

Erdheim-Chester disease (ECD)

ECD

Lipid Granulomatosis

1930: Jakob **Erdheim**
William **Chester**

50-70才 (7 - 84才) 男女比3 : 1

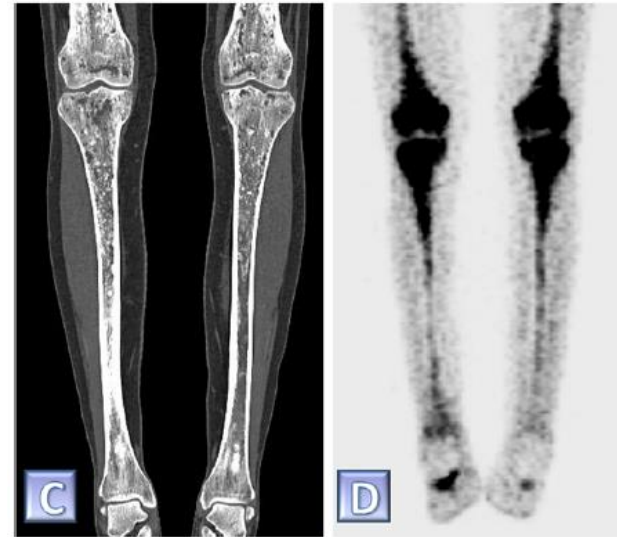
CD68+, S100+/-, CD1a-

- foamy macrophagesの集簇
- 慢性炎症
- 線維化
- 臓器障害

稀な発症

US ECD alliance 170例、海外142例
仏 1995年から165例

左右対称性の骨硬化



Orphanet J Rare Disease 2013 Mazor

〈これまでの治療〉

- INFα
- 2CdA
- Anakinra(IL-1 受容体antagonist)
- Infliximab (TNFα抗体)
- Sirolimus

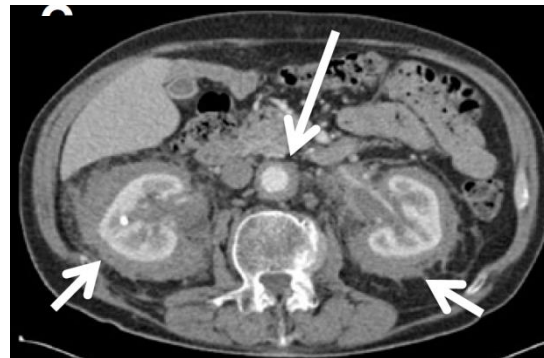
3年 Mortlity rate 60% → 20%



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ECDに特徴的な所見

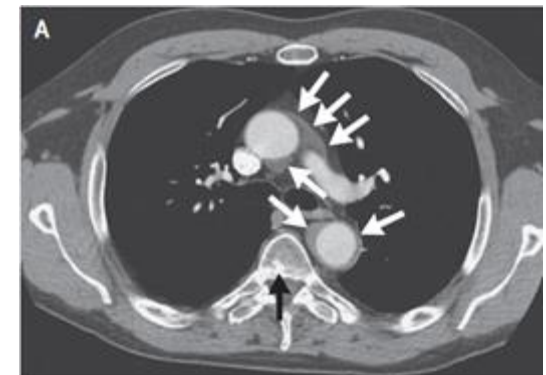
- 骨病変 > 95%
両側大腿骨sclerosis
- retroperitoneal fibrosis
- coarcted aorta



Estrada-Veras, et al. Blood advances 2017;1(6) 357-66.



Nikpanah, et al. European Radiology 2018;28,3751-59



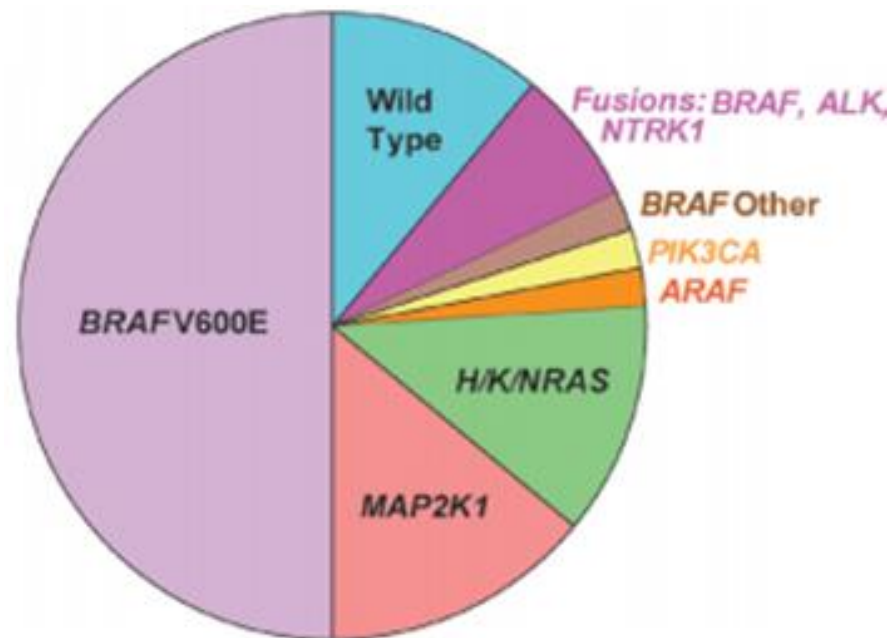
Mills, et al. NEJM 2008 359(7) 736-47.

Erdheim-Chester disease (ECD)

ECDの症状

Organ system and clinical findings	NIH patients,* n (%)
Bone	57 (95)
Kidney	39 (65)
Periaortic encasement	37 (62)
Hypogonadism	36 (60)
Lung	31 (52)
Bone pain	28 (47)
Maxilla and mandible§	24 (47)
Diabetes insipidus	28 (47)
CNS disease infiltration	23 (38)
Retro-orbital area ± exophthalmos	15 (27)
Heart (pseudotumor in RA)	22 (37)
Xanthelasma	20 (33)
Skin	15 (25)
Pericardial disease	5 (8)

Abder-Wahab, et al. 2017 ASH mini review 14 (4)



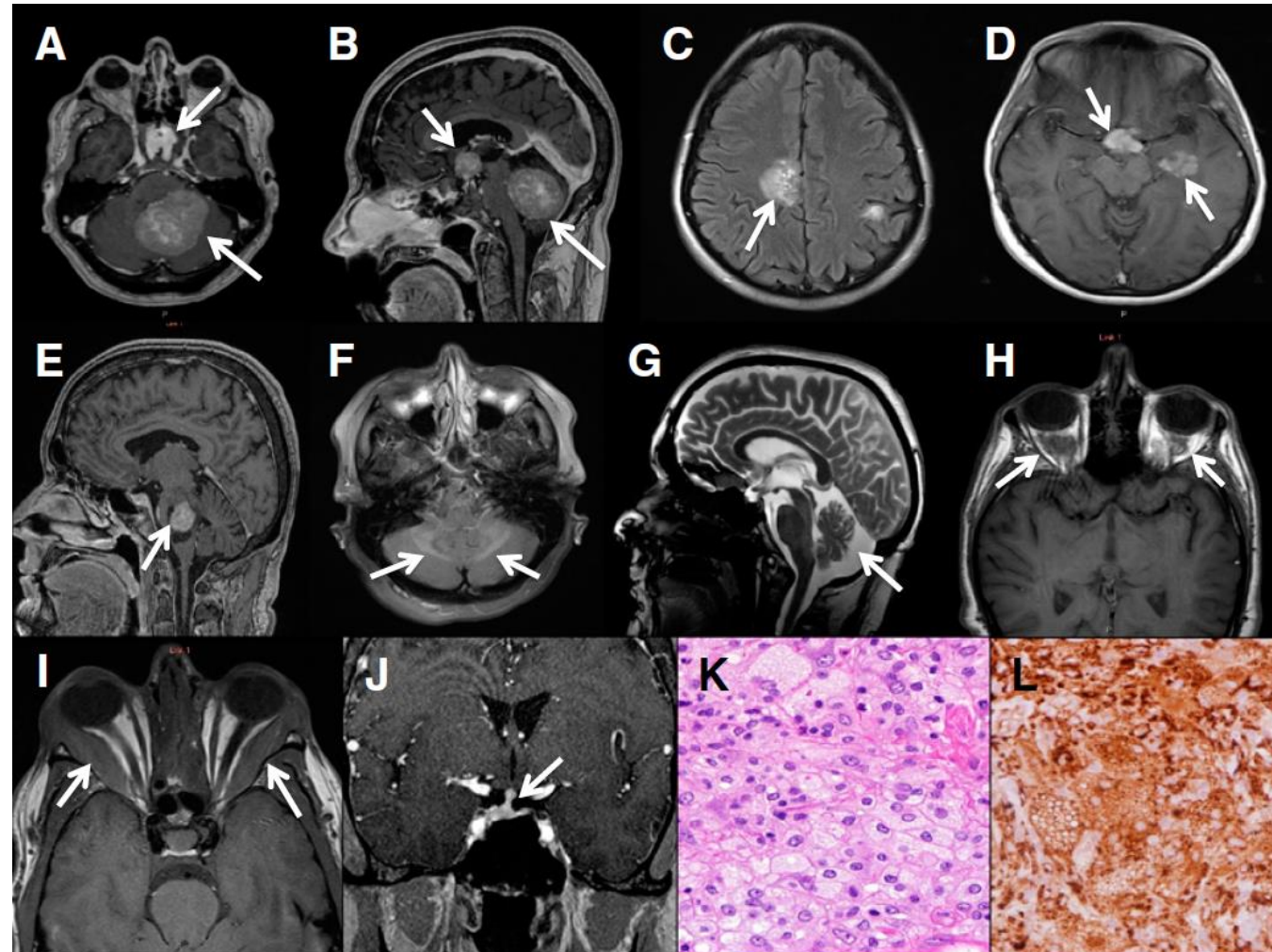
- 80%以上の症例にMAPK pathwayのmutation
- ECDの20%ちかくの症例にLCHを合併
- 尿崩症, NDを生ずることもLCHと共通

Haroche J, et al. *Blood*. 2012 Sep 27;120(13):2700-3.
Estrada-Veras, et al. *Blood advances*. 2017;1(6):357-66.

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ECDに対するMAPK inhibitor

BASKET study

ECD 22例, LCH 4例
Vemurafenib

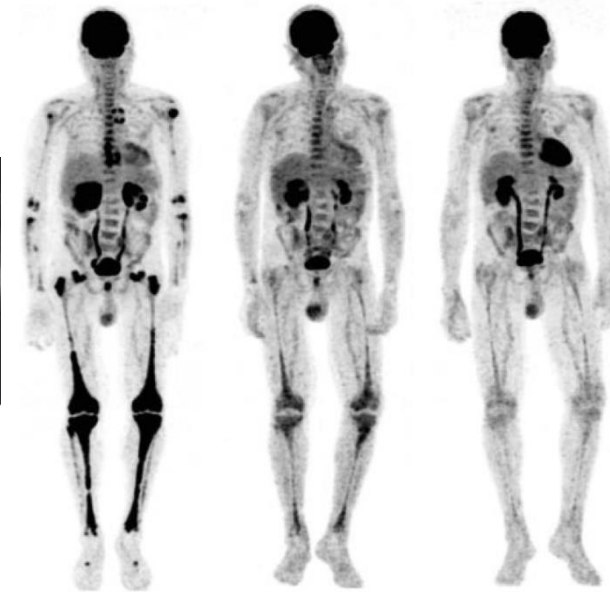
Diamond, et al. JAMA Oncol. 2018;4(3):384-88.



Before



M12



Before
Vemurafenib

Vemurafenib
1 month

Vemurafenib
4 months

LOVE study

54 例

Vemurafenib/Dabrafenib 51例

Cobimetinib 15例

治療反応+ 88%

V600E+のECDでは91%

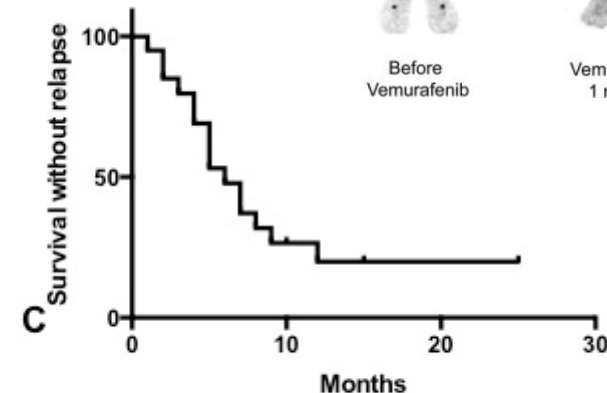
20人 Med 20か月内服後に中止

2人 増悪のため中止

15人 75%はその後まもなく再発 med 6mo

inhibitor開始時よりも勢いをもって再発

11/54 (20.4%) 副作用のため内服中止



Duration (months) 0 1 2 3 4 5 6 7 8 9 10 12 15 25
Number of patients 20 20 19 16 15 13 10 9 7 6 5 4 2 1

Haroche J, et al. Blood. 2013 121(9):1495-1500.

Haroche J, et al. Blood. 2017 130(11):1377-80.

Haroche J, et al. JCO. 2015 33(5):411-8.