitors.
Evolution	CR could be obtained, but is promptly followed by relapse progressing rapidly to an AML, rarely ALL.
Prognosis	Median survival: 6 months. Although the number of reported cases is low, EMS seems to be disease with bad prognosis that generally progresses to acute leukemia.

Cytogenetics

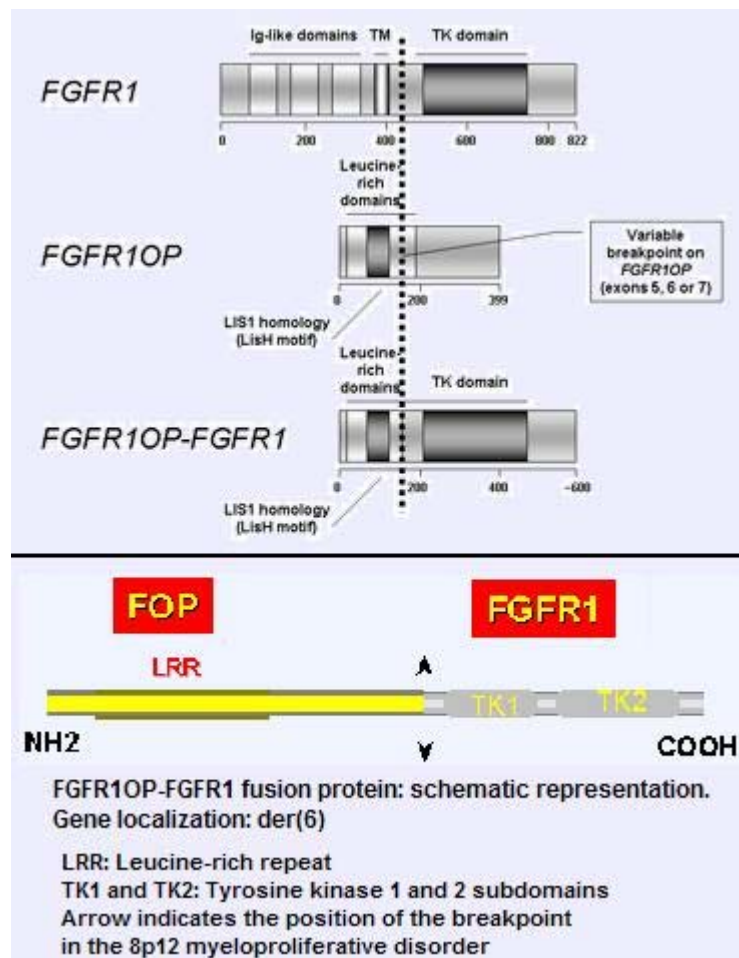
Cytogenetics	Available data shows that sometimes the t(6;8)(q27;p12) is not the sole abnormality.
Morphological	BM: 46,XX,t(6;8)(6pter-6q27::8p12-8pter;6qter-6q27::8p12-8qter) BM: 46,XY,t(6;8)(q27;p11) [100%] BM: 46,XY,t(6;8)(q27;p11) [100%] BM: 46,XY,t(6;8)(q27;p11.2) BM: 46,XX,t(6;8)(q27;p11.2),+8,+10,-18,-19,+dic(18;19)(p11.2;p13.3) BM: 46,XX,t(6;8)(q27;p12),+der(6)add(6)(q27) [66%]; 46,XX,t(6;8)(q27;p12) [34%] BM: 45,XY,t(6;8)(q27;p12),-7 [100%]
Cytogenetics Molecular	Mega YAC 959-A -4 (1260kb) from CEPH; FGFR1-specific cosmid 134.8
Variants	t(6;8)(q27;p12) is one of the reported rearrangements of 8p11 that fuses FGFR1 with other partner genes.

Genes involved and Proteins

Gene Name	FGFR1
Location	8p12
Note	This gene is involved in several fusions.
Dna / Rna	24 exons spanning about 55.9 Kb on 8p12. Transcription is from centromere to telomere. Based on Entrez data, FGFR1OP has seven different transcripts. Based on Ensembl data it has five different transcripts.
Protein	According to UniProt-SwissProt FGFR1 (FGFR1_HUMAN) or fibroblast growth factor receptor 1 is a receptor for basic fibroblast growth factor located in the membrane. Binding of FGF1 and heparin promotes autophosphorylation on tyrosine residues and activation of the receptor. FGFR1 contains 3 Ig-like C2-type (immunoglobulin-like) domains and a protein kinase domain. It belongs to the protein tyrosine kinase family, fibroblast growth factor receptor subfamily. Defects in FGFR1 have been associated with Pfeiffer syndrome (PS) or acrocephalosyndactyly type V (ACS5), hypogonadotropic hypogonadism (IHH), Kallmann syndrome type 2 (KAL2) ; osteoglophonic dysplasia (OGD) ; or osteoglophonic dwarfism, non-syndromic trigonocephaly or metopic craniosynostosis, and the EMS/SCLL due to fusion with other genes and constitutive activation of this receptor.
Gene Name	FGFR1OP (formerly known as FOP, FGFR1 oncogene partner)
Location	6q27
Note	This gene is involved only in this fusion.
Dna / Rna	13 exons spanning about 43.2 Kb on 6q27. Transcription is from centromere to telomere. Based on Entrez data, FGFR1OP has two different transcripts. Based on Ensembl-Vega data it has up to 6 different transcripts.
Protein	According to UniProt-SwissProt FGFR1OP (FR1OP_HUMAN) is a centrosomal protein associated with gamma-tubulin and required for anchoring microtubules to the centrosomes. Other centrosomal proteins have been described as fusion partner of tyrosine kinases like FGFR1. FGFR1OP is a hydrophilic protein that contains several leucine-rich regions with consensus sequences L-X2-L-X35-L-X35-L (in some of them leucine is substituted by either valine or isoleucine) in its amino and carboxy termini. It has a putative role as a regulator of normal proliferation and differentiation of the erythroid lineage and could belong to a novel family of the leucine-rich proteins. FGFR1OP also contains a Lis-homology (LisH) motif found in more than 100 eukaryotic proteins. These motifs are believed to be involved in microtubule dynamics and organization, cell migration and chromosome segregation; several of them are associated with genetic diseases. Its expression is ubiquitous but is higher in heart, liver, muscle, kidney, intestine, colon, adrenal gland, prostate, testis, and pancreas.

Result of the chromosomal anomaly

Hybrid gene



Schematic representation of the fusion FGFR1OP-FGFR1 resulting from the t(6;8)(q27;p12). Top figure courtesy José Luis Vizmanos : From top to bottom: structure of FGFR1, FGFR1OP and the putative chimeric FGFR1OP-FGFR1. TM, transmembrane domain; TK, tyrosine kinase domain. The breakpoints on FGFR1OP are variable as described in refs. 4, 5 and 10; Bottom figure courtesy Marie-Josèphe Pébusque

Description	Three different hybrid genes have been described, based on different breakpoints on the FGFR1OP gene. An in-frame fusion between FGFR1OP exon 6 and FGFR1 exon 9 was described; later, two variants in different patients, both in-frame with FGFR1 exon 9, one of them involving FGFR1OP exon 5 and the other involving FGFR1OP exon 7 was described. The presence of two different transcripts (one with a breakpoint in FGFR1OP exon 6 and the other with a breakpoint in exon 7) was reported.
Transcript	5' FGFR1OP-FGFR1 3'
Detection	See ref. 4 below.
Fusion Protein Description	The fusion gene is predicted to encode an aberrant tyrosine kinase composed of the putative leucine-rich N-terminal region of FOP, and the FGFR1 intracellular region. Like other fusions involving RTKs, FGFR1OP-FGFR1 lacks the FGFR1 transmembrane domain.
Oncogenesis	Through constitutive activation of FGFR1 signal transduction pathways, via putative dimerization of the fusion protein via the FOP leucine-rich repeats FGFR1OP shares features in common with other tyrosine kinase fusion partners, namely widespread expression and the presence of putative oligomerization domains. There is experimental proof that expression of FOP-FGFR1 in primary bone marrow cells induced by retroviral transduction generates a rapid MPD in mice. However.

lymphoproliferation and progression to acute phase were not observed in the murine model.

External links

Other database	t(6;8)(q27;p12)	Mitelman database (CGAP - NCBI)
Other database	t(6;8)(q27;p12)	CancerChromosomes (NCBI)
Other database	Mitelman database (CGAP - NCBI)	
Other database	CancerChromosomes (NCBI)	
Other database	FGFR1 TICdb	

To be noted

Additional cases are needed to delineate the epidemiology of this rare entity:
you are welcome to submit a paper to our new [Case Report](#) section.

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Updated 05-2007 José Luis Vizmanos

Citation

This paper should be referenced as such :

Pébusque MJ . t(6;8)(q27;p12). Atlas Genet Cytogenet Oncol Haematol. December 2000 .
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